

# **Waters ACQUITY UPC<sup>2</sup> Bibliography**

**A compendium of references  
to scientific journal articles  
based on the technique of  
UltraPerformance  
Convergence Chromatography  
(UPC<sup>2</sup>)**

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## 1. Towards eco - friendly secondary plant metabolite quantitation: Ultra high performance supercritical fluid chromatography applied to common vervain (*Verbena officinalis* L.)

Nora Gibitz - Eisath, Miriam Eichberger, Regina Gruber, Christoph Seger, Sonja Sturm, Hermann Stuppner

2019 – Journal of Separation Science

### Abstract

This report presents the first ultra high performance supercritical fluid chromatography diode array detector based assay for simultaneous determination of iridoid glucosides, flavonoid glucuronides, and phenylpropanoid glycosides in *Verbena officinalis* (Verbenaceae) extracts. Separation of the key metabolites was achieved in less than 7 min on an Acquity UPC2 Torus Diol column using a mobile phase gradient comprising subcritical carbon dioxide and methanol with 0.15% phosphoric acid. Method validation for seven selected marker compounds (hastatoside, verbenalin, apigenin - 7 - O - glucuronide, luteolin - 7 - O - glucuronide, apigenin - 7 - O - diglucuronide, verbascoside, and luteolin - 7 - O - diglucuronide) confirmed the assay to be sensitive, linear, precise, and accurate. Head - to - head comparison to an ultra high performance liquid chromatography comparator assay did prove the high orthogonality of the methods. Quantitative result equivalence was evaluated by Passing - Bablok - correlation and Bland - Altman - plot analysis. This cross - validation revealed, that one of the investigated marker compound peaks was contaminated in the ultra high performance liquid chromatography assay by a structurally related congener. Taken together, it was proven that the ultra high performance supercritical fluid chromatography instrument setup with its orthogonal selectivity is a true alternative to conventional reversed phase liquid chromatography in quantitative secondary metabolite analysis. For regulatory purposes, assay cross - validation with highly orthogonal methods seems a viable approach to avoid analyte overestimation due to coeluting, analytically indistinguishable contaminants.

<https://doi.org/10.1002/jssc.201900854>

## 2. Ultra-performance convergence chromatography, a more efficient method for chemical quality evaluation of Gaoben medicinal materials compared with the ultra-performance liquid chromatography

Xiaoyi Zhang, Jiushi Liu, Shiman Gao, Rongchang Chen, Yaodong Qi, Bengang Zhang, Xiaobo Sun, Haitao Liu, Peigen Xiao

2019 – Journal of Chromatography A

Highlights: An UPC2 method was developed for chemical quality evaluation of Gaobens. Comparative analysis on the chemical constituents of Gaobens by UPC2 and UPLC. Chemometrics analysis on the results of UPC2 showed effective discriminability. The compounds analyzed by UPC2 method showed important chemotaxonomic significance. UPC2 is a powerful supplement to UPLC for chemical quality evaluation in aromatic TCM.

### Abstract

Ultra-performance convergence chromatography (UPC2), which combines the advantages of both reversed phase liquid chromatography (RPLC) and gas chromatograph (GC), is a novel, eco-friendly analytical method and could be a powerful supplement for RPLC and GC. Based on these characteristics, an UPC2 method was developed for the chemical analysis of Gaoben medicinal materials including six batches of *Ligusticum sinense*, six batches of *Ligusticum jeholense* and six batches of *Conioselinum vaginatum* and compared with the results by ultra-performance liquid chromatography (UPLC) method at the same time. Six compounds were determined by UPC2 method, and eight compounds were quantitatively analyzed by UPLC method. Hierarchical cluster analysis (HCA) and principle component analysis (PCA) methods were used to elucidate the resemblance relationship among these 18 samples. The results showed the samples from same species analyzed by UPC2 method were grouped together respectively. However, UPLC method could not distinguish these three kinds of Gaoben medicinal materials effectively. The compounds determined by UPC2 method showed the chemical taxonomic significance than those of UPLC method, and were more suitable for chemical quality evaluation of Gaoben medicinal materials from different regions. This showed good complementarity between UPC2 and UPLC methods. And the UPC2 method might provide a more efficient analytical method for the chemical quality evaluation of medicinal materials rich in volatile oils, which would be a powerful supplement to the current quality evaluation.

### 3. Defining a system suitability limit to decide on column deterioration and to facilitate column transfers in chiral supercritical fluid chromatography

Sven Declerck, Yvan Vander Heyden, Debby Mangelings

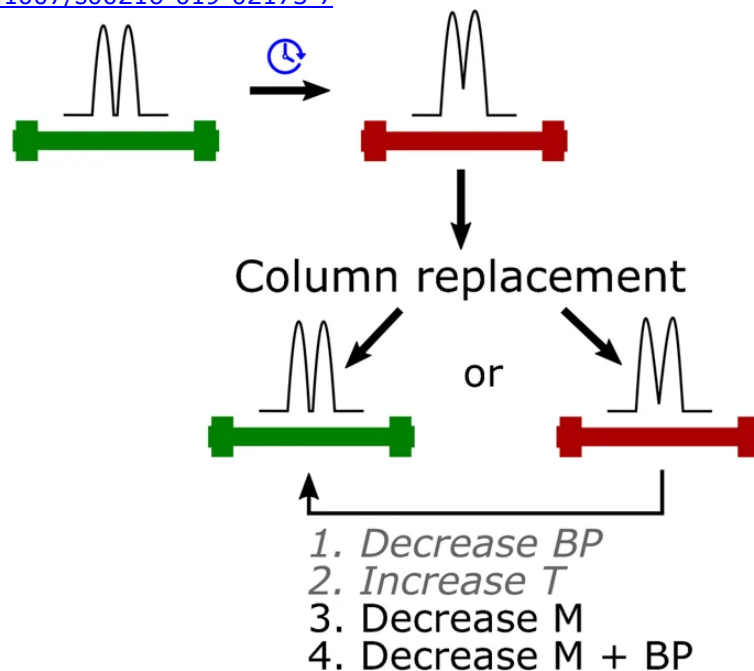
2019 – Analytical and Bioanalytical Chemistry

Keywords: Supercritical fluid chromatography, Enantioseparations, Intermediate-precision study, System suitability, Transfer, UPC2

#### Abstract

The separation of enantiomers is an important requirement during the entire drug life cycle in the pharmaceutical industry. High-performance liquid chromatography and supercritical fluid chromatography (SFC) are the main chromatographic techniques used to separate enantiomers. Since chiral stationary phases are often extensively used once a method has been developed, columns will age and must be replaced after a certain period. However, no practical guidelines exist to determine when a column is deteriorated or to decide whether a transfer to another column (with the same chiral selector) is successful. In this study, a system suitability limit for resolution was defined, based on an intermediate (time-different) precision study in SFC on four immobilized polysaccharide-based columns that only differed in manufacturer or particle size. This system suitability limit could be used to decide on column deterioration or as a requirement to evaluate whether a separation transfer was successful. Some method adaptations may be necessary to obtain successful transfers. An approach was proposed, which helped the analyst to make successful transfers.

<https://doi.org/10.1007/s00216-019-02173-7>



### 4. Development of S-Fluxametamide for Bioactivity Improvement and Risk Reduction: Systemic Evaluation of the Novel Insecticide Fluxametamide at the Enantiomeric Level

Runan Li, Xinglu Pan, Qinqin Wang, Yan Tao, Zenglong Chen, Duoduo Jiang, Chi Wu, Fengshou Dong, Jun Xu, Xingang Liu, Xiaohu Wu, Yongquan Zheng

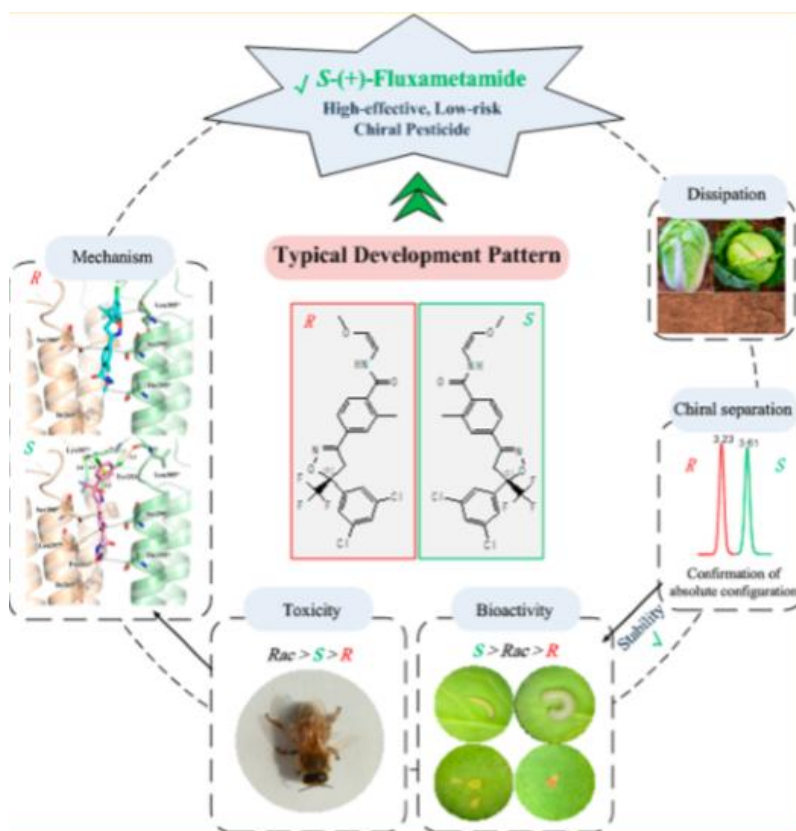
2019 – Environ. Sci. Technol.

#### Abstract

Increasing numbers of novel pesticides have been applied in agriculture. However, traditional evaluation of pesticides does not distinguish between their enantiomers, which may lead to

inaccurate results. In this study, systematic research on the chiral insecticide fluxametamide was conducted at the enantiomeric level. The methods for enantioseparation and semipreparative separation of fluxametamide enantiomers were developed. The optical rotation and absolute configuration of two enantiomers were determined, and their stability was verified in solvents and soils. Enantioselective bioactivities against four target pests (*Plutella xylostella*, *Spodoptera exigua*, *Aphis gossypii*, and *Tetranychus cinnabarinus*) were tested. Acute toxicities of fluxametamide enantiomers toward honeybees were also evaluated. S-(+)-Isomer exhibited 52.1–304.4 times and 2.5–3.7 times higher bioactivity than R-(–)-isomer and rac-fluxametamide, respectively. Meanwhile, rac-fluxametamide was more toxic than S/R-isomer, and S-(+)-isomer showed >30-fold higher acute toxicity than R-(–)-isomer. Molecular docking studies were performed with  $\gamma$ -aminobutyric acid receptor (GABAR) to monitor the mechanism of stereoselective bioactivity. The better Grid score of S-(+)-fluxametamide (–60.12 kcal/mol) than R-(–)-enantiomer (–56.59 kcal/mol) indicated higher bioactivity of S-(+)-isomer than of R-(–)-isomer. The dissipation of fluxametamide in cabbage, Chinese cabbage, and soil was nonenantioselective under field conditions. Development of S-(+)-fluxametamide could maintain the high-efficacy and low-risk properties, which should attract attention of producers, applicators, and managers of pesticides.

<https://doi.org/10.1021/acs.est.9b03697>



## 5. Walk-up SFC-MS for Fast Purification of reaction Mixtures within Discovery Chemistry

Craig White

2019 – Chromatography Today August Article

Purification is often regarded as the bottleneck to delivering pure compounds for biological assays within Discovery Research. Medicinal chemists depend on simple processes and robust instrumentation for rapid purification of intermediates and final products, whilst expending as little time and effort as possible. Reverse phase LC-MS platforms are typically used, often with an open-access interface which for the chemist, simplifies sample submission, method selection and batching of samples. The widely accepted limitation of reverse phase LC purification, however, is the time required to remove the post purification aqueous solution and provide a dry isolated product. Supercritical Fluid Chromatography (SFC) is a technique that delivers fractions in a small volume of

organic solvent, significantly reducing the post purification processing time. SFC is an established technique within Lilly for queue-based chiral and achiral purification submissions. Until recently, SFC instrumentation has not had a robust hardware and software interface, and as such, has been generally inaccessible to the medicinal chemist in a walk-up environment. In this short application note, we describe our experience with the deployment of SFC-MS for walk-up purification, considering both the challenge to the analytical chemist, and the benefit it affords to the medicinal chemist.



Walk-up-SFC-MS  
for Fast Purification

## 6. Supercritical Fluid Chromatography × Ultra-High Pressure Liquid Chromatography for Red Chilli Pepper Fingerprinting by Photodiode Array, Quadrupole-Time-of-Flight and Ion Mobility Mass Spectrometry (SFC × RP-UHPLC-PDA-Q-ToF MS-IMS)

Paola Donato, Daniele Giuffrida, Marianna Oteri, Veronica Inferrera, Paola Dugo, Luigi Mondello  
2019 – Food Analytical Methods

### Abstract

The coupling of normal phase and reversed phase liquid chromatography (NP-LC × RP-LC) is one of the most effective ways to increase orthogonality in two-dimensional comprehensive separations, being the two retention mechanisms truly independent. However, such coupling is not straightforward to implement, due to immiscibility of the mobile phases, poor peak focusing at the head of the secondary column (2D), signal interferences and peak deterioration. In this research, supercritical fluid chromatography (SFC) was used in the first dimension (1D), coupled to ultra high pressure LC (UHPLC), to alleviate incompatibility issues and provide a number of advantages related to the use of supercritical CO<sub>2</sub>. An on-line SFC × RP-UHPLC system was implemented in an automated fashion, around two 2-position, six-port switching valves equipped with octadecyl silica cartridges for effective trapping and focusing of the analytes eluted from 1D. A water make-up flow added to the SFC effluent permitted to efficiently focus the solutes on the sorbent material and to reduce interferences of the expanded CO<sub>2</sub> on the 2D separation. In addition to photodiode array and quadrupole-time-of-flight mass spectrometry detection, ion mobility separation based on analyte mass, shape and size added a fourth separation dimension for carotenoid fingerprinting in a red chilli pepper sample.

<https://doi.org/10.1007/s12161-018-1307-x>

## 7. Evaluation of silica from different vendors as the solid support of anion - exchange chiral stationary phases by means of preferential sorption and liquid chromatography

Michal Kohout, Štěpán Hovorka, Jana Herciková, Maciej Wilk, Petr Sysel, Pavel Izák, Vilém Bartůněk, Cornelia von Baeckmann, Jan Pícha, Peter Frühauf

2019 – Journal of Separation Science

### Abstract

Chromatographic performance of a chiral stationary phase is significantly influenced by the employed solid support. Properties of the most commonly used support, silica particles, such as size and size distribution, and pore size are of utmost importance for both superficially porous particles and fully porous particles. In this work, we have focused on evaluation of fully porous particles from three different vendors as solid supports for a brush - type chiral stationary phase based on 9 - O - tert - butylcarbamoyl quinidine. We have prepared corresponding stationary phases under identical experimental conditions and determined the parameters of the modified silica by physisorption measurements and scanning electron microscopy. Enantioselectivity properties of the chiral stationary phases have been studied using preferential sorption experiments. The same material was slurry - packed into chromatographic columns and the chromatographic properties have been evaluated in liquid chromatography. We show that preferential sorption can provide valuable information about the influence of the pore size and total pore volume on the interaction of analytes of different size with the chirally - modified silica surface. The data can be used to understand



differences observed in chromatographic evaluation of the chiral stationary phases. The combination of preferential sorption and liquid chromatography separation can provide detailed information on new chiral stationary phases.

<https://doi.org/10.1002/jssc.201900731>

## 8. PESTICIDES ENANTIOMER ANALYSIS: METHODOLOGICAL APPLICATIONS IN ENVIRONMENT, FOOD AND NON TARGET ORGANISMS

Minmin Li

2019 - Dissertations and theses : Doctoral thesis

### Abstract

Pesticides are components used to protect crops from pests and disease in fields but also in the food chain allowing securing the food supply with the efficient use of ever-scarcer natural resources. The FAO estimated an average of 26% to 40% of crop yields that are lost annually due to weeds, pests and diseases. To ensure safety and sustainability with pesticide use, the fundamental principle lies behind the EU and China pesticide legislation. It is very important to combine the protection of human health, wildlife and the environment with the improvement of agricultural productivity. Also, the assessment for novel chiral postharvest pesticides is necessary to follow their future in food and environment. Therefore, in this thesis, we firstly investigated the analysis methods, the limits of quantification (LOQs) were estimated to be 1.0 µg/kg for 2,4-D, carbendazim, thiabendazole, and prochloraz, and 1.5 µg/kg for iprodione in food matrices. The mean recoveries were in the range of 70.4-113.9%. The analysis uses the ultra-performance convergence chromatography coupled with triple quadruple mass spectrometry (UPC2-MS/MS) following by the QuEChERs as sample preparation. The coefficients of determination ( $r^2$ ) exceeded 0.9954 in the solution calibration and all matrix-matched calibrations, and the LODs of CYF enantiomers were 2.8-4.9 µg/kg and the LOQ was 50 µg/kg. Acceptable average recoveries were within 84.95% to 119.9% at three concentration levels and the RSDs ranged from 0.75% to 9.36% of all cases. Based on chemometric methods, the residue levels of these five pesticides in commercial juice may be further decreased using a reconstitution step. Afterward, the PF of the peeling process was the lowest with degradation of (+) -CYF and (-) -CYF by around 65.4% and 66.2%, respectively. The reduction of CYF enantiomers in the process of fermentation was in accordance with the first-order of kinetics, in which the half-lives of (-) -CYF and (+) -CYF were 4.25, 4.05 days in apple wine making, and 3.18, 3.19 days in apple vinegar-making, respectively. Also, the degradation dynamics of CYF followed first-order kinetics. Under aerobic conditions, the differences in black soil, krasnozem and fluvo-aquic soil were significantly different ( $p < 0.05$ ).

Finally, the CYF enantiomers selectively recognize proteins and affect metabolic pathways. This mechanism of interfering hormones was found to be up-regulated by the estrogen receptor family protein FAM102A by proteomic analysis. Preliminary studies have shown that the development of (+)-CYF is more active and less toxic than rac-CYF. However, the toxicity of (+)-CYF to bees requires longer observation duration, at least over 48 hours.

In summary, this thesis increased the understanding of the chemometric-assisted method, especially their time saving during extracting and cleaning. The supercritical fluid chromatography combined with tandem mass spectrometry support a perfect separation with the advantages of low viscosity, high separation efficiency, and environmental benefits. From the food processing factor data, we found that the residue levels of water-soluble pesticides in commercial juice may be further decreased using a reconstitution step. Apples with pesticide residue levels lower than the maximum residue levels can be assessed, and the resulting apple juice can be consumed directly. In addition, they easily degraded other compounds and these compounds could be converted into each other, the enantioselective usually occurred in the enzyme, especially in chiral environment. Through bioassay and protein experiments, chiral pesticides expressed enantioselective toxicity, which may be due to differences in binding between with protein and chiral structure.

<http://hdl.handle.net/2268/240352>

## 9. Rapid determination of 13 ultraviolet absorbents in plastic food contact materials by ultra-performance convergence chromatography

Qiu Y, Li G, Long M, Li Y, Xia Z

2019 - Chinese Journal of Chromatography



A rapid method based on ultra-performance convergence chromatography (UPC2) was developed for the analysis of 13 ultraviolet (UV) absorbents in plastic food contact materials. The UV absorbents were extracted from plastic food contact materials by supersonic extraction with methanol, purified by C18 solid phase extraction column, and analyzed via UPC2 before filtration with an organic filtration membrane (0.22  $\mu\text{m}$ ). An ACQUITY UPC2 HSS C18 SB chromatographic column (150 mm $\times$ 3.0 mm, 1.8  $\mu\text{m}$ ) was used for the detection of the UV absorbents. An effective separation was achieved within 4 min under the optimized conditions. The mobile phases were supercritical carbon dioxide and isopropanol as a modifier. The results showed that the 13 UV absorbents exhibited good linear relationships in the respective linear ranges with the correlation coefficients no less than 0.9985. The limits of detection (S/N=3) were in the range of 0.05-0.15 mg/kg. The recoveries were from 86.8% to 115.7%, and the relative standard deviations were between 0.73% and 5.61%. This method is rapid, convenient, accurate and reliable, and can be used for the rapid determination of the 13 UV absorbents in plastic food contact materials.

<https://doi.org/10.3724/sp.j.1123.2019.03026>

## 10. Enantioselective Olfactory Effects of the Neonicotinoid Dinotefuran on Honey Bees (*Apis mellifera* L.)

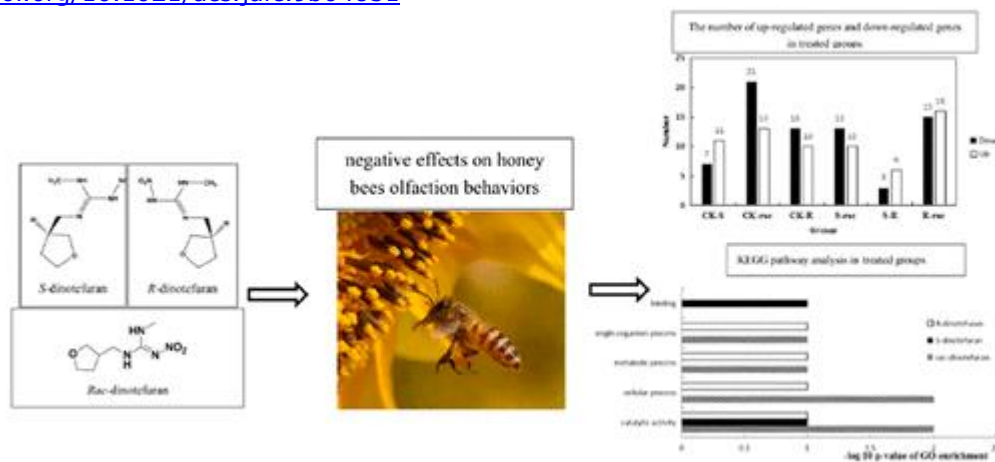
2019 – J. Agric. Food Chem.

Keywords: dinotefuran, honey bees, sublethal olfaction effects, enantioselective toxicity, UPC2

### Abstract

Sublethal exposure to neonicotinoids affects honey bee olfaction, but few studies have investigated the sublethal effects of the enantioselective neonicotinoid dinotefuran on honey bee olfaction. This study assessed the sublethal olfactory toxicity of dinotefuran enantiomers to honey bees. Compared to R-dinotefuran, S-dinotefuran had higher acute oral toxicity, sucrose sensitivity effects, octopamine concentrations, lower learning ability, and memory effects on honey bees. High-throughput circular RNA sequencing of the honey bee brain revealed that R-dinotefuran caused more gene regulatory changes than S-dinotefuran. Gene ontology enrichment and Kyoto Encyclopedia of Genes and Genomes pathway analyses demonstrated that the SERCA, Kca, and Maxik genes may be related to the enantioselective effects of dinotefuran isomers on honey bee olfaction. These results indicated that the current ecotoxicological safety knowledge about chiral dinotefuran effects on honey bees should be amended.

<https://doi.org/10.1021/acs.jafc.9b04851>



## 11. Umpolung Strategy for $\alpha$ - Functionalization of Aldehydes for the Addition of Thiols and other Nucleophiles

Jakob Blom, Dr. Gabriel J. Reyes - Rodríguez, Henriette N. Tobiesen, Johannes N. Lamhauge, Marc V. Iversen, Casper L. Barløse, Dr. Niels Hammer, Matilde Rusbjerg, Prof. Dr. Karl Anker Jørgensen  
2019 – Angewandte Chemie

### Abstract

Nucleophile-nucleophile coupling is a challenging transformation in organic chemistry. Herein we present a novel umpolung strategy for  $\alpha$  - functionalization of aldehydes with nucleophiles. The strategy uses organocatalytic enamine activation and quinone - promoted oxidation to access O - bound quinol - intermediates that undergo nucleophilic substitution reactions. These quinol -

intermediates react with different classes of nucleophiles. The focus is on an unprecedented organocatalytic oxidative  $\alpha$  - thiolation of aldehydes. The reaction scope is demonstrated for a broad range of thiols and extended to chemoselective bioconjugation, and applicable to a large variety of aldehydes. This strategy can also encompass organocatalytic enantioselective coupling of  $\alpha$  - branched aldehydes with thiols forming quaternary thioethers. Studies indicate a stereoselective formation of the intermediate followed by a stereospecific nucleophilic substitution reaction at a quaternary stereocenter, with inversion of configuration.

<https://doi.org/10.1002/anie.201911793>

## 12. Separation of Unprecedented Degradants of Domperidone by Ultra-Performance Convergence Chromatography and Their Structure Elucidation

V V S R N Anji Karun Mutha, Chakravarthy Chandra, B Vijayabhaskar, Prabhakar S Achanta, Jagadeesh Narkedimilli, Muralidharan Kaliyaperumal, Raghu Babu Korupolu, Susheela Bai Gajbhiye, Chidananda Swamy Rumalla

2019 – Journal of Chromatographic Science

### Abstract

Domperidone, a gastroprokinetic agent, is a common drug to treat emesis. It was subjected to acid, base-mediated hydrolysis, peroxide-mediated oxidation, photolysis and thermal degradation according to ICH guidelines to observe stability of the selected drug under the stress conditions. Although the drug is resistant to base hydrolysis, photolysis and thermal stressors, two degradants (DP-ISO1 and DP-ISO2) were formed in acid mediated hydrolysis. Oxidation with hydrogen peroxide also resulted in one product (DP-OX). All three degradants were isolated from the crude reaction mixture by preparative high-performance liquid chromatography and supercritical fluid chromatography. Structures of isolated compounds were unambiguously characterized as 5-chloro-1-(1-(3-(6-chloro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)propyl)piperidin-4-yl)-1,3-dihydro-2H-benzo[d]imidazol-2-one (DP-ISO1), 5-chloro-1-(3-(4-(5-chloro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)piperidin-1-yl)propyl)-1,3-dihydro-2H-benzo[d]imidazol-2-one (DP-ISO2), 4-(5-chloro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)-1-(3-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)propyl)piperidine 1-oxide (DP-OX) by analysis of mass spectrometry, 1D and 2D nuclear magnetic resonance spectra. To the best of our knowledge, DP-ISO1 and DP-ISO2 are new and DP-OX was previously reported as domperidone impurity.

<https://doi.org/10.1093/chromsci/bmz066>

## 13. An offline two-dimensional supercritical fluid chromatography $\times$ reversed phase liquid chromatography tandem quadrupole time-of-flight mass spectrometry system for comprehensive gangliosides profiling in swine brain extract

Wei Si, Yanfang Liu, Yuansheng Xiao, Zhimou Guo, Gaowa Jin, Jingyu Yan, Aijin Shen, Han Zhou, Fan Yang, Xinmiao Liang

2019 – Talanta

Highlights: An offline SFC  $\times$  RPLC two-dimensional system was constructed for GLS analysis for the first time. A GLS fast screening and automatic identification strategy was established by in-house library with self-developed software.

### Abstract

79 gangliosides were tentatively identified in swine brain extract and 20 of them were new. Gangliosides, widely distributed in tissues and body fluid, have been connected to the therapy of cancer and brain related diseases. The complexity of the gangliosides structures with different polar moieties coexisting, a carbohydrate moiety and a ceramide chain, make it a great challenge in separation and analysis science. This study aimed to develop a strategy on the basis of high-accuracy data collected by an offline two-dimensional (2D) supercritical fluid chromatography (SFC)  $\times$  reversed phase liquid chromatography (RPLC)/quadrupole time-of-flight (Q-ToF) system, and to integrate an in-house library with self-developed software for fast screening and identification of gangliosides from a complex sample (swine brain extract). Subsequent positive-mode MS/MS was used to validate the identified gangliosides. Finally, 153 gangliosides were separated and 79 of them were identified by the in-house library and self-developed software, 4-fold more than those by manual identification (18 gangliosides). Among the identified ones, 20 were detected in swine brain for the first time. This study established an offline 2D SFC  $\times$  RPLC system and provided a new

method for fast screening and automatic identification of gangliosides in complex mixtures. It will be conducive to further study of biological functions of gangliosides.

<https://doi.org/10.1016/j.talanta.2019.120366>

#### 14. Homochiral Metal–Organic Frameworks for Enantioselective Separations in Liquid Chromatography

M. Nieves Corella-Ochoa, Jesús B. Tapia, Heather N. Rubin, Vanesa Lillo, Jesús González-Cobos, José Luis Núñez-Rico, Salvador R.G. Balestra, Neyvis Almora-Barríos, Marina Lledós, Arnau Güell-Bara, Juanjo Cabezas-Giménez, Eduardo C. Escudero-Adán, Anton Vidal-Ferran, Sofía Calero, Melissa Reynolds, Carlos Martí-Gastaldo, José Ramón Galán-Mascarós

2019 - J. Am. Chem. Soc

##### Abstract

Selective separation of enantiomers is a substantial challenge for the pharmaceutical industry. Chromatography on chiral stationary phases is the standard method, but at a very high cost for industrial-scale purification due to the high cost of the chiral stationary phases. Typically, these materials are poorly robust, expensive to manufacture, and often too specific for a single desired substrate, lacking desirable versatility across different chiral analytes. Here, we disclose a porous, robust homochiral metal–organic framework (MOF), TAMOF-1, built from copper(II) and an affordable linker prepared from natural L-histidine. TAMOF-1 has shown to be able to separate a variety of model racemic mixtures, including drugs, in a wide range of solvents of different polarity, outperforming several commercial chiral columns for HPLC separations. Although not exploited in the present article, it is worthy to mention that the preparation of this new material is scalable to the multikilogram scale, opening unprecedented possibilities for low-energy chiral separation at the industrial scale.

<https://doi.org/10.1021/jacs.9b06500>

#### 15. Enantiospecific UPC2 SFC-MS method for separation and quantification of R & S-Eliglustat tartrate in presence of its stereo isomers and degradation impurities

Umamaheshwar Puppala, Koduri S.V. Srinivas, K. Venkateshwara Reddy, Muralidharan Kaliyaperumal, Srinivasa Rao Pakalapatia

2019 -Materials Today: Proceedings

Keywords: Eliglustat tartrate (EGT), UPC2 SFC-MS, Chiral separation, Forced degradation, Validation

##### Abstract

Eliglustat tartrate is an oral inhibitor of glucosylceramide synthase used in the treatment of Gaucher's disease. This drug is administered as enantio-specific trans-(R,R) isomer and there is a possibility to have three more potential stereo isomers due to two chiral centers, owing to the toxicological difference between stereoisomers chiral method with high sensitivity is required to detect low level contaminations. A method for enantiomeric separation and quantification of trans-(R,R) Eliglustat tartrate in presence of other isomers trans-(S,S) Eliglustat, cis-(R,S) Eliglustat, cis-(S,R) Eliglustat was developed and validated using ultra-high performance supercritical fluid chromatography with tandem mass spectrometry (UPC2 SFC-MS) which is termed as a green chromatographic technique. Chiral separation was developed using Chiralcel OX-3 (4.6 \* 150 mm) 3 µm column which has 4 chloro, 3 methyl phenyl carbamate as chiral selector, with a flow rate of 3 g/min using CO<sub>2</sub> and 0.5% diethyl amine in ethanol: methanol (1:1) as a co-solvent. The effect on the enantioseparation by varying chiral additives, gradient conditions and content of organic modifier were investigated. The method has good linearity with concentration ranges from 0.25 to 7.5 µg mL<sup>-1</sup>. The detection limit was 0.08 µg mL<sup>-1</sup> and quantification limit was 0.25 µg mL<sup>-1</sup>. Forced degradation studies were performed and all the degradation impurities were separated from product peak, the molecular weight of impurities were identified by using UPC2-Mass spectrometer. The method was validated in line to ICH guidelines in terms of linearity, accuracy, precision, LOQ, LOD and robustness.

<https://doi.org/10.1016/j.matpr.2019.07.629>

#### 16. Simultaneous detection of nitrosamines and other sartan-related impurities in active pharmaceutical ingredients by supercritical fluid chromatography

**Abstract**

Since July 2018, the pharmacological class of "sartans" has been the subject of considerable media and analytical interest, as it became known that they are contaminated with nitrosamines such as N-nitrosodimethylamine (NDMA), N-nitrosodiethylamine (NDEA) and N-nitrosodiisopropylamine (NDiPA). Previous compendial methods are not able to detect these new contaminants. Using the latest and innovative Quality-by-Design (QbD) approach, it has now been possible to develop an analytical method that enables to investigate sartans, such as valsartan and losartan. Also a large class of different nitrosamines in the ppb range and sartan-related impurities can thus be determined simultaneously in a single analysis using supercritical fluid chromatography (SFC). By using SFC, a broad spectrum of nonpolar and very polar impurities can be separated and analyzed in under 20 min. The analytical method developed is validated for limit testing according to ICH Q2(R1) and fulfills default thresholds of EMA and FDA for testing of drug substances and genotoxic impurities. Additionally, it can also be adapted to other pharmaceuticals that may be contaminated with nitrosamines, since tetrazole synthesis as the underlying cause of nitrosamine contamination is important for a set of other non-sartan drug substances.

<https://doi.org/10.1016/j.jpba.2019.04.049>

### **17. 11 $\alpha$ -Hydroxyprogesterone, a potent 11 $\beta$ -hydroxysteroid dehydrogenase inhibitor, is metabolised by steroid-5 $\alpha$ -reductase and cytochrome P450 17 $\alpha$ -hydroxylase/17,20-lyase to produce C11 $\alpha$ -derivatives of 21-deoxycortisol and 11-hydroxyandrostenedione in vitro**

Rachelle Gent, Therina du Toit, Amanda C.Swart

2019 -The Journal of Steroid Biochemistry and Molecular Biology

**Abstract**

11 $\alpha$ -Hydroxyprogesterone (11 $\alpha$ OHP4) and 11 $\beta$ -hydroxyprogesterone (11 $\beta$ OHP4) have been reported to be inhibitors of 11 $\beta$ -hydroxysteroid dehydrogenase (11 $\beta$ HSD) type 2, together with 11 $\beta$ -hydroxytestosterone and 11 $\beta$ -hydroxyandrostenedione, and their C11-keto derivatives being inhibitors of 11 $\beta$ HSD1. Our in vitro assays in transiently transfected HEK293 cells, however, show that 11 $\alpha$ OHP4 is a potent inhibitor of 11 $\beta$ HSD2 and while this steroid does not serve as a substrate for the enzyme, the aforementioned C11-oxy steroids are indeed substrates for both 11 $\beta$ HSD isozymes. 11 $\beta$ OHP4 is metabolised by 11 $\beta$ HSD2 yielding 11-ketoprogesterone with 11 $\beta$ HSD1 catalysing the reverse reaction, similar to the reduction of the other C11-oxy steroids. In the same model system, novel 11 $\alpha$ OHP4 metabolites were detected in its conversion by steroid-5 $\alpha$ -reductase (SRD5A) types 1 and 2 yielding 11 $\alpha$ -hydroxydihydroprogesterone and its conversion by cytochrome P450 17A1 (CYP17A1) yielding the hydroxylase product, 11 $\alpha$ ,17 $\alpha$ -dihydroxyprogesterone, and the 17,20 lyase product, 11 $\alpha$ -hydroxyandrostenedione. We also detected both 11 $\alpha$ OHP4 and 11 $\beta$ OHP4 in prostate cancer tissue— ~23 and ~32 ng/g respectively with 11K17 levels >300 ng/g. In vitro assays in PC3 and LNCaP prostate cancer cell models, showed that the metabolism of 11 $\alpha$ OHP4 and 11 $\beta$ OHP4 was comparable. In LNCaP cells expressing CYP17A1, 11 $\alpha$ OHP4 and 11 $\beta$ OHP4 were metabolised with negligible substrate, 4%, remaining after 48 h, while the steroid substrate 11 $\beta$ ,17 $\alpha$ -dihydroxyprogesterone (21dF) was metabolised to C11-keto C19 steroids yielding 11-ketotestosterone.

Despite the fact that 11 $\alpha$ OHP4 is not metabolised by 11 $\beta$ HSD2, it is a substrate for SRD5A and CYP17A1, yielding C11 $\alpha$ -hydroxy C19 steroids as well as the C11 $\alpha$ -hydroxy derivative of 21dF—the latter associated with clinical conditions characterised by androgen excess. With our data showing that 11 $\alpha$ OHP4 is present at high levels in prostate cancer tissue, the steroid may serve as a precursor to unique C11 $\alpha$ -hydroxy C19 steroids. The potential impact of 11 $\alpha$ OHP4 and its metabolites on human pathophysiology can however only be fully assessed once C11 $\alpha$ -hydroxyl metabolite levels are comprehensively analysed.

<https://doi.org/10.1016/j.jsbmb.2019.04.018>

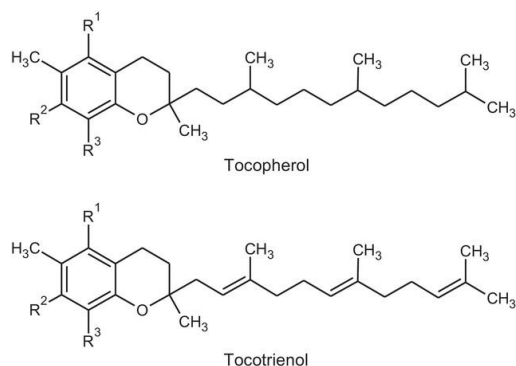
### **18. Applications of packed and capillary supercritical fluid chromatography in the separation of tocochromanols**

Mei Han Ng, Ahmad Kushairi Din

**Abstract**

Tocochromanols consisting of tocopherols and tocotrienols, is collectively known as vitamin E. Similarity in their structures, physical and chemical properties rendered the tocochromanols to be subject of chromatography interest. Supercritical fluid chromatography is a highly efficient tool for the separation and analysis of tocochromanols. Separation and analysis of tocochromanols using supercritical fluid chromatography had been carried out in the past using capillary or packed columns. Each of these techniques offer their own advantages and drawbacks. Besides being used for analysis, packed column supercritical fluid chromatography found applications as a purification and content enrichment tool. Emergence of new equipment and stationary phase technologies in recent years also helped in making supercritical fluid chromatography a highly efficient tool for the separation and analysis of tocochromanols. This paper gives an insight into the use of capillary and packed columns in supercritical fluid chromatography for the separation and/or analysis of tocochromanols. The types of stationary phase used, as well as chromatographic conditions are also discussed.

<https://doi.org/10.1002/jssc.201900342>



Name	R1	R2	R3
Alpha	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>
Beta	CH <sub>3</sub>	H	CH <sub>3</sub>
Gamma	H	CH <sub>3</sub>	CH <sub>3</sub>
Delta	H	H	CH <sub>3</sub>

## 19. A review of pretreatment and analytical methods of biogenic amines in food and biological samples since 2010

Zhang Yu-jia, Zhang Yuan, Zhou Yu, Li Guo-hui, Yang Wen-zhen, Feng Xue-song

2019 – Journal of Chromatography A

Highlights: Comprehensive information of classification and physiological activity of biogenic amines. Updated information on sample pretreatment and analytical methods of biogenic amines. Separation conditions, analytical conditions and validation information are compared.

**Abstract**

Biogenic amines (BAs), mainly produced by amino acid decarboxylation, are widespread in foods and human organisms. Appropriate intake of BAs is beneficial to the human body, while excessive consumption may cause discomfort. Meanwhile, BAs are a kind of chemical marker for evaluating meat freshness. For these reasons, simple, rapid and efficient methods have been developed for the determination of BAs in food and biological products. This review introduces the provenance, classification and physiological activity of eight essential BAs and summarizes the dominant pretreatment and analysis methods since 2010. Pretreatment technologies mainly include the "dilute and shoot" method, ultrasonic assisted extraction, solid-phase extraction, matrix solid-phase dispersion, dispersive liquid-liquid microextraction, etc. Determination methods include liquid chromatography coupled to ultraviolet or fluorescence detectors, liquid chromatography tandem mass spectrometry, capillary electrophoresis, biosensors and so on.

<https://doi.org/10.1016/j.chroma.2019.07.015>



## 20. A strategy to reduce the dose of multichiral agricultural chemicals: The herbicidal activity of metolachlor against *Echinochloa crusgalli*

Lu Zhao, Yue Gao, Jingian Xie, Qiong Zhang, Fangjie Guo, Shuren Liu, Weiping Liu

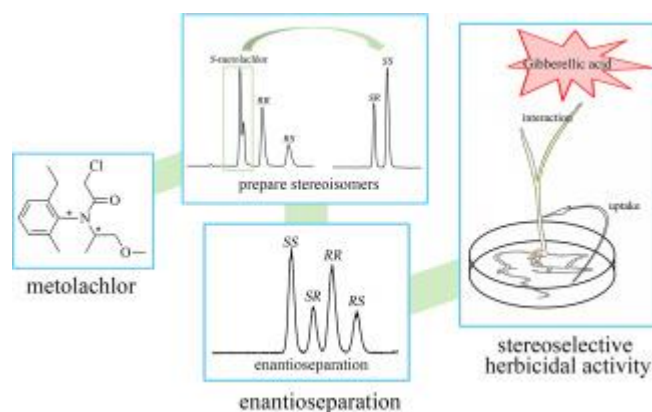
2019 - Science of The Total Environment

Highlights: S-metolachlor and four stereoisomers of metolachlor were first prepared successfully. UPC2-MS/MS was rapid and sensitive in separating the four metolachlor stereoisomers. Chiral carbon feature plays a major role in the stereoisomeric herbicides. Inhibition on GA synthesis is an important reason for stereoselective herbicides.

### Abstract

Agricultural chemicals are normally used as mixtures of several isomers, e.g., enantiomers. In theory, in order to minimize the pesticides dose, it is desirable to use the most target-active isomer. Metolachlor is a typical multichiral herbicide belonging to amide herbicides. An asymmetric carbon atom and a chiral axis yield four stereoisomers. In this study, a novel laboratory method was developed to prepare the S-metolachlor and the four stereoisomers using high performance liquid chromatography. The separated isomers had a purity of >99%, with their absolute configurations assigned by electronic circular dichroism. The enantioseparation by ultra performance convergence chromatography tandem mass spectrometry was also performed for the rapid and sensitive detection of metolachlor stereoisomers. The enantioselective herbicidal activity toward the target weed (*Echinochloa crusgalli*) was systematically assessed for the first time by measuring the morphology of the weed after treatment with rac-, S-metolachlor and the four stereoisomers, respectively. Among the commercial pesticides, S-metolachlor was more effective in weed inhibition than rac-metolachlor, and to the four stereoisomers, the herbicidal activities were ranked as: SS > SR >> RS > RR, and the RR-isomer even had some stimulative effect to the weed growth at lower concentration (1 ppm). Thus, we concluded that in these cases, the chiral carbon feature played a major role in herbicidal activity rather than the chiral axis feature, and the higher bioactivity of the S-isomers was confirmed by more effective uptake and stronger interaction with target enzymes that were involved in the gibberellic acid biosynthesis. Although the SS-isomer shows the highest herbicidal activity, controlling the major chiral feature is still much easier and more economical than controlling two chiral features.

<https://doi.org/10.1016/j.scitotenv.2019.06.521>



## 21. SAT-344 11 $\alpha$ -Hydroxyprogesterone, a Potent 11 $\beta$ -Hydroxysteroid Dehydrogenase Inhibitor, Is Metabolised In Vitro by Adrenal Steroidogenic Enzymes

Rachelle Gent, Amanda Swart

2019 - Journal of the Endocrine Society

### Abstract

The C11-oxy C21 steroids, 11 $\alpha$ OHP4 (11 $\alpha$ -hydroxyprogesterone) and 11 $\beta$ OHP4 (11 $\beta$ -hydroxyprogesterone), have to date been characterised only in terms of their inhibition of 11 $\beta$ -hydroxysteroid dehydrogenase (11 $\beta$ HSD). However, 11 $\beta$ OHP4 is also a substrate of 11 $\beta$ HSD2 and is converted to 11-ketoprogesterone which is subsequently metabolised to active C11-oxy androgens.



Although our studies indicate that 11 $\alpha$ OHP4 is not a substrate for 11 $\beta$ HSD2, it may be metabolised by the steroidogenic enzymes of the backdoor pathway. While circulating 11 $\alpha$ OHP4 and 11 $\beta$ OHP4 levels are not routinely analysed in physiological and pathophysiological conditions, 11 $\beta$ OHP4 was only recently included in the analysis of steroid hormones associated with adrenal disorders with 11 $\alpha$ OHP4 being overlooked. We have demonstrated that both 11 $\alpha$ OHP4 and 11 $\beta$ OHP4 are present in prostate cancer tissue samples while the in vitro metabolism of 11 $\beta$ OHP4 contributes to the production of the potent C11-oxy C19 steroid, 11-ketodihydrotestosterone, in the C11-oxy backdoor pathway. We therefore hypothesised that 11 $\alpha$ OHP4 would be metabolised to C11-oxy C19 steroids. The in vitro metabolism of 11 $\alpha$ OHP4 was therefore assayed in HEK293 cells transiently transfected with 5 $\alpha$ -reductase (SRD5A) and cytochrome P450 17A1 (CYP17A1). Ultra-performance convergence chromatography tandem mass spectrometry (UPC2-MS/MS) analysis identified 5 $\alpha$ -pregnan-11 $\alpha$ -ol-3,20-dione in the conversion by SRD5A1 and SRD5A2 (50% converted in 2.5 and 1.5 hrs, respectively), the initial step in the backdoor pathway. Moreover, novel steroid metabolites were detected in the metabolism of 11 $\alpha$ OHP4 by CYP17A1 in the production of the 11 $\alpha$ -hydroxy derivatives of 21-deoxycortisol and 11-hydroxyandrostenedione. These were successfully confirmed by UPC2-MS/MS and chromatographically separated from the 11 $\beta$ -hydroxylated forms. The metabolism of 11 $\alpha$ OHP4 and 11 $\beta$ OHP4 was subsequently assayed in several whole cell models in which these novel intermediates were detected as well as quantifiable levels of C11-oxy C19 steroids in the conversion of 11 $\beta$ OHP4. In conclusion, in vitro metabolism by SRD5A, indicates that 11 $\alpha$ OHP4 is metabolised in the C11-oxy backdoor pathway with conversion by CYP17A1 yielding 11 $\alpha$ -hydroxylated C19 steroids. Data suggest that 11 $\alpha$ OHP4 may add to active C11-oxy C19 steroids with the 11 $\alpha$ -intermediates attenuating the inhibitory potential of the steroids leading to the production of 11KDHT. However, the conversion of 11 $\alpha$ OHP4 by SRD5A and CYP17A1 is less efficient than that of 11 $\beta$ OHP4—indicating that the contribution of 11 $\alpha$ OHP4 to the active androgen pool would be markedly lower, suggesting a potential mechanism controlling the flux towards active C11-oxy androgens. Although the contribution to the androgenic pool remains unclear, the role of 11 $\alpha$ OHP4 is more complex than that of one being labelled just as an inhibitor of 11 $\beta$ HSD2.

<https://doi.org/10.1210/js.2019-SAT-344>

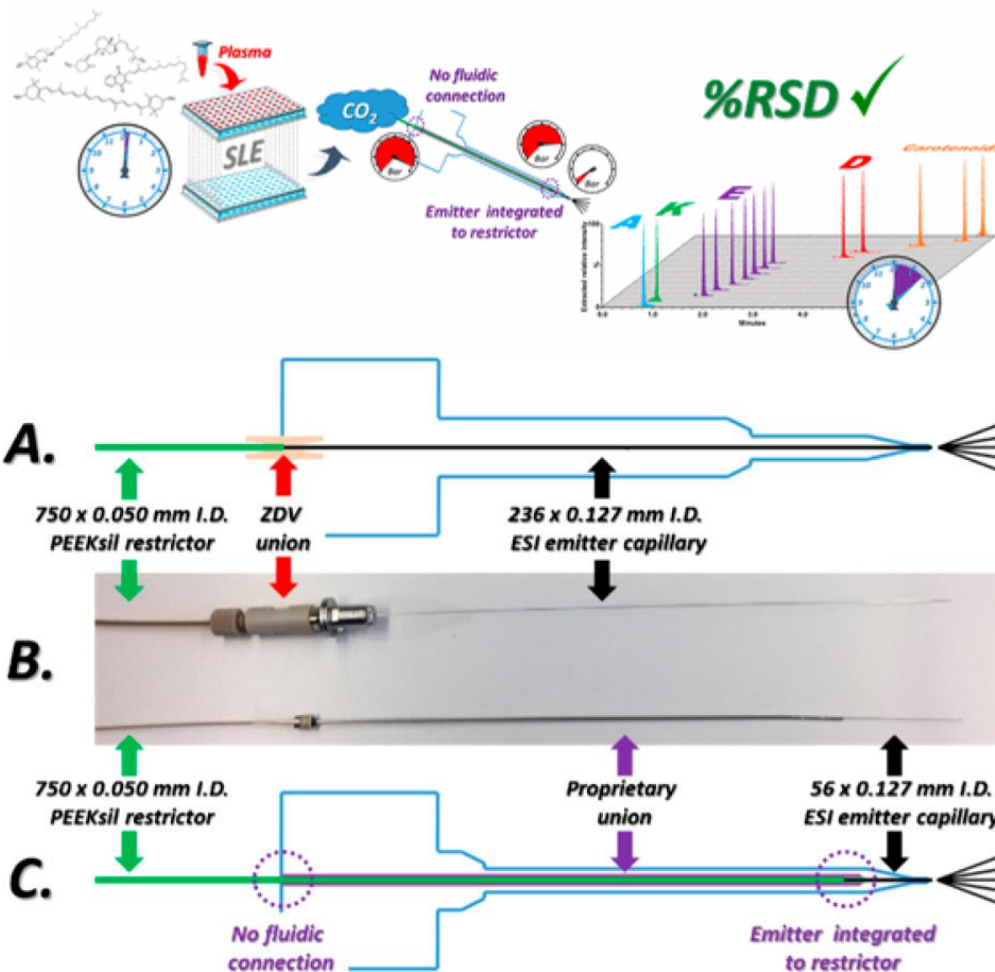
## 22. Quantitative Profiling of Endogenous Fat-Soluble Vitamins and Carotenoids in Human Plasma Using an Improved UHPSFC-ESI-MS Interface

Filomena Petruzzello, Alexandre Grand-Guillaume Perrenoud, Anita Thorimbert, Michael Fogwill, and Serge Rezz

2017 – Analytical Chemistry

### Abstract

Analytical solutions enabling the quantification of circulating levels of liposoluble micronutrients such as vitamins and carotenoids are currently limited to either single or a reduced panel of analytes. The requirement to use multiple approaches hampers the investigation of the biological variability on a large number of samples in a time and cost efficient manner. With the goal to develop high-throughput and robust quantitative methods for the profiling of micronutrients in human plasma, we introduce a novel, validated workflow for the determination of 14 fat-soluble vitamins and carotenoids in a single run. Automated supported liquid extraction was optimized and implemented to simultaneously parallelize 48 samples in 1 h, and the analytes were measured using ultrahigh-performance supercritical fluid chromatography coupled to tandem mass spectrometry in less than 8 min. An improved mass spectrometry interface hardware was built up to minimize the post-decompression volume and to allow better control of the chromatographic effluent density on its route toward and into the ion source. In addition, a specific make-up solvent condition was developed to ensure both analytes and matrix constituents solubility after mobile phase decompression. The optimized interface resulted in improved spray plume stability and conserved matrix compounds solubility leading to enhanced hyphenation robustness while ensuring both suitable analytical repeatability and improved the detection sensitivity. The overall developed methodology gives recoveries within 85–115%, as well as within and between-day coefficient of variation of 2 and 14%, respectively.



<http://dx.doi.org/10.1021/acs.analchem.7b01476>

### 23. Rapid and Green Separation of Mono- and Diesters of Monochloropropanediols by Ultrahigh Performance Supercritical Fluid Chromatography–Mass Spectrometry Using Neat Carbon Dioxide as a Mobile Phase

Firas Jumaah, Renata Jędrkiewicz, Justyna Gromadzka, Jacek Namieśnik, Sofia Essén, Charlotta Turner, and Margareta Sandahl

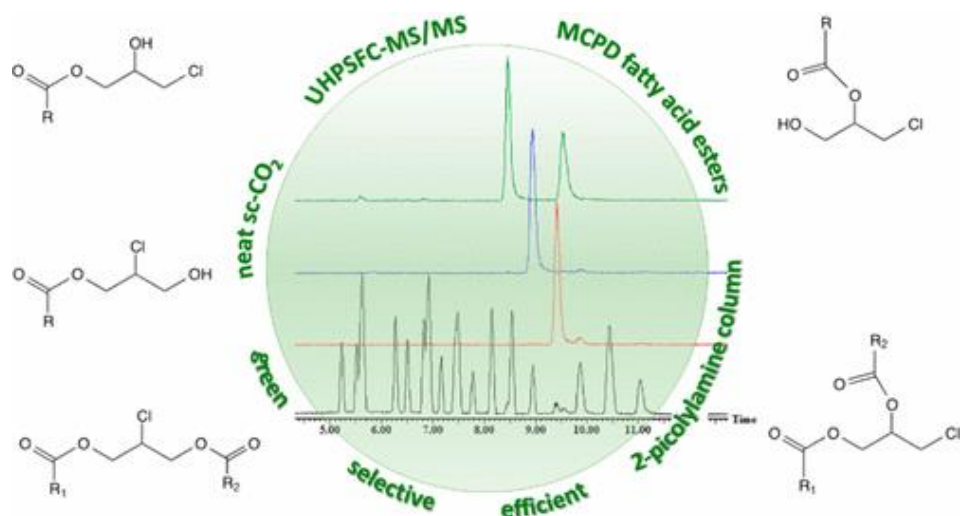
2017 – Journal of Agricultural and Food Chemistry

Keywords: 2-MCPD esters; 3-MCPD esters; chloropropanol; mass spectrometry; method development; orthogonal column screening; SFC; UPC2

#### Abstract

This study demonstrates the effect of column selectivity and density of supercritical carbon dioxide (SC-CO<sub>2</sub>) on the separation of monochloropropanediol (MCPD) esters, known as food toxicants, using SC-CO<sub>2</sub> without addition of cosolvent in ultrahigh performance supercritical fluid chromatography–mass spectrometry (UHPSFC–MS). This study shows that over 20 2-monochloropropanediol (2-MCPD) and 3-monochloropropanediol (3-MCPD) mono- and diesters are separated on a 2-picolylamine column in less than 12 min. The presence and position of a hydroxyl group in the structure, the number of unsaturated bonds, and the acyl chain length play a significant role in the separation of MCPD esters. The flow rate, backpressure, and column oven temperature, which affect the density of the mobile phase, were shown to have a substantial impact on retention, efficiency, and selectivity. The developed method was successfully applied for the determination of MCPD esters in refined oils and showed a close to excellent green analysis score using the Analytical Eco-Scale.

<http://dx.doi.org/10.1021/acs.jafc.7b02857>



## 24. Environmentally Friendly Procedure Based on Supercritical Fluid Chromatography and Tandem Mass Spectrometry Molecular Networking for the Discovery of Potent Antiviral Compounds from *Euphorbia semiperfoliata*

Louis-Félix Nothias, Stéphanie Boutet-Mercey, Xavier Cachet, Erick De La Torre, Laurent Laboureur, Jean-François Gallard, Pascal Retailleau, Alain Brunelle, Pieter C. Dorrestein, Jean Costa, Luis M. Bedoya, Fanny Roussi, Pieter Leyssen, José Alcami, Julien Paolini, Marc Litaudon, and David

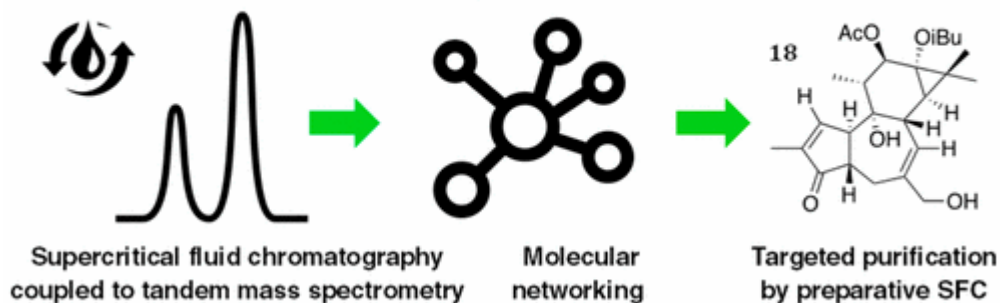
2017 – Journal of Natural Products

### Abstract

A supercritical fluid chromatography-based targeted purification procedure using tandem mass spectrometry and molecular networking was developed to analyze, annotate, and isolate secondary metabolites from complex plant extract mixture. This approach was applied for the targeted isolation of new antiviral diterpene esters from *Euphorbia semiperfoliata* whole plant extract. The analysis of bioactive fractions revealed that unknown diterpene esters, including jatrophane esters and phorbol esters, were present in the samples. The purification procedure using semipreparative supercritical fluid chromatography led to the isolation and identification of two new jatrophane esters (13 and 14) and one known (15) and three new 4-deoxyphorbol esters (16–18). The structure and absolute configuration of compound 16 were confirmed by X-ray crystallography. This compound was found to display antiviral activity against Chikungunya virus ( $EC_{50} = 0.45 \mu\text{M}$ ), while compound 15 proved to be a potent and selective inhibitor of HIV-1 replication in a recombinant virus assay ( $EC_{50} = 13 \text{ nM}$ ). This study showed that a supercritical fluid chromatography-based protocol and molecular networking can facilitate and accelerate the discovery of bioactive small molecules by targeting molecules of interest, while minimizing the use of toxic solvents.

<http://dx.doi.org/10.1021/acs.jnatprod.7b00113>

### Efficient and Environmentally Friendly Procedure to Target and Purify Secondary Metabolites



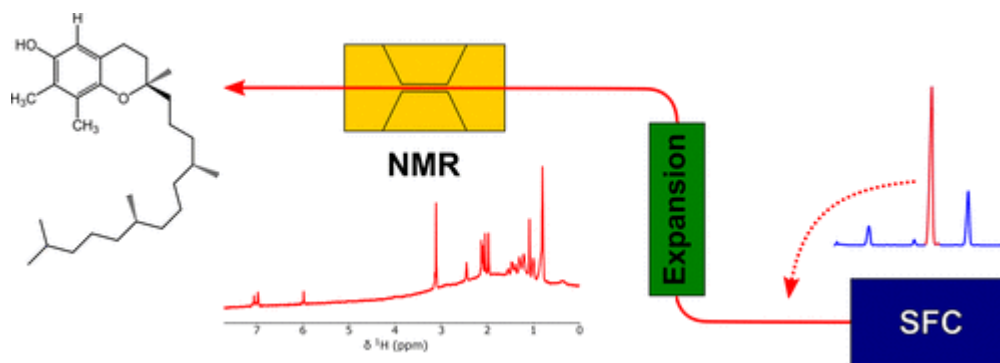
## 25. Hyphenation of Supercritical Fluid Chromatography and NMR with In-Line Sample Concentration

F. H. M. van Zelst, S. G. J. van Meerten, P. J. M. van Bentum, and A. P. M. Kentgens

2018 – Analytical Chemistry

### Abstract

By coupling supercritical fluid chromatography (SFC) and nuclear magnetic resonance (NMR) in-line, a powerful analytical method arises that enables chemically specific analysis of a broad range of complex mixtures. However, during chromatography, the compounds are diluted in the mobile phase, in this case supercritical CO<sub>2</sub> (scCO<sub>2</sub>), often resulting in concentrations that are too low to be detected by NMR spectroscopy or at least requiring excessive signal averaging. We present a hyphenated SFC-NMR setup with an integrated approach for concentrating samples in-line, which are diluted in scCO<sub>2</sub> during chromatography. This in-line concentration is achieved by controlled in-line expansion of the scCO<sub>2</sub>. As a proof of concept four isomers of vitamin E (tocopherol) were isolated by SFC, concentrated in-line by expanding CO<sub>2</sub> from 120 to 50 bar, and finally shuttled to the NMR spectrometer fitted with a dedicated probehead for spectroscopic characterization of microfluidic samples. The abundant isomers were readily detected, supporting the viability of SFC-NMR as a powerful analytical tool.



<http://dx.doi.org/10.1021/acs.analchem.8b02357>

## 26. Detection and Quantitation of ACCUTRACE S10, a New Fiscal Marker Used in Low-Duty Fuels, Using a Novel Ultrahigh-Performance Supercritical Fluid Chromatography–Mass Spectrometry

G. John Langley, Julie Herniman, Anastarsia Carter, Edward Wilmot, Maria Ashe, and Jim Barker

2018 – Energy & Fuels

### Abstract

A new ultrahigh-performance supercritical fluid chromatography–mass spectrometry (UHPSFC–MS) method has been developed using electrospray ionization (ESI) to detect and quantify a new fiscal fuel marker, ACCUTRACE S10, that was introduced into fuel in the U.K. and Ireland from April 1, 2015. S10 is synthesized by the Dow Chemical Company and is used as a replacement for ultraviolet–visible (UV–vis) fuel markers, such as quinizarin, Euromarker, and Solvent Red 24. It is UV–invisible, is doped at a low level (2.5 ppm), and was designed for detection using modern gas chromatography–mass spectrometry (GC–MS) instrumentation. All currently proposed methods for the determination of the ACCUTRACE S10 fuel marker in diesel fuel (automotive diesel oil, with current specifications of EN 590 and ASTM D975) use GC–MS, and two-dimensional (2D) GC–MS is necessary to detect the marker at tank dilutions. However, the lower limit of detection (LLOD) and lower limit of quantification (LLOQ) for S10 are severely compromised using legacy GC–MS instrumentation, and measurement at tank dilutions is not feasible. ACCUTRACE S10 exhibited unusual ionization characteristics when analyzed by atmospheric pressure ionization techniques; the ionization is modeled and discussed; and the strong ionization response is used to develop a new approach for detection and quantitation of the new fuel maker. The novel UHPSFC–MS

method uses this phenomenon, allows injection of undiluted fuels, and affords detection and quantitation at doping and tank dilution levels.

<http://dx.doi.org/10.1021/acs.energyfuels.8b02459>

## 27. Effect of quercetin supplementation on the growth, feed efficiency and serum hormone levels of New Zealand White rabbits

M.K. North, A. Dalle Zotte & L.C. Hoffman

2019 – South African Journal of Animal Science

Keywords: Cortisol, UPC2/MS/MS, feed conversion ratio, flavonoid, growth, rabbit, somatotropin, thyroid hormones

### Abstract

Meat rabbits could provide a new avenue for agricultural development in South Africa, and flavonoids may be able to improve their live performance. This study investigated the effects of quercetin dihydrate (0 and 2 g/kg feed) on the growth parameters and serum-free triiodothyronine (ft3), free thyroxine, somatotropin, and cortisol levels of growing rabbits. It also provides the first growth and feed conversion ratio (FCR) data for South African New Zealand Whites. Control (Ctrl) and quercetin-supplemented (Qrc) diets were provided to 34 (16 male, 18 female) and 32 (15 male, 17 female) rabbits, respectively, from 5 to 12 weeks old. Live performance was measured weekly, and serum hormone levels were determined at 11 weeks old. Overall, the rabbits performed well for live weight and growth rate, growing from  $1052 \pm 13.4$  g to  $3192 \pm 45.3$  g (5 - 12 weeks). Females had higher cortisol levels than males, as found for other species (female = 10.9 ng/mL, male = 3.89 ng/mL). Qrc rabbits tended to have a higher overall FCR than Ctrl rabbits (Ctrl = 3.83, Qrc = 4.01), possibly due to lower feed digestibility, and had smaller sex differences in growth and FCR than Ctrl rabbits, possibly owing to xenoestrogenic activity. They also tended to have higher ft3 levels than Ctrl rabbits (Ctrl = 3.62 ng/mL, Qrc = 4.98 ng/mL), possibly owing to the inhibition of binding to transthyretin. However, it does not seem that the provision of quercetin is commercially justified for improving the live performance of rabbits.

<http://dx.doi.org/10.4314/sajas.v48i6.17>

## 28. Triacylglycerol, fatty acid, and phytochemical profiles in a new red sorghum variety (Ji Liang No. 1) and its antioxidant and anti-inflammatory properties

Yaqiong Zhang, Ming Li, Hang Gao, Bo Wang, Xu Tongcheng, Boyan Gao, Liangli (Lucy) Yu

2019 – Food Science and Nutrition

Keywords: anti-inflammation, antioxidant, phenolic, red sorghum, triacylglycerol

### Abstract

In this study, a new red sorghum variety (Ji Liang No. 1) was investigated for its triacylglycerol (TAG) and fatty acid profiles, carotenoid and tocopherol compositions, total phenolic, total flavonoid and phenolic acid contents, and antioxidant and anti-inflammatory properties. A total of 17 TAGs were identified in the red sorghum oil. Linoleic and oleic acids were the primary fatty acids, contributing more than 80% of the total fatty acids.  $\beta$ -Carotene was the primary carotenoid at a level of 26.14  $\mu\text{g/g}$ .  $\alpha$ -,  $\gamma$ -, and  $\delta$ -tocopherols were at levels of 0.19, 4.08, and 0.10  $\mu\text{g/g}$ , respectively. Moreover, acetone–water (60:40, v/v) extract of the red sorghum exhibited the greatest total phenolic content of 2.77 mg GAE/g and total flavonoid content of 5.44 mg RE/g. The extract had scavenging capacities against DPPH, ABTS+, and peroxy radicals and suppressed LPS-stimulated IL-1 $\beta$ , IL-6, and COX-2 mRNA expressions in a dose-dependent manner. Ferulic, p-coumaric, isoferulic, and p-hydroxybenzoic acids were found in the red sorghum, with ferulic acid as the predominant phenolic acid and mostly in an insoluble bound form. These data indicated a potential utilization of the red sorghum in health-promoting functional food or supplemental products.

<https://doi.org/10.1002/fsn3.886>

## 29. Application of immunocastration in a commercial Dohne Merino ram flock before weaning

T. Needham<sup>1</sup>, H. Lambrechts & L.C. Hoffman

2019 – South African Journal of Animal Science

Keywords: Carcass, GnRH, immunocastrate, Improvac, sheep, Blood sampling, testosterone, Acquity UPC2-MS/MS

### Abstract



The influence of pre-weaning immunocastration on the growth, incidences of reaction to vaccination, serum testosterone concentration and slaughter performance of ram lambs was determined and compared to that of physically castrated lambs. Immunocastration was performed using two doses of 2 mL Improvac® administered subcutaneously in the shoulder, alternating sides per vaccination, using a Sterimatic® needle guard system. The first vaccination was administered to 50 lambs with an average weight ( $\pm$  SD) of  $16.0 \pm 3.05$  kg, and the second vaccination was carried out six weeks later, when the lambs weighed on average ( $\pm$  SD)  $20.5 \pm 4.11$  kg. An additional 50 lambs were physically castrated using elastrator bands at the same time as the primary vaccination given to the immunocastrates. Data were collected during four sessions over the 25-week period, at time points which fitted into the normal management activities of the commercial operation (Weeks 1, 6, 16 and at slaughter). During these sessions, all lambs were weighed, and blood samples were collected from immunocastrates. The immunocastration injection site was also scored for adverse reactions. Immunocastration was successful in preventing testosterone secretion for the duration of the trial and no differences were reported regarding weight gain or slaughter performance between the treatments. The Sterimatic® and Stericap® system, as used in this study, proved to be an easy-to-use and safe system for the commercial administration of Improvac®, with no adverse reactions to vaccinations recorded at the injection sites. Pre-weaning immunocastration in lambs is thus possible, and the growth rate, carcass weight and carcass fatness of immunocastrates are similar to that of elastrator-castrated lambs.

<http://dx.doi.org/10.4314/sajas.v48i6.15>

### 30. One-pot organocatalytic/multicomponent approach for the preparation of novel enantioenriched non-natural selenium-based peptoids and peptide-peptoid conjugates

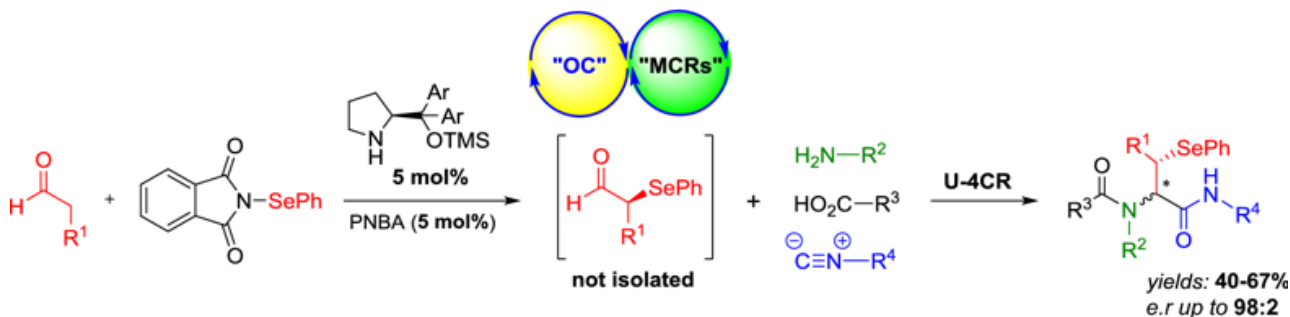
Alexander F. de la Torre, Akbar Ali, Fábio Z. Galetto, Antonio, L. Braga, José A. C. Delgado, Márcio W. Paixão

2019 – Molecular Diversity

Keyword: ACQUITY UPC2, Trefoil Amy 1 chiral column, Trefoil Cel 1chiral column

#### Abstract

A combined organocatalytic and multicomponent synthetic approach was designed for the preparation of selenium-based peptoids and peptide-peptoid conjugates. This single-step synthetic protocol comprises the organocatalytic asymmetric insertion of phenylselenium in the aldehyde moiety followed by the Ugi four-component reaction which results in obtaining the desired compounds in good-to-moderate yields and with good-to-excellent levels of stereoselectivity.



<https://doi.org/10.1007/s11030-019-09923-w>

### 31. Separation and detection of aqueous atmospheric aerosol mimics using super critical fluid chromatography-mass spectrometry

Daisy N. Grace, Melissa B. Sebold, and Melissa M. Galloway

2019 – Journal Atmospheric Measurement Techniques

#### Abstract

Atmospheric particles contain thousands of compounds with many different functional groups and a wide range of polarities. Typical separation methods for aqueous atmospheric systems include reverse-phase liquid chromatography or derivatization of the analytes of interest followed by gas chromatography. These methods can be time-consuming and do not easily separate highly polar aqueous molecules. This study uses supercritical fluid chromatography-mass spectrometry to



separate the methylglyoxal – ammonium sulfate reaction mixture as a proxy for aqueous atmospheric aerosol mimics. Several column compositions, mobile phase modifiers, and column temperatures were examined to determine their effect on separation and the optimum conditions for separation in a minimal amount of time and sample preparation. Polar columns such as the Viridis UPC2™ BEH column combined with a mobile phase gradient of carbon dioxide and methanol provided the best separation of compounds in the mixture. This separation method can be extended to analyze other aqueous atmospheric systems, including the mixtures of other aldehydes or organic acids with ammonium or small amines  
<https://doi.org/10.5194/amt-2019-42>

### **32. The 11 $\beta$ -hydroxysteroid dehydrogenase isoforms: pivotal catalytic activities yield potent C11-oxy C19 steroids with 11 $\beta$ HSD2 favouring 11-ketotestosterone, 11-ketoandrostenedione and 11-ketoprogesterone biosynthesis**

Rachelle Gent, Therina duToit, Liezl M. Bloem, Amanda C. Swart

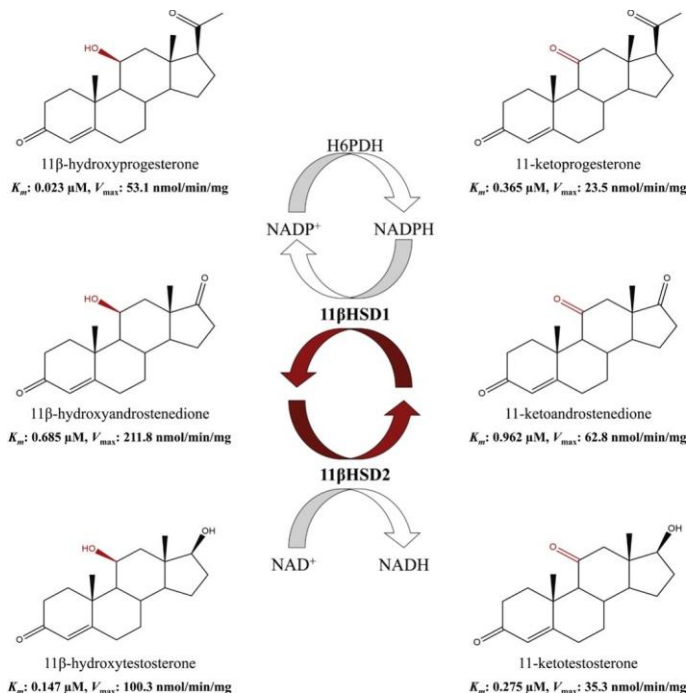
2019 – The Journal of Steroid Biochemistry and Molecular Biology

Keywords: 11 $\beta$ -hydroxysteroid dehydrogenase (11 $\beta$ HSD), Adrenal 11 $\beta$ -hydroxyandrostenedione (11OHA4, 11OHAD), Polycystic ovary syndrome (PCOS), 21-hydroxylase deficiency (21OHD, 21-OH CAH), Castration resistant prostate cancer (CRPC), Cytochrome P450 17 $\alpha$ -hydroxylase/17,20-lyase (CYP17A1), Cortisol, Cortisone

#### **Abstract**

The 11 $\beta$ -hydroxysteroid dehydrogenase (11 $\beta$ HSD) types 1 and 2 are primarily associated with glucocorticoid inactivation and reactivation. Several adrenal C11-oxy C19 and C11-oxy C21 steroids, which have been identified in prostate cancer, 21-hydroxylase deficiency and polycystic ovary syndrome, are substrates for these isozymes. This study describes the kinetic parameters of 11 $\beta$ HSD1 and 11 $\beta$ HSD2 towards the C11-keto and C11-hydroxy derivatives of the C19 and C21 steroids. The apparent  $K_m$  and  $V_{max}$  values indicate the more prominent 11 $\beta$ HSD2 activity towards 11 $\beta$ -hydroxy androstenedione, 11 $\beta$ -hydroxytestosterone and 11 $\beta$ -hydroxyprogesterone in contrast to the 11 $\beta$ HSD1 reduction of the C11-keto steroids, as was demonstrated in the LNCaP cell model in the production of 11-ketotestosterone and 11-ketodihydrotestosterone. Data highlighted the role of 11 $\beta$ HSD2 and cytochrome P450 17A1 in the contribution of C11-oxy C21 steroids to the C11-oxy C19 steroid pool in the C11-oxy backdoor pathway. In addition, 11 $\beta$ HSD2 activity, catalysing 11-ketotestosterone biosynthesis, was shown to be key in the production of prostate specific antigen and in the progression of prostate cancer to castration resistant prostate cancer. The study at hand thus provides evidence that 11 $\beta$ HSD isozymes play key roles in pathophysiological states, more so than was previously put forward.

<https://doi.org/10.1016/j.jsbmb.2019.02.013>



### 33. Ultra-performance convergence chromatography with tandem mass spectrometry-assisted method for rapid enantioseparation and determination of fluazifop-butyl in tobacco and soil.

Yang F, Tang G, Liu S, Fan Z, Wang Y, Deng H, Bian Z, Li Z

2019 – Chirality

Keywords: enantioselective separation, fluazifop - butyl herbicide, tandem mass spectrometry, ultra - performance convergence chromatography

#### Abstract

A quick, green, and sensitive method for chiral separation and determination of fluazifop - butyl enantiomers in tobacco and soil was established by ultra - performance convergence chromatography with tandem mass spectrometry (UPC2 - MS/MS). The baseline separation was obtained on an ACQUITY UPC2 Trefoil CEL2 column in 4 minutes with CO<sub>2</sub> and methanol as mobile phase. Column temperature, auto back pressure regulator pressure (ABPR), and modifier solvent were optimized to obtain the best separation efficiency. Under the optimal conditions, the recoveries of both enantiomers were 82.8% to 99.5% with relative standard deviations (RSDs) less than 5.5% at three different concentration levels in two matrices. Good coefficients of determination ( $R^2 \geq 0.9976$ ) were achieved over the concentration range of 10 to 500 ng/mL. The limits of detection (LODs) for all enantiomers in the two matrices varied from 1.6 to 2.1  $\mu\text{g/kg}$ , and the limits of quantification (LOQs) did not exceed 7.0  $\mu\text{g/kg}$ . The proposed method was then successfully applied to analyze authentic samples, confirming that it was a green, convenient, and reliable strategy for the analysis of fluazifop - butyl enantiomers in tobacco and soil.

<https://doi.org/10.1002/chir.23062>

### 34. Development of a robust SFC method for evaluation of compatibility for a novel antituberculous fixed-dose combination

Valentina Petruševska, Iva Krtalić, Andrea Rašića and Ana Mornar

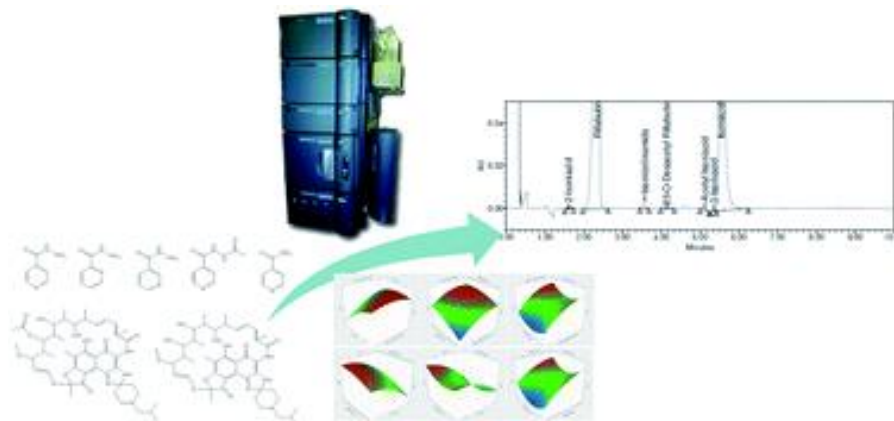
2019 – Journal of Analytical Methods

#### Abstract

A fast and simple supercritical fluid chromatography method for the simultaneous determination of two antituberculous drugs, isoniazid and rifabutin, and their impurities from a new proposed fixed-dose combination (FDC) was developed. Isoniazid and rifabutin are used in antituberculous therapy as single active substance medications. Although FDCs have proved beneficial in general,

compatibility issues for some combinations have been reported. The development of a suitable analytical method was, therefore, necessary to assess the applicability of these two active substances for a new FDC formulation. Two active components and their related compounds were successfully separated in only 7 min using an Acquity UPC2™ Torus DEA, 130 Å, 1.7 µm, 3.0 × 100 mm column. Compressed CO<sub>2</sub> was modified with a mixture of methanol–2-propanol–water–triethylamine, in ratio 70 : 28 : 2 : 0.1 (v/v/v/v), to obtain gradient elution. Quality-by-design principles were implemented to accomplish a reliable and robust analytical method. Modeling software (JMP®, version 13.2.1) was utilized for the Design of Experiments. Mathematical models for the relationship of column temperature, pressure, modifier composition and flow rate to five critical quality attributes were generated. A comprehensive method development approach facilitated detection of influencing factors and significant second-order terms indicating factors' interaction and nonlinear effects. The new proposed method was successfully validated for specificity, linearity, sensitivity, accuracy, precision, stability, filter study and robustness in compliance with internationally accepted guidelines. Acceptable validation results were obtained for both concentration level ranges (assay and impurities determination). Finally, the applicability of the method was tested for commercially available samples of both active substances.

<https://doi.org/10.1039/C9AY00117D>



### 35. Simultaneous identification and determination of eleven tyrosine kinase inhibitors by supercritical fluid chromatography-mass spectrometry

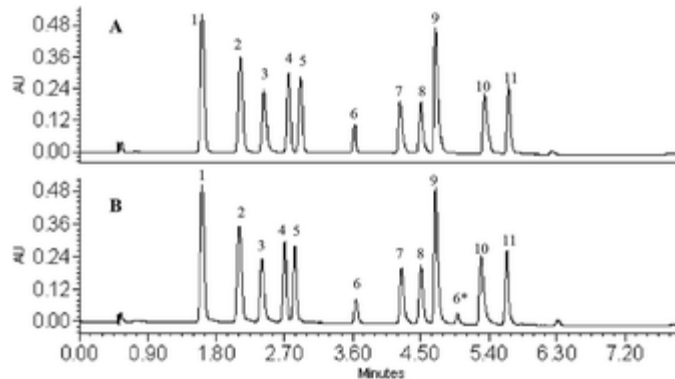
Shaomin Zhang, Wei Jin and Yongjian Yang

2019 – Journal of Analytical Methods

#### Abstract

A rapid analytical method using supercritical fluid chromatography (SFC) coupled to mass spectrometry for the simultaneous identification and determination of eleven tyrosine kinase inhibitors (TKIs) was developed and validated. For quantitative assay, a tested solution with a high concentration of 0.4 mg mL<sup>-1</sup> was applied for SFC determination. For identification purposes, a diluted solution with a concentration down to 1 µg mL<sup>-1</sup> was introduced into a SFC-MS system to gain confirmative information. Six different columns were examined in this study and the best separation was achieved on an Acquity UPC2 Torus DIOL column (3.0 mm × 100 mm, 1.7 µm) using a gradient program. The effects of different additives, column temperature and back pressure were investigated. Negative and positive modes were compared using Xevo G2-XS QTOF after SFC separation. The results showed that the response of TKIs in positive mode was much higher than that in negative mode and thus positive mode was adopted. The method validation was performed in the concentration range of 1–600 µg mL<sup>-1</sup> for all TKIs with a coefficient of determination (R<sup>2</sup>) greater than 0.9995. The developed method was applied to several samples collected from the market. Two out of them in powder form were identified to be afatinib with a content of 0.94 mg mg<sup>-1</sup> and osimertinib with a content of 0.92 mg mg<sup>-1</sup>. Another sample in capsule form was identified to be osimertinib with a content of 57 mg per capsule.

<https://doi.org/10.1039/C9AY00332K>



### 36. Determination of Optical Purity of Lactic Acid-Based Chiral Liquid Crystals and Corresponding Building Blocks by Chiral High-Performance Liquid Chromatography and Supercritical Fluid Chromatography

Anna Poryvai, Terezia Vojtylová-Jurkovicová, Michal Šmahel, Natalie Kolderová, Petra Tomášková, David Sýkora and Michal Kohout

2019 – Molecules

Keywords: chiral liquid crystals; optical purity; chiral separation; super critical fluid chromatography; enantioseparation of liquid crystals; mass spectrometry detection; mesomorphic properties

#### Abstract

Liquid crystals (LCs) are among the most prominent materials of the current information age, mainly due to their well-known application in liquid crystal displays (LCDs). Their unique electro-optical properties stem from their ability to form organised structures (mesophases) on the transition from solid state to isotropic liquid. Molecules of LCs in a mesophase still maintain the anisotropy of solid crystals, while simultaneously exhibiting the fluidity of liquids, which gives the system the ability to react immediately to external stimuli such as electric or magnetic fields, light, mechanical stress, pressure and, of course, temperature. For the proper function of LC-based devices, not only chemical, but also optical purity of materials is strongly desirable, since any impurity could be detrimental to the self-assembly of the molecules. Therefore, in this study we aimed to verify synthetic methods published in the literature, which are used nowadays to prepare chiral building blocks based on lactic acid, for their enantioselectivity. Moreover, we have focused on the development of an analytical chiral separation method for target liquid crystalline materials. Using a chiral polysaccharide-based column operated in liquid chromatography mode, we show that not all published methods of LC synthesis are enantioselective, which could lead to significant differences in the properties of the resulting materials. We show that high-performance liquid chromatography with UV detection and supercritical fluid chromatography with UV and mass spectrometry detection enable full control over the chemical and optical purity of the target LCs and the corresponding chiral building blocks. For the first time, we utilise supercritical fluid chromatography with mass detection for the direct chiral analysis of liquid crystalline materials and impurities formed during the synthesis.

<https://doi.org/10.3390/molecules24061099>

### 37. A chiral unified chromatography–mass spectrometry method to analyze free amino acids

Adrien Raimbault, Magdalena Dorebska, Caroline West

2019 – Analytical and Bioanalytical Chemistry

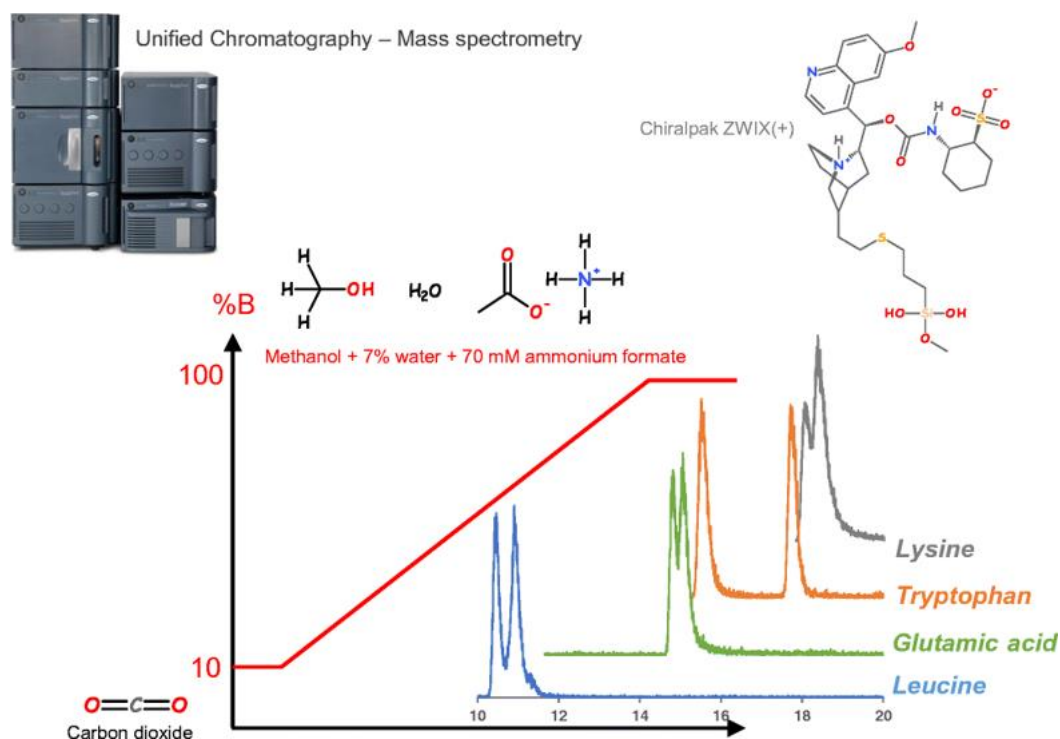
Keywords: Amino acids, Enhanced-fluidity liquid chromatography, Food supplements, Supercritical fluid chromatography, Unified chromatography

#### Abstract

In this project, we aimed at analyzing native (or free) amino acids with supercritical fluid chromatography coupled to mass spectrometric detection, with modern instruments and methods, and maintaining as simple a mobile phase as possible to ensure applicability of the method. The purpose was twofold: (i) a generic method allowing for satisfactory elution of a wide range of amino acids (acidic, basic, or neutral residue) and (ii) resolution of the enantiomeric pairs. The Chiralpak

ZWIX (+) and (-) stationary phases were selected as they are well-known for the enantioresolution of amino acids in liquid chromatographic modes. A wide range elution gradient, starting with a large concentration of carbon dioxide (90%) and finishing at 100% solvent (methanol containing 70 mM ammonium formate and 7% water) allowed the elution of 18 native proteinogenic amino acids out of 19 injected. In these conditions, enantioselectivity was achieved for 16 of them. The basic amino acids (arginine, histidine, and lysine) were the most difficult to elute in these conditions, resulting in rather poor peak shapes. Cysteine was never observed in any of the conditions tested. Sample application was attempted with two food supplements, tablets containing a mixture of 17 proteinogenic amino acids and capsules containing taurine and theanine that were not present in the standards used for the method development. The sample preparation method was very simple, involving dissolution of the tablets and capsules in acidified water, filtration, and dilution with methanol. Mass spectrometric detection (electrospray ionization with single-quadrupole mass detection) allowed for unambiguous identification of most amino acids, except for the leucine and isoleucine isomers that were not separated by the generic gradient. The observation of taurine and theanine also suggests that the method should be generally applicable to other native amino acids than the proteinogenic amino acids selected for the development of this method. As peak shapes and signal-to-noise ratios could still be improved, further developments are wanted to upgrade this method. Due to the wide gradient (10 to 100% co-solvent in carbon dioxide), the method cannot truly be called either supercritical fluid chromatography (SFC) or enhanced-fluidity liquid chromatography (EFLC), but should be related to "unified chromatography" (UC), joining SFC and HPLC.

<https://doi.org/10.1007/s00216-019-01783-5>



### 38. Development and optimization of a supercritical fluid chromatography tandem mass spectrometry method for the high - throughput determination of nimodipine in beagle plasma

Weiping Wang, Pengyan Li, Fengying Wu, Zhen Wang, Tianhong Zhang

2019 – Journal of Separation Science

Keywords: Mass spectrometry, nimodipine, pharmacokinetics, supercritical fluid chromatography

#### Abstract

A simple, sensitive and efficient supercritical fluid chromatography tandem mass spectrometry method was established for the determination of nimodipine in beagle plasma. One - step protein precipitation with acetone was used to extract the analytes from the plasma. Nitrendipine was used

as the internal standard. The chromatographic separation was achieved on an ACQUITY UPC2™ BEH 2 - EP column, and a gradient elution program was applied at a flow rate of 1.5 mL/min. The detection was carried out on a triple quadrupole tandem mass spectrometer with an electrospray ionization source operating in positive ion mode. Quantification was performed using multiple reaction monitoring of the transitions of  $m/z$  419.3→301.3 for NMD and  $m/z$  361.4→315.2 for IS. A satisfactory linearity was obtained over the concentration range of 0.5 - 800.0 ng/mL ( $r > 0.996$ ). The intra - and inter - day precision and accuracy results were less than 9.1 % across the quality control levels. The  $C_{max}$  and  $AUC_{0-t}$  values of the test and reference formulations were  $279.28 \pm 211.46$  and  $265.13 \pm 149.26$  ng/mL,  $25608.00 \pm 17553.65$  and  $28553.67 \pm 20207.92$  ng·min/mL, respectively. The validated method was successfully applied to reveal the pharmacokinetic profiles of nimodipine in beagle dogs after oral administration. Moreover, the analytical method could be used for further bioequivalence studies.

<https://doi.org/10.1002/jssc.201900134>

### 39. Rapid quantitative analysis of six flavonoids in licorice by ultra-performance convergence chromatography

Li LI, Wenyi ZHU, Jingxiu YANG, Xiaolan LIU, Yinmao DONG

2019 – Food Science and Technology

Keywords: licorice; UPC2/PDA; quantify; flavonoids

#### Abstract

This study was to establish a rapid quantitative method for determination of six characteristic flavonoids, including licochalcone A (1), liquiritigenin (2), glabridin (3), isoliquiritigenin (4), liquiritoside (5), and isoliquiritoside (6) in licorice by a ultra-performance convergence chromatography (UPC2) apparatus equipped with a photodiode-array detector (PDA). Methods: The flavonoids studied were separated on an ACQUITY UPC2™ Torus 2-PIC column ( $2.1 \times 100$  mm,  $1.7 \mu\text{m}$ ) using gradient elution (85:15–70:30) with a mobile phase consisting of  $\text{CO}_2$  and methanol: formic acid (99.8:0.2, v/v), back pressure of 2,000 psi, flow rate of 0.8 mL/min, and detection at 254 nm. This method was further applied for the analysis of the flavonoids present in 10 batches of licorice roots samples. Results: Good linearity ( $R^2 = 0.9990$ – $0.9998$ ) was achieved and limits of detection (LOD) and quantification (LOQ) ranging from 0.12 to 0.49  $\mu\text{g/mL}$  and 0.46 to 1.61  $\mu\text{g/mL}$ , respectively. The relative standard deviations (RSD) for repeatability and reproducibility were 2.30–2.80% and 2.30–2.98%, respectively. The flavonoids distributed differently in *Glycyrrhiza uralensis*, *Glycyrrhiza glabra*, and *Glycyrrhiza inflata*. Conclusion: The established rapid quantitative analysis method was environment friendly and suitable to the quality control of species licorice.

<http://orcid.org/0000-0002-2983-9147>

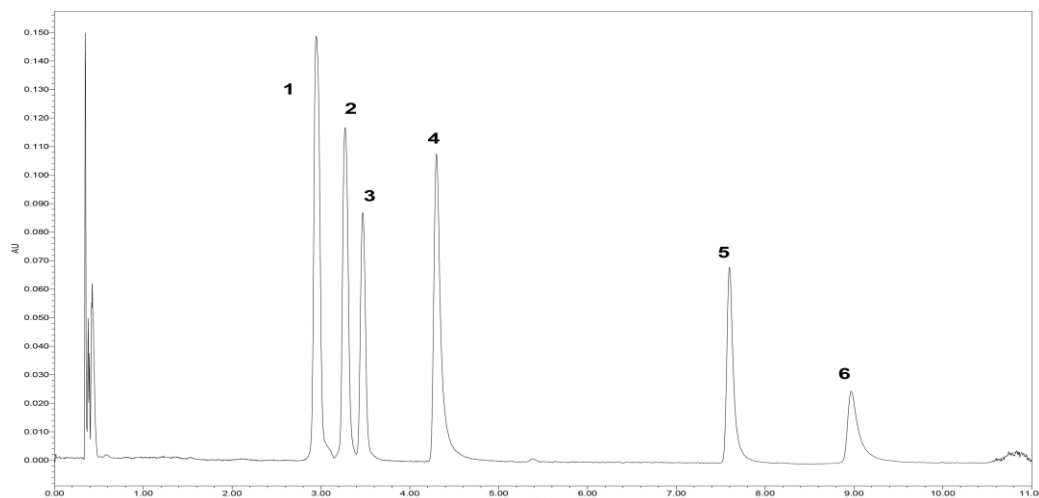


Figure 1 Typical chromatogram of standard mixture of six flavonoids. Peaks numbering: licochalcone A (1), liquiritigenin (2), glabridin (3), isoliquiritigenin (4), liquiritoside (5), isoliquiritoside (6).



#### 40. Quantitative analysis of different batches of raw, wine-processed, and vinegar - processed *Paeoniae Alba Radix* using ultra-performance convergence chromatography coupled with photo diode array detection

Liu Yang, Hai Jiang, Xinyue Guo, Ajiao Hou, Wenjing Man, Xudong Xing, Meiling Yan, Bingyou Yan, Qihong Wang, Haixue Kuang

2019 – Biomedical Chromatography / Early View

##### Abstract

Supercritical fluid chromatography is a safe and ecofriendly analytical technique that has not been fully applied to the analysis of traditional Chinese medicine. This is the first study on the separation of six quality markers—paeoniflorin, albiflorin, benzoyl paeoniflorin, oxypaeoniflorin, gallic acid and benzoic acid—from raw, wine - baked and vinegar - baked *Paeoniae Alba Radix* (PAR) by Supercritical fluid chromatography. Optimum separation was achieved on an HSS C18 SB column (100 × 3.0 mm, 1.8 μm particles) with a gradient elution of high - purity carbon dioxide as mobile phase A and methanol–acetonitrile (70:30, v/v) with 0.10% phosphoric acid as mobile phase B. The flow rate was set at 0.7 mL/min for 15.0 min. The method was validated in terms of the overall intraday and interday precision, with relative standard deviations (RSDs) of 0.87–2.87 and 1.47–3.63%, respectively. The recoveries were 98.10–103.60% with an RSD of 1.00–3.40%. The stability of the RSD values was in the range 1.10–3.78%. The developed approach was successfully applied and provides a valuable reference for the quality assessment of PAR and processed PAR. The results also revealed that the standardization of processing technology is of great significance to the fluctuations in quality before and after the processing of traditional Chinese medicine.

<https://doi.org/10.1002/bmc.4485>

#### 41. Fast Simultaneous Determination of Eight Sudan Dyes in Chili Oil by Ultra-High-Performance Supercritical Fluid Chromatography

Yunjia Yang, Jing Zhang, Jie Yin, and Yi Yang

2019 – Journal of Analytical Methods in Chemistry

##### Abstract

A rapid and simple ultra-high-performance supercritical fluid chromatography (UHPSFC) with photodiode array (PDA) method was developed and validated for simultaneous determination of eight Sudan dyes in chili oil. In particular, a pair of isomer, Sudan red B and Sudan IV, was included in the analysis. After being diluted with dichloromethane, the analytes were separated on an Acquity UPC2 HSS C18 SB column with gradient elution using CO<sub>2</sub> as the mobile phase and acetonitrile/methanol (v/v, 45/55, containing 0.1% formic acid) as the organic modifier. Analytes were quantified by external calibration curves over ranges of 0.5–50 mg/L, with correlation coefficients above 0.999. The method gave recoveries of the target compounds (spiked at levels of 1, 5, and 25 mg/kg) ranging from 82.6 to 108.3%, with intraday and interday relative standard deviations of less than 8.0% and 8.6%, respectively. The limits of detection (LODs) and the limits of quantification (LOQs) for eight dyes were from 0.10 to 0.30 mg/kg and 0.30–1.00 mg/kg, respectively. This method was applied for the analysis of chili oil samples collected from the supermarket in Beijing. This validated that the UHPSFC-PDA method provides a useful strategy for the simultaneous determination of Sudan dyes in chili oil for routine analysis.

<https://doi.org/10.1155/2019/3731028>

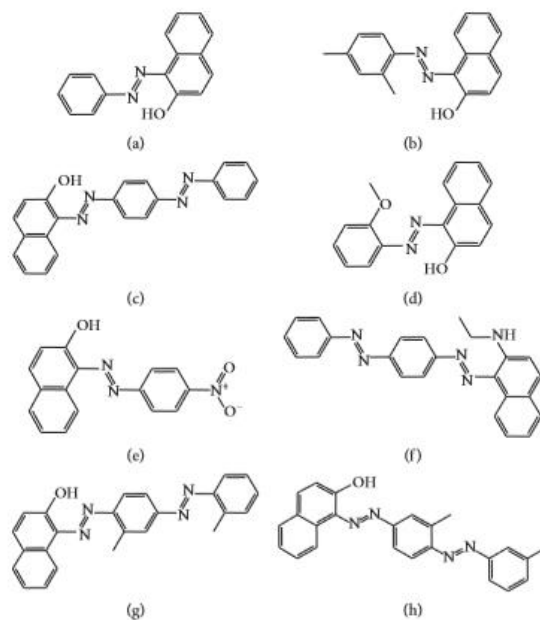


FIGURE 1: Chemical structure of eight Sudan dyes. (a) Sudan I. (b) Sudan II. (c) Sudan III. (d) Sudan red G. (e) Para red. (f) Sudan red 7B. (g) Sudan IV. (h) Sudan red B.

## 42. Determination of multi-class antibiotic residues in compost by microwave-enhanced accelerated solvent extraction and ultra performance convergence chromatography with tandem mass spectrometry

Xue-feng Lu, Yang Zhou, Jian Zhang, Yu-peng Ren

2019 – Journal of Separation Science

### Abstract

This work reports the development and application of a multi - class compound analysis method for the determination of 20 antibiotic residues in compost. Samples were processed by microwave - enhanced accelerated solvent extraction at 120° C for 7.5 min. Salting - out homogeneous liquid - liquid extraction was used to remove water and water - soluble impurities from the extract before ultra performance convergence chromatography with tandem mass spectrometry analysis. By using the supercritical fluid (carbon dioxide) and organic solvent (methanol) as the mobile phase, the 20 antibiotics and the internal standard were well separated in 8.2 min without obvious matrix effect. Method validation was performed and good trueness (relative error in the range of  $\pm 5.0\%$ ) and precision (inter - and intraday relative standard deviations  $< 10.8\%$ ) were obtained. Method detection and quantitation limits were 0.8-1.9 and 2.7-7.1 ng/g, respectively. Recoveries were assessed at three concentration levels (10, 60, and 400 ng/g) and acceptable mean values (70.4-111.9%) were found. This method has also been used to analyze real samples, and the average concentrations of antibiotics (excepting the concentrations  $<$  method quantitation limits) were determined up to 123.6 ng/g. The results showed the method could be helpful for the analysis of multi - class antibiotics in environmental samples.

<https://doi.org/10.1002/jssc.201801032>

## 43. The Benefits of Ultra-High-Performance Supercritical Fluid Chromatography in Determination of Lipophilic Vitamins in Dietary Supplements

Lucie Nováková, Magdaléna Sejkorová, Kateřina Smolková, Kateřina Plachká, František Švec

2019 – Chromatographia

Keywords: Ultra-high-performance supercritical fluid chromatography, Ultra-high-performance liquid chromatography, Liquid-liquid extraction, Vitamin E Dietary supplements, Method validation

## Abstract

Nine tocopherol derivatives including four tocopherols, four tocotrienols, and one esterified form of  $\alpha$ -tocopherol acetate were analyzed using ultra-high-performance supercritical fluid chromatography (UHPSFC) with diode array detection. The separation was carried out on BEH 2-EP column using shallow gradient elution of 1–4% methanol and CO<sub>2</sub> in 5 min. Complementary ultra-high-performance liquid chromatography method was developed using Ascentis Express F5 core-shell stationary phase and isocratic elution with 75% acetonitrile/methanol (1:1) and 25% water. This separation took 12 min that is the shortest liquid chromatography run in analysis of all tocopherol derivatives reported so far. However, our UHPSFC method resulted in more than two times faster analysis, and allowed direct injection of heptane solutions and extracts from liquid-liquid extraction. These features made UHPSFC a method of choice for subsequent analysis of dietary supplements containing different forms of vitamin E. Sample preparation methods were optimized for individual dosage forms of drops, capsules, tablets, and granulate.

<https://doi.org/10.1007/s10337-018-3666-2>

$\alpha$ -tocopherol:  $R_1 = \text{CH}_3$

$\beta$ -tocopherol:  $R_1 = \text{H}, R_2 = \text{CH}_3$

$\gamma$ -tocopherol:  $R_1 = \text{CH}_3, R_2 = \text{H}$

$\delta$ -tocopherol:  $R_1 = \text{H}$

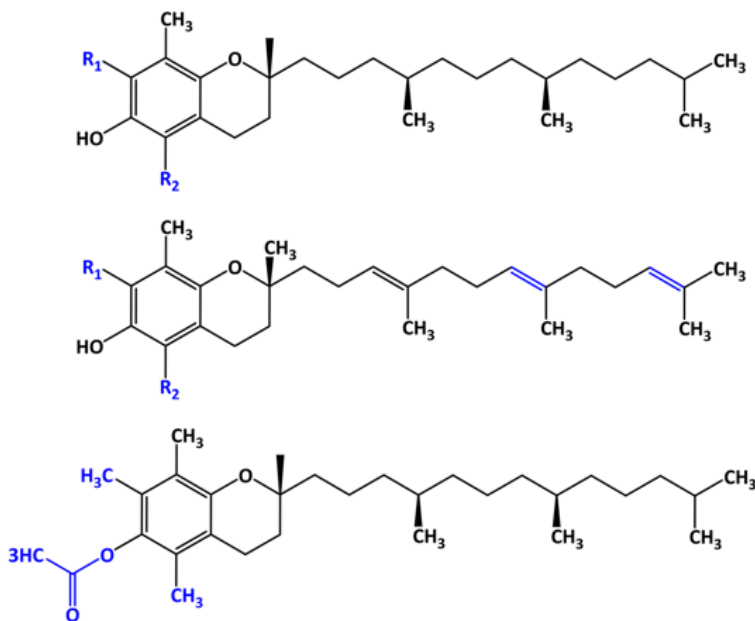
$\alpha$ -tocotrienol:  $R_1 = \text{CH}_3$

$\beta$ -tocotrienol:  $R_1 = \text{H}, R_2 = \text{CH}_3$

$\gamma$ -tocotrienol:  $R_1 = \text{CH}_3, R_2 = \text{H}$

$\delta$ -tocotrienol:  $R_1 = \text{H}$

$\alpha$ -tocopherol acetate:



## 44. Methods for assessment of Vitamin K – Chapter 5

Renata M.Górska

2019 – Laboratory Assessment of Vitamin Status

Keywords: Phylloquinone, Vitamin K, Menaquinones, Urinary vitamin K metabolites, Undercarboxylated vitamin K-dependant proteins, HPLC, LCMS, SFC

### Abstract

There is a great need for the development of robust, reliable methods for the quantitative determination of vitamin K. This chapter provides an overview of the important principles and practices relating to vitamin K measurement in diagnostic and research settings. It include what we feel will be helpful for laboratories in the setting up of analytical methods and also in the interpretation of the results. The difficulties and limitations of the methods are also discussed. Our goal is to give the reader several successful examples of methods used for the assessment of vitamin K status.

## 45. The utility of ultra-high performance supercritical fluid chromatography–tandem mass spectrometry (UHPSFC-MS/MS) for clinically relevant steroid analysis

Karl-Heinz Storbeck, Lorna Gilligan, Carl Jenkinson, Elizabeth S. Baranowski, Jonathan L. Quanson, Wiebke Arlt, Angela E.Taylor

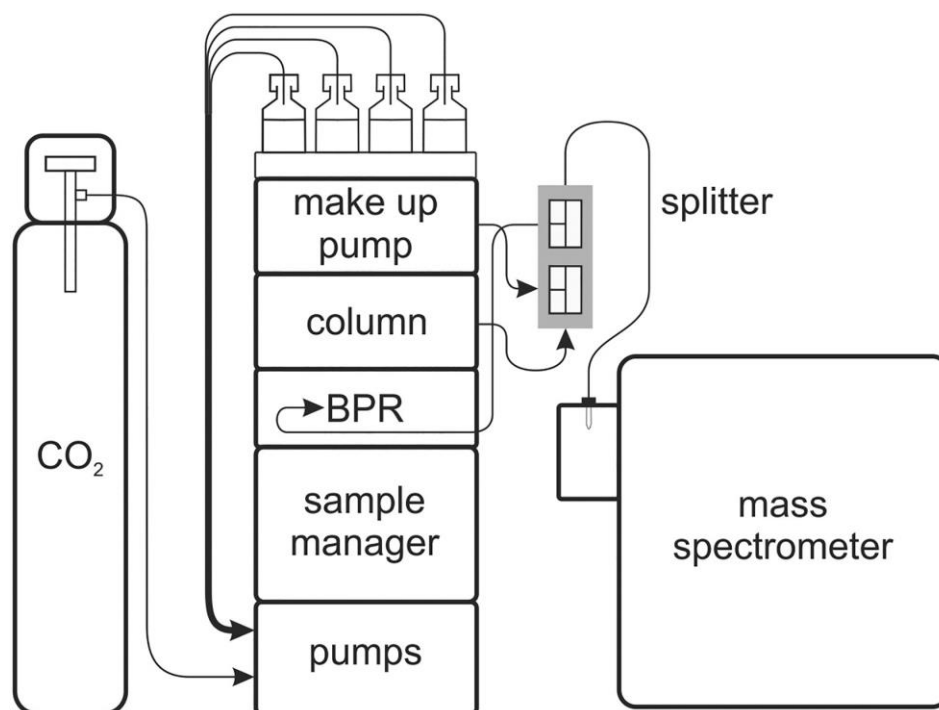
2018 – Journal of Chromatography B

Keywords: Ultra-high performance supercritical fluid chromatography–tandem mass spectrometry, Ultra-high performance liquid chromatography–tandem mass spectrometry, Gas chromatography–mass spectrometry, Steroid analysis

**Abstract**

Liquid chromatography tandem mass spectrometry (LC-MS/MS) assays are considered the reference standard for serum steroid hormone analyses, while full urinary steroid profiles are only achievable by gas chromatography (GC-MS). Both LC-MS/MS and GC-MS have well documented strengths and limitations. Recently, commercial ultra-high performance supercritical fluid chromatography–tandem mass spectrometry (UHPSFC-MS/MS) systems have been developed. These systems combine the resolution of GC with the high-throughput capabilities of UHPLC. Uptake of this new technology into research and clinical labs has been slow, possibly due to the perceived increase in complexity. Here we therefore present fundamental principles of UHPSFC-MS/MS and the likely applications for this technology in the clinical research setting, while commenting on potential hurdles based on our experience to date.

<https://doi.org/10.1016/j.jchromb.2018.03.033>



## 46. Chemical profile and adulteration detection of olive oils

Yinghua Luo

2018 – Maryland Theses and Dissertations

**Abstract**

A combination of ultra-performance convergence chromatography (UPC2) combined with quadrupole time-of-flight mass spectrometry (Q-TOF MS) analyses was utilized to determine the triacylglycerols (TAGs) composition and sn-positions of olive, corn, soybean and sunflower oils, for better understanding of their nutritional value and shelf stability. Ten commercial olive oil samples were analyzed, and a total of 23 TAGs were detected, of which O-O-O was the most abundant TAG in the olive oil samples, followed by P-O-O, O-O-S and O-O-L. The TAGs composition of olive oils were compared to that of the local commercial soybean, corn and sunflower oils. Comparing soybean, corn and sunflower oils with olive oils, L-L-L, P-L-L, B-L-L and M-L-L could be detected in the soybean, corn and sunflower oils but not in the olive oils. Po-O-Po, O-Po-O and G-O-O could be detected only in olive oil and O-O-O was much greater in olive oils. Using UPC2-Q-TOF MS, pure soybean, corn, and sunflower oils could be differentiated from pure olive oil samples based on their triacylglycerol compositions. However, UPC2-Q-TOF MS analysis could not detect olive oils adulterated with small amount of soybean, corn or sunflower oils. UPC2-Q-TOF MS system combined with multivariate data

analysis was tested for potential utilization in detecting of olive oil adulterated by soybean, corn or sunflower oils. A combined UPC2-Q-TOF MS and multivariate data analysis approach was developed to potentially detect the olive oil adulterated with other vegetable oils at 0.5% (v/v) level. In addition, 10 representative marker ions of TAGs were selected to create a model using PCA, which could be used to differentiate pure olive oil from the olive oils adulterated with small amounts of soybean, corn and sunflower oils. The UPC2 system coupled with Q-TOF-MS approach can examine TAG sn-position compositions of olive oils with improved resolution of TAGs and reduced use of organic solvent. UPC2-Q-TOF MS may also be a more environmentally friendly approach for the rapid and accurate analysis of TAGs composition in edible oils and fats, as well as biologically lipids. UPC2-Q-TOF MS system combined with multivariate data analyses may be a possible approach for edible oil adulteration detection.

<https://doi.org/10.13016/hjvp-2i7e>

## 47. Supercritical Fluid Chromatography – eBook

2019 – Book – Volume 2 -Gerard Rosse (Ed)

### Abstract

Supercritical Fluid Chromatography (SFC) provides a timely overview of SFC application areas which were unimaginable just a decade ago. This two-volume series opens with an overview of the history and expectant future of SFC and continues with recent applications in the pharmaceutical industry and other fascinating areas of science. SFC has found its place in the pharmaceutical industry with an increasing body of applications for chiral and achiral molecules in both the research and development phases of the drug discovery process. As illustrated in this two-volume series, the current interest in SFC extends well beyond the pharmaceutical industry. Chapters encompassing applications for polar and non-polar mixtures of importance are covering widely disparate areas in substance abuse, natural products including cannabinoids, bioactive lipids, flavor and fragrance. With its broad balance and coverage, this two-volume book constitutes a unique educational platform to students and scientists for many years to come. The major objective of this book editions is to inspire and stimulate readers to continue exploring the possibilities of exploiting supercritical fluids as a particular media for analysis, purifications and synthesis

<https://books.google.com/books?hl=en&lr=&id=nk2FDwAAQBAJ&oi=fnd&pg=PT10&ots=YUTUEu-8Mt&sig=pEXmmKavd2pkK7RYU6nnJ6TwHuY#v=onepage&q&f=false>

## 48. Unravelling the effects of mobile phase additives in supercritical fluid chromatography—Part II: Adsorption on the stationary phase

Caroline West, Elise Lemasson

2019 - Journal of Chromatography A

Keywords: Adsorption, Ionic interactions, Selectivity, Solvation parameter model, Supercritical fluid chromatography

### Abstract

The mobile phases employed in current practice of supercritical fluid chromatography (SFC) are usually composed of a mixture of pressurized carbon dioxide and a co-solvent. The co-solvent is most often an alcohol and may contain a third component in small proportions, called an additive (acid, base or salt). In the first part of this series, the effects of mobile phase additives on the polarity and apparent pH of the mobile phase were explored. In the present paper, we examine the effects pertaining to adsorption of additives on the stationary phase. Ammonium acetate was selected as a representative case, because it is often employed in current practice. To favour its solubility and further improve chromatographic quality, a small portion of water is also advocated. First, the equilibration time is observed to be largely increased in the presence of an additive, especially when mobile phase compositions containing only low proportions of methanol co-solvent are employed. Secondly, the effects of ammonium acetate are more thoroughly assessed with a modified version of the solvation parameter model (five Abraham descriptors and two descriptors to take account of positive and negative charges on ionizable species). On a hybrid silica stationary phase (ACQUITY UPC2 BEH), the effects of increasing concentration of ammonium acetate (0–25 mM in the methanol co-solvent) are investigated. The retention of acidic species is the most strongly affected, with a continuous retention increase when additive concentration increases. The retention of basic and neutral species is also moderately affected. Then thirty-two stationary phases based on sub-2 µm totally porous particles or sub-3 µm superficially porous particles are characterized with and without 20 mM ammonium acetate and 2% water in the methanol co-solvent. The effects of

adsorbed additive on the interaction capabilities are discussed. Finally, the interest of introducing the additive in the dilution solvent, a method that was sometimes recommended to simplify the workflow, is also discussed with a model basic compound.

#### Highlights

- Additives effects on stationary phase interactions are explored in details.
- Adsorbed additives render polar stationary phases more similar than without them.
- Column equilibration may be extremely long when low proportions of solvent are used.
- Additives in the dilution solvent are unadvisable due to poor reproducibility

<https://doi.org/10.1016/j.chroma.2019.02.002>

## 49. Development and validation of ultra-high performance supercritical fluid chromatography method for quantitative determination of nine sunscreens in cosmetic samples

Maria A. Khalikova, Eric Lesellier, Eric Chapuzet, Dalibor Šatínský, Caroline West

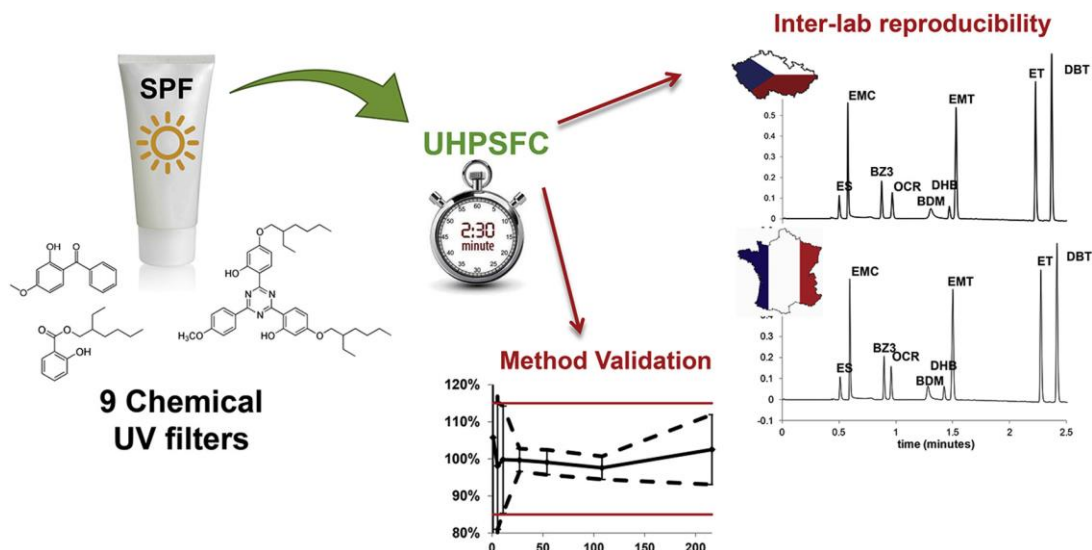
2018 - Analytica Chimica Acta

Keywords: Accuracy profile, Inter-laboratory reproducibility, Sunscreen, Supercritical fluid chromatography, UV filter

#### Abstract

A fast and simple ultra-high performance supercritical fluid chromatography (UHPSFC) method has been developed for the determination of nine sunscreens (UV filters), namely 2-ethylhexyl-2-hydroxybenzoate (ES), ethylhexyl-methoxycinnamate (EMC), benzophenone-3 (BZ3), octocrylene (OCR), bis-ethylhexyloxyphenol-methoxyphenyl triazine (EMT), butyl-methoxydibenzoyl-methane (BDM), diethylamino-hydroxybenzoyl-hexyl-benzoate (DHB), ethylhexyl-triazone (ET), and diethylhexyl-butamido-triazone (DBT) in cosmetic samples. The separation was achieved with Acquity UPC2 Torus 2-PIC (100 × 3.0 mm, 1.7 μm) column. The influence of key chromatographic parameters on resolution was evaluated. The optimal mobile phase was a gradient mixture of carbon dioxide and methanol containing ammonium acetate, at flow rate 1.2 mL min<sup>-1</sup>. The back-pressure of the system was set to 150 bar and the temperature to 40 °C. The compounds were determined with diode-array detection at 280 nm, 305 nm and 340 nm depending on absorbance maxima. The proposed UHPSFC method provided separation of the nine target sunscreens within 2.5 min without labor-consuming sample pretreatment procedure. The method was validated according to the concept of the total error and the accuracy profile. The inter-laboratory reproducibility was evaluated between two independent laboratories (in France and Czech Republic). The reliability of the developed method was shown by application to commercial sunscreen-containing cosmetic sample obtained from French market. The measured limits of quantification showed the suitability of the proposed method for determination of UV filters considering the European Union requirements.

<https://doi.org/10.1016/j.aca.2018.06.013>





## 50. Triacylglycerols composition analysis of olive oils by ultra-performance convergence chromatography combined with quadrupole time-of-flight mass spectrometry

Yinghua Luo, Yaqiong Zhang, Fanghao Yuan, Boyan Gao, Ziyuan Wang, Liangli (Lucy) Yu  
2018 – International Journal of Food Science and Technology

### Abstract

Triacylglycerols (TAGs) compositions of ten commercial olive oil samples were analysed using an ultra-performance convergence chromatography (UPC2) combined with a quadrupole time-of-flight mass spectrometry (Q-TOF MS). A total of twenty-three TAGs were characterised based on their Q-TOF MS accurate molecular weight and MS2 fragment ion profiles, and seventeen of those were reported in olive oils for the first time. O-O-O was the most abundant TAG in all tested olive oil samples, followed by P-O-O, O-O-S and O-O-L. G-G-B had the lowest relative concentration in all the TAGs, ranging 0.02-0.08% of the total sample weight. The results from this study are important for further understanding the nutritional value and stability of olive or other edible oils.

<https://doi.org/10.1111/ijfs.14008>

## 51. Profiling of modified nucleosides from ribonucleic acid digestion by supercritical fluid chromatography coupled to high resolution mass spectrometry

Laurent Laboureur, Vincent Guérineau, Sylvie Auxilien, Satoko Yoshizawa, David Touboul  
2018 – Journal of Chromatography A

Keywords: Supercritical fluid chromatography, High resolution mass spectrometry, Epigenetic, Nucleoside, RNA

### Abstract

A method based on supercritical fluid chromatography coupled to high resolution mass spectrometry for the profiling of canonical and modified nucleosides was optimized and compared to classical reverse-phase liquid chromatography in terms of separation, number of detected modified nucleosides and sensitivity. Limits of detection and quantification were measured using statistical method and quantifications of twelve nucleosides of a tRNA digest from E. coli are in good agreement with previously reported data. Results highlight the complementarity of both separation techniques to cover the largest view of nucleoside modifications for forthcoming epigenetic studies.

## 52. Interest of achiral-achiral tandem columns for impurity profiling of synthetic drugs with supercritical fluid chromatography

Caroline West, Elise Lemasson, Sophie Bertin, Philippe Hennig, Eric Lesellier  
2018 – Journal of Chromatography A

Keywords: High-resolution separations, Impurity profiling, Orthogonal methods, Performance comparison, Pharmaceutical ingredients, Tandem columns

### Abstract

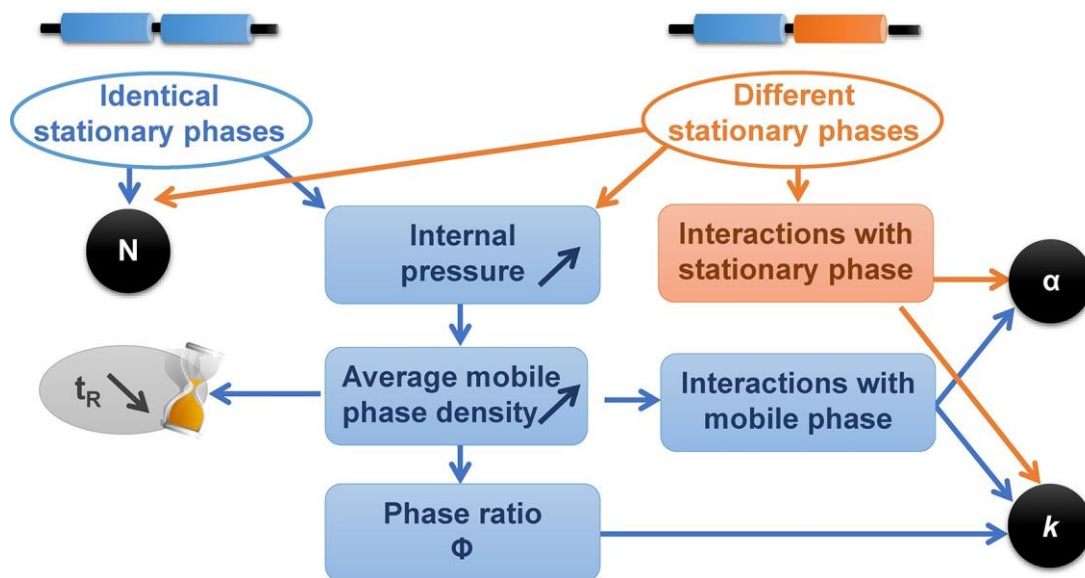
To achieve the most complete impurity profiling of synthetic drugs with a single chromatographic technique, high resolution is required, which may be gained with a combination of high efficiency and versatile selectivity, allowing to separate most similar analytes. Compared to a single-column chromatographic method, coupling complementary stationary phases promises both an increase in efficiency and an increase in selectivity possibilities. With supercritical fluid chromatography (SFC), the use of long columns is facilitated by the low viscosity of the mobile phase. In this paper, we investigate the interest of coupling two achiral stationary phases (Acquity UPC2 HSS C18 SB and Nucleoshell HILIC) that were previously observed to have excellent complementarity in SFC to carry out impurity profiling on 25 individual drug substances containing varied numbers and amounts of impurities. The single-column gradient methods are compared to tandem-column gradient methods with the two possible ordering of columns (C18 phase in first or second position) based on selectivity, peak capacity, sensitivity, UV-estimated purity of the active pharmaceutical ingredient and number of impurities detected with UV-estimated concentration >0.04%. It appears that it could be more beneficial to have two columns coupled in a single analysis than two consecutive methods with the

single columns. The overall analysis time are nearly the same, but with more informative chromatograms in about 35% cases.

Highlights:

- Coupling two columns is an easy way to assemble selectivities in SFC.
- Tandem columns improve peak capacity and sensitivity over single columns.
- Some column combinations are more effective than others.
- The analysis time reduction with tandem columns is currently restricted by system pressure limits.

<https://doi.org/10.1016/j.chroma.2017.12.061>



### 53. Application and enantiomeric residue determination of diniconazole in tea and grape and apple by supercritical fluid chromatography coupled with quadrupole-time-of-flight mass spectrometry

Zhang Xinzhong, Zhao Yuechen, Cui Xinyi, Wang Xinru, Shen Huishan, Chen Zongmao, Huang Chun, Narendra Meruva, Zhou Li, Wang Fang, Wu Luchao, Luo Fengjian

2018 – Journal of Chromatography A

Keywords: Enantiomeric residue analysis, Diniconazole, Apple, Grape, Tea, Supercritical fluid chromatography coupled with quadrupole-time-of-flight mass spectrometry (SFC-Q-TOF/MS)

#### Abstract

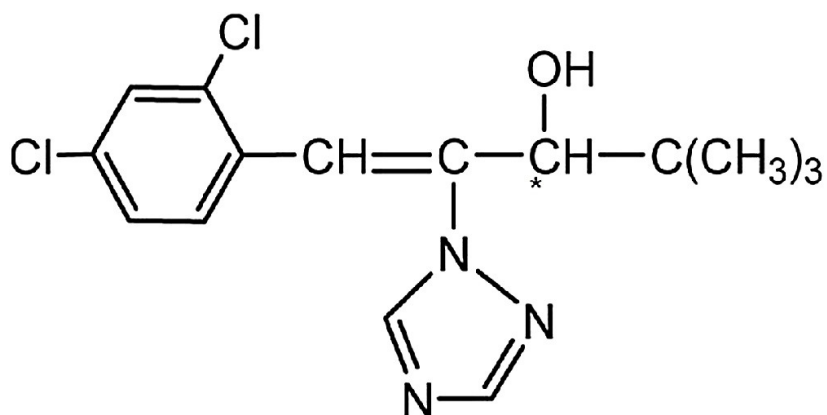
A chiral separation and residue determination method for diniconazole enantiomers in tea, apple, and grape was developed and validated by supercritical fluid chromatography coupled with quadrupole-time-of-flight mass spectrometry (SFC-Q-TOF/MS). The two diniconazole enantiomers were separated on a Chiral CCA column, and the chromatographic conditions (mobile phase proportion and modifier, column temperature, backpressure, and auxiliary solvent) were optimized. The optimal SFC-Q-TOF/MS conditions were selected as a mobile phase of CO<sub>2</sub>/isopropanol (IPA) (v/v, 96/4), flow rate at 2.0 mL/min, automated back pressure regulator (ABPR) at 2000 psi, column temperature at 25 °C and under electrospray ionization positive mode with the best auxiliary solvent of 2 mmol/L ammonium acetate in methanol/water (v/v, 1/1) at 0.20 mL/min flow rate. Residues in tea and fruit samples were extracted by acetonitrile/water (v/v, 4/1 for fruit and 2/1 for tea), purified by Cleanert TPT or Pesti-Carb solid phase extraction column, then analyzed by SFC-Q-TOF/MS with matrix-matched external standard quantification method. The elution order of diniconazole enantiomers on CCA column was R-(-)-diniconazole at first, and S-(+)-diniconazole at second. The standard curve concentration levels of R-(-)-diniconazole and S-(+)-diniconazole in samples ranged from 0.01 mg/L to 1.00 mg/L with the correlation coefficients greater than 0.99. The spiked recoveries of R-(-)-diniconazole and S-(+)-diniconazole in apple and grape at three levels of 0.005, 0.05 and 0.25 mg/kg were in the range of 69.8% to 102.1%, with relative standard

deviations (RSDs) ( $n = 6$ ) between 3.5% and 10.4%, and the limits of quantitation (LOQs) below 0.005 mg/kg. The spiked recoveries in black tea at three levels of 0.01, 0.10, and 0.50 mg/kg were in the range of 85.6% to 90.6%, with the RSDs ( $n = 6$ ) ranging from 3.9% to 9.5%, and LOQ of 0.01 mg/kg. This residue analysis and determination method for diniconazole enantiomers in apple, grape and tea samples is convenient, reliable, and meets the residue analysis requirement. Also it is applied for the residue fates of R-(-)-diniconazole and S-(+)-diniconazole during the fresh tea leaves growing, green tea processing and black tea processing. The degradation half-times (DT50) between R-(-)-diniconazole and S-(+)-diniconazole in the fresh tea leaves growing were 2.9 d and 3.1 d, respectively. The concentrations of R-(-)-diniconazole and S-(+)-diniconazole decreased gradually with time and on the 14th day after application were lower than 10% of the initial concentration. The average enantiomer fractions (EFs) of R-(-)-diniconazole and S-(+)-diniconazole at 2 h, 2, 5, 7, 10 and 14 d after application in fresh tea leaves were 0.505, 0.526, 0.523, 0.558, 0.453 and 0.489, respectively. This result is similar to the result of our last research for the enantiomers of cis-epoxiconazole-another triazole fungicide residues in fresh tea leaves. And in the whole black tea processing, 37.1%–49.3% and 35.9%–57.9% of R-(-)-diniconazole and S-(+)-diniconazole decreased, respectively. The total processing factors (PFs) of R-(-)-diniconazole and S-(+)-diniconazole for the black tea procedure were 0.507–0.629 and 0.421–0.641, respectively. The EFs of R-(-)-diniconazole and S-(+)-diniconazole in black tea processing ranged from 0.432 to 0.532. However, in the whole green tea processing, 22.3%–32.6% and 21.7%–40.3% of R-(-)-diniconazole and S-(+)-diniconazole decreased, respectively. The difference between black tea and green tea is nearly 15%, and in green tea is less decreased than in black tea. The total PFs of R-(-)-diniconazole and S-(+)-diniconazole for the green tea procedure were 0.674–0.777 and 0.597–0.783, respectively. The EFs of R-(-)-diniconazole and S-(+)-diniconazole in green tea processing ranged from 0.473 to 0.504. The PFs illustrated that for R-(-)-diniconazole and S-(+)-diniconazole decrease, the rolling and fermentation were the critical steps in black tea processing, and the rolling was the critical step in green tea processing, respectively.

#### Highlights:

- Optimized SFC-Q-TOF/MS separation method for diniconazole enantiomers on CCA column was developed. R-(-)-diniconazole was eluted at first and S-(+)-diniconazole at second.
- Highly efficient and accuracy residue analysis method in tea, apple and grape was demonstrated. LOQs were significantly lower than the MRLs of diniconazole in various agriculture products.
- DT50 in fresh tea leaves were 2.9 and 3.1 days for R-(-)- and S-(+)-diniconazole, respectively.
- Rolling and fermentation are the critical steps affecting digestion in black tea processing, and rolling in green tea processing.

<https://doi.org/10.1016/j.chroma.2018.10.051>



## 54. Recent Developments in the Analysis of Carotenoids by Mass Spectrometry

Antonio Pérez-Gálvez and María Roc

Keywords: Extraction methods of carotenoids, liquid chromatography, ionization procedures, mass spectrometry, metabolomics, fragmentation pathways and carotenoid identification, data analysis from mass spectra, software tools

#### **Abstract**

Mass spectrometry has become an indispensable tool for the analysis of carotenoids in photosynthetic tissues, foods, and biological materials from different sources to accurately establish their pigment profile, to provide evidences to distinguish the different structural arrangements, and to obtain biological meaning from metabolic processes where carotenoids participate during the development of their natural functions and activities. The recent progresses in the hyphenated HPLC systems with hybrid mass spectrometers, which enhance the acquisition of independent and complementary physicochemical properties for the identification of carotenoids, are detailed in this chapter. A reasonable guide for the implementation of post-processing routines, assisted by modern software tools, and the key issues for the analysis of the characteristic product ions are also defined in this contribution to help the readers in the understanding of the potential capabilities of mass spectrometry in the field of carotenoid pigments.

<http://dx.doi.org/10.5772/intechopen.79755>

### **55. First inter-laboratory study of a Supercritical Fluid Chromatography method for the determination of pharmaceutical impurities**

Amandine Dispas, Roland Marini, Vincent Desfontaine, Jean-Luc Veuthey, Dorina Kotoni, Luca Gioacchino Losacco, Adrian Clarke, Charlene Muscat Galea, Debby Mangelings, Brandon M. Jocher, Erik L. Regalado, Katerina Plachká, Lucie Nováková, Benjamin Wuyts, Isabelle François, Michael Gray, Andrew J. Aubin, Abhijit Tarafder, Maxime Cazes, Christophe Desvignes, Loic Villemet, Morgan Sarrut, Adrien Raimbault, Elise Lemasson, Eric Lesellier, Caroline West, Tomas Leek, Mengling Wong, Lulu Dai, Kelly Zhang, Alexandre Grand-Guillaume Perrenoud, Claudio Brunelli, Philippe Hennig, Sophie Bertin, Fabien Mauge, Nathalie Da Costa, William P. Farrell, Madeleine Hill, Niranjana Desphande, Manish Grangrade, Santosh Sadaphule, Ravi Yadav, Sandesh Rane, Shankar Shringare, Marion Iguiniz, Sabine Heinisch, Julien Lefevre, Estelle Corbel, Nicolas Roques, Yvan Vander Heyden, Davy Guillaume, Philippe Hubert

2018 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: Supercritical Fluid Chromatography (SFC); Inter-laboratory study; Collaborative study; Reproducibility; Pharmaceutical impurities; Salbutamol sulfate

#### **Abstract**

Supercritical Fluid Chromatography (SFC) has known a strong regain of interest for the last 10 years, especially in the field of pharmaceutical analysis. Besides the development and validation of the SFC method in one individual laboratory, it is also important to demonstrate its applicability and transferability to various laboratories around the world. Therefore, an inter-laboratory study was conducted and published for the first time in SFC, to assess method reproducibility, and evaluate whether this chromatographic technique could become a reference method for quality control (QC) laboratories. This study involved 19 participating laboratories from 4 continents and 9 different countries. It included 5 academic groups, 3 demonstration laboratories at analytical instrument companies, 10 pharmaceutical companies and 1 food company. In the initial analysis of the study results, consistencies within- and between-laboratories were deeply examined. In the subsequent analysis, the method reproducibility was estimated taking into account variances in replicates, between-days and between-laboratories. The results obtained were compared with the literature values for liquid chromatography (LC) in the context of impurities determination. Repeatability and reproducibility variances were found to be similar or better than those described for LC methods, and highlighted the adequacy of the SFC method for QC analyses. The results demonstrated the excellent and robust quantitative performance of SFC. Consequently, this complementary technique is recognized on equal merit to other chromatographic techniques.

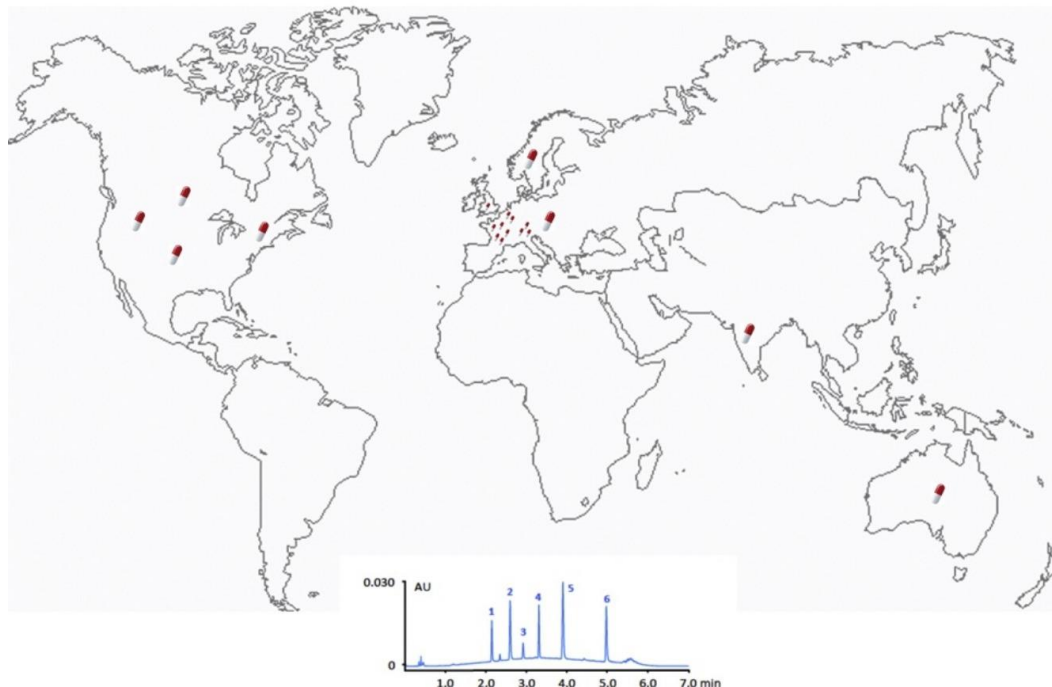
#### Highlights

- Inter-laboratory study was conducted for the first time in SFC.
- This study involved 19 participating laboratories from 4 continents and 9 different countries.
- Results consistencies within- and between-laboratories were deeply examined.
- The method reproducibility was estimated taking into account variances in replicates, between-days and between-laboratories.

- Repeatability and reproducibility variances were found to be similar or better than those described for LC methods.

<https://doi.org/10.1016/j.jpba.2018.08.042>

#### Supercritical Fluid Chromatography Inter-laboratory study



## 56. Identification and quantification of triacylglycerols in human milk fat using ultra-performance convergence chromatography and quadrupole time-of-flight mass spectrometry with supercritical carbon dioxide as a mobile phase

Xinghe Zhang, Ce Qi, Yiren Zhang, Wei Wei, Qingzhe Jin, Zhimin Xu, Guanjun Tao, Xingguo Wang  
2018 – Food Chemistry

Keywords: Human milk; Fat; Triacylglycerols; Mass spectrometry; Supercritical fluid

### Abstract

An ultra-performance convergence chromatography (UPC2) method coupled with quadrupole time-of-flight mass spectrometry (Q-TOF-MS), was developed for the determination of complicated triacylglycerols (TAGs) in human milk fat. The use of supercritical carbon dioxide as the mobile phase improved the chromatographic separation of the TAGs significantly. By optimizing the scan modes of Q-TOF-MS and selecting parent ions for MS/MS ionization, the fragment ions of each TAG including TAG isomers with overlapping retention time were adequately resolved for identification and quantification. A total of 95 different TAGs were identified in the human milk samples from Chinese mother volunteers, with O-P-L representing the main TAG, followed by O-P-O and O-L-L. In addition, the compositions and contents of TAGs in different fats and oils were successfully measured. The developed method can serve as an advanced and reliable analytical tool for the determination of complicated TAGs in various biological samples.

### Highlights

- A method was established to analyze complex triacylglycerols mixture by UPC2-Q-TOF-MS.
- A total of 95 triacylglycerols in human milk fat can be detected.
- Triacylglycerols isomers having the same parent ion and overlapping retention time could be determined.

<https://doi.org/10.1016/j.foodchem.2018.09.150>



## 57. A rapid analysis of piroxicam in beagle plasma applying evaporation-free liquid-liquid extraction by supercritical fluid chromatography-tandem mass spectrometry

Xiaoting Li, Yan Gao, Jia Liu, Gongtian Zhang, Tianhong Zhang

2018 – Journal of Chromatography B

Keywords: Piroxicam; SFC-MS/MS; Bioequivalence; Pharmacokinetics

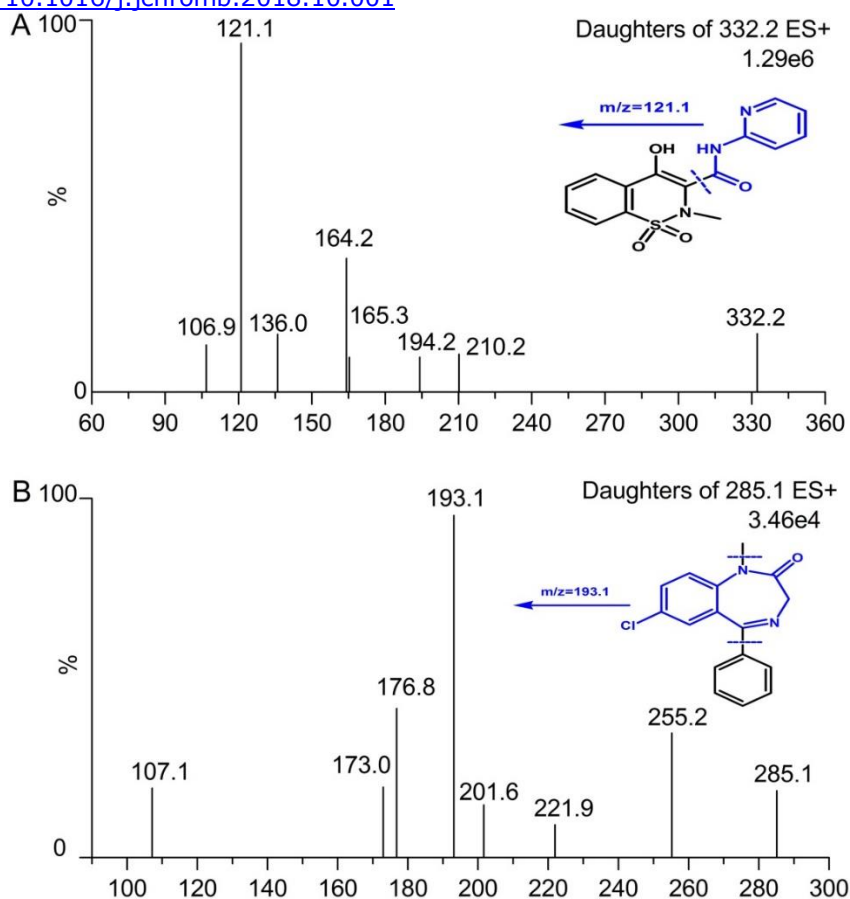
### Abstract

Bioequivalence study is highly prized to piroxicam (PIRO), since its generic products have been widely used worldwide. The present work was undertaken to explore the pharmacokinetic behaviors and bioequivalence of two branded PIRO tablets in beagle dogs using the supercritical fluid chromatography tandem mass spectrometry (SFC-MS/MS) method. Here, a fast evaporation-free liquid-liquid extraction (EF-LLE) method using ethyl acetate was developed for extracting PIRO from beagle dog plasma. To improve the response as well as peaks elution and symmetry of analytes, several key factors were investigated including post-column compensation, stationary phase, mobile phase, column temperature, back pressure and flow rate, and finally the analytes were eluted on an ACQUITY UPC2™ BEH 2-EP column (100 × 3 mm, 1.7 μm) within only 2.5 min in optimal conditions. The performance of the established method was evaluated, good linearity was found over the concentration range of 5–5000 ng/mL ( $R_2 \geq 0.994$ ) with a lower limit of quantification (LLOQ) of 5 ng/mL. Accuracy of all quality control (QC) samples were between 96.6% and 99.6% with a satisfactory intra and inter-day precision (RSD values < 6.6%). The proposed rapid, sensitive, user-friendly and high throughput method will be an alternative way for PIRO analysis in biological samples.

### Highlights

- A rapid and straightforward analytical method was exploited using SFC-MS/MS.
- An evaporation-free LLE method was firstly used in PIRO biological sample preparation.
- A satisfied sensitivity (LLOQ 5 ng/mL) and short elution time (2.5 min) were achieved.
- Less plasma usage is more consistent with animal ethical requirements.

<https://doi.org/10.1016/j.jchromb.2018.10.001>





## 58. An environmentally friendly method for the enantioseparation and determination of benalaxyl in tobacco and soil by ultra - performance convergence chromatography with tandem mass spectrometry

Fei Yang, Gangling Tang, Zhonghao Li, Ziyang Fan, Ying Wang, Shanshan Liu, Zhaoyang Bian, Huimin Deng

2018 - Journal of Separation Science

Keywords: benalaxyl, enantioseparation, fungicide, tandem mass spectrometry, ultra - performance convergence chromatography

### Abstract

For the purpose of chiral separation and determination of benalaxyl enantiomers in tobacco and soil, we developed a rapid, green and sensitive method using ultra - performance convergence chromatography with tandem mass spectrometry. The samples were extracted and purified by quick, easy, cheap, effective, rugged and safe method before injection. The baseline separation was obtained on a chiral column in 5 min with carbon dioxide and ethanol as mobile phase. Separation parameters were optimized for the best separation efficiency. Under the optimal conditions, the recoveries of both enantiomers were 77.1–98.4% with relative standard deviations less than 5.0% at spiked level of 0.1, 2.0 and 5.0 mg/kg in two matrices. Good coefficients of determination were achieved over the concentration range of 10–250 ng/mL. The limit of detection and the limit of quantification for all enantiomers ranged from 0.43 to 0.72  $\mu$ g/kg, and from 1.25 to 2.15  $\mu$ g/kg, respectively. The results show that ultra - performance convergence chromatography with tandem mass spectrometry provides a reliable, green, and rapid method for the separation and determination of benalaxyl enantiomers in tobacco and soil. This method has important theoretical significance for studying the enantioselectivity and bioactivity of benalaxyl in the environment and organism.

<https://doi.org/10.1002/jssc.201800861>

## 59. Practical Strategies for Successful Scaling from UPC2 to Preparative SFC

Jacquelyn Runco

2018 – Chromatography Today article

### Abstract

Techniques for scaling separation methods from analytical to preparative in traditional liquid chromatography are well understood and easily accomplished. Many of the same factors that influence successful scaling in HPLC are also important in SFC, such as maintaining identical column length, particle size and stationary phase, along with determining system and extra column volumes in order to account for and anticipate differences in peak shape and retention time [1]. Also, depending on the choice of diluent and injection volume, the sample injection strategy needs to be considered.

<https://www.chromatographytoday.com/article/supercritical-fluid-sfcgreen-chromatography/45/waters-corporation/practical-strategies-for-successful-scaling-from-upc2-to-preparative-sfc/2430/view>

## 60. A novel, fast and sensitive supercritical fluid chromatography-tandem mass spectrometry (SFC-MS/MS) method for analysis of arachidonic acid metabolites

S. J. Kumari A. Ubhayasekera, Santosh R. Acharyaa and Jonas Bergquist

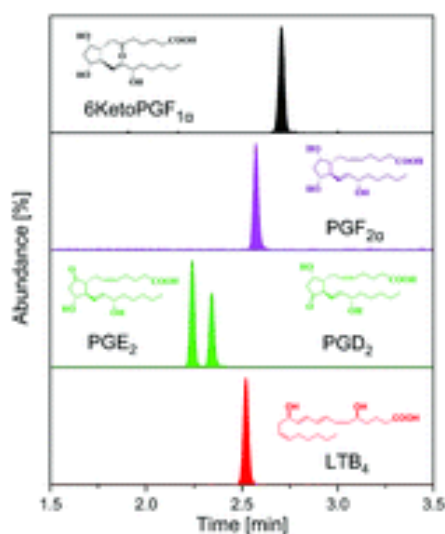
2018 – Analyst

Keywords:

### Abstract

The development of a rapid, sensitive and reliable method for the quantification of bioactive arachidonic acid metabolites (AA-metabolites) in biological samples is quite challenging due to the minute concentration, short half-life and their structural complexity arising from different isomers. In this study, a simple, fast and environmentally friendly supercritical fluid chromatography-tandem mass spectrometry (SFC-MS/MS) method was developed and validated for simultaneous measurement of five (PGD<sub>2</sub>, PGE<sub>2</sub>, PGF<sub>2</sub> $\alpha$ , 6KetoPGF<sub>1</sub> $\alpha$  and LTB<sub>4</sub>) AA-metabolites in biological

samples. These analytes were extracted by protein precipitation followed by separation and quantification. The analysis was completed within 3 minutes. The matrix matched linear calibration ranged from 0.5–100 ng mL<sup>-1</sup> ( $r^2 \geq 0.995$ ), whilst, the limit of quantification of PGD<sub>2</sub>, PGE<sub>2</sub>, PGF<sub>2 $\alpha$</sub> , and LTB<sub>4</sub> was 0.5 ng mL<sup>-1</sup> and was 2.5 ng mL<sup>-1</sup> for 6KetoPGF<sub>1 $\alpha$</sub> . The interday and intraday precisions of the method were less than 15% while the accuracy of most of the analytes varied between 83 and 109%. Finally, as a proof of concept, the method was successfully applied for the determination of eicosanoids in human samples, which expands the possibility to explore physiological states, disease phenotypes, and novel biomarkers.  
<https://doi.org/10.1039/C8AN00788H>



## 61. SFC for chiral separations in bioanalysis

Lukas C. Harps, Jan F. Joseph, Maria K. Parr

2019 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: Enantiomer; Chiral separation; Biological specimen; Bioanalysis; Chiral stationary phase; Supercritical fluid chromatography

### Abstract

This review covers literature investigating methods for enantioselective chromatography using supercritical fluids as mobile phase constituents (SFC) in the field of bioanalysis. It provides an overview on method development and screening approaches published in scientific literature 2014–2018. Chiral stationary phases are used to create a chiral environment that allows for discrimination of enantiomers. Especially polysaccharide-based stationary phases are used in methods of recent investigations. In comparison to HPLC chiral SFC separation provides more selective cavity effects of inclusion-type chiral separation phases. Modifier and additive choices as well as further operating conditions like backpressure, temperature and flow rate are summarized and critically discussed. Further on, observed sample pretreatment and possible detection techniques are presented. SFC hyphenated to mass detection was found of major relevance and is therefore further discussed. Coupling of SFC with different detectors allows for straightforward use in bioanalysis. Interfacing MS detectors is generally performed including a make-up pump. Thus, applied make-up conditions were also reviewed. While most of the chiral separations in HPLC are performed in normal phase mode, and thus, challenge MS hyphenation, SFC-MS hyphenation can be easily achieved. This allows for convenient application in chiral trace analyses, often required in bioanalysis. Even worse in enantioseparation than in achiral chromatography, method development in SFC suffers from a lack of knowledge in separation mechanisms and thus approaches are often quite unique and most often achieved by screening using a One-Factor-at-a-Time (OFAT) design. Broad screening experiments with methodical approaches still appear as method of choice for now.

## 62. Characterization of Novel Polymer-Based Pyridine Stationary Phases for Supercritical Fluid Chromatography

Caroline West, Elise Lemasson, Kanji Nagai, Tohru Shibata, Pilar Franco, Sophie Bertin, Philippe Hennig, Eric Lesellier

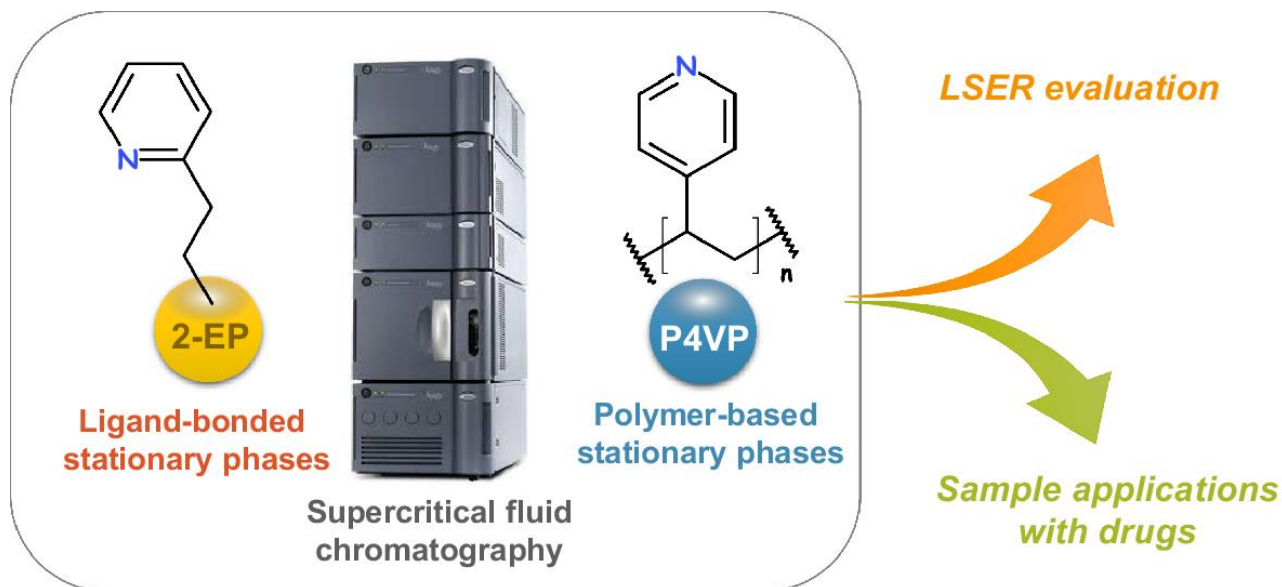
2018 – Chromatographia

Keywords: Supercritical fluid chromatography (SFC), Linear solvation energy relationships (LSER), Quantitative structure–retention relationships (QSRR), Solvation parameter model, Polymeric stationary phases

#### Abstract

2-Ethylpyridine-bonded silica is one of the most famous stationary phases employed in supercritical fluid chromatography, especially for the analysis of basic compounds and even without an additive in the mobile phase. In the present paper, we present the synthesis and characterization of three original stationary phases based on poly(vinylpyridine) polymers supported on silica. The position of nitrogen atom relative to the polymer chain was varied to be in the 2, 3, or 4 position. All these phases were prototypes, while the poly(4-vinylpyridine) phase was subsequently commercialized (DCPak P4VP from Daicel Corporation). The stationary phases obtained are characterized in supercritical fluid chromatography with carbon dioxide–methanol mobile phase, with a modified version of the solvation parameter model, to take account of ionic interactions. The three phases are also compared to a 2-ethylpyridine-bonded silica phase and a 2-picolyamine-bonded silica phase. It appears that the polymer-based pyridine phases are significantly more retentive than brush-type pyridine phases and adequately shield residual silanol groups to prevent unwanted interactions with basic compounds. The different selectivities and chromatographic performances are also evidenced with sample applications on pharmaceutical compounds, notably with a selection of 140 drug candidates.

<https://doi.org/10.1007/s10337-018-3598-x>



### 63. Measuring Thiols in Single Cultivar South African Red Wines Using 4,4-Dithiodipyridine (DTDP) Derivatization and Ultraperformance Convergence Chromatography-Tandem Mass Spectrometry

Mpho Mafata, Maria A. Stander, Baptiste Thomachot and Astrid Buica

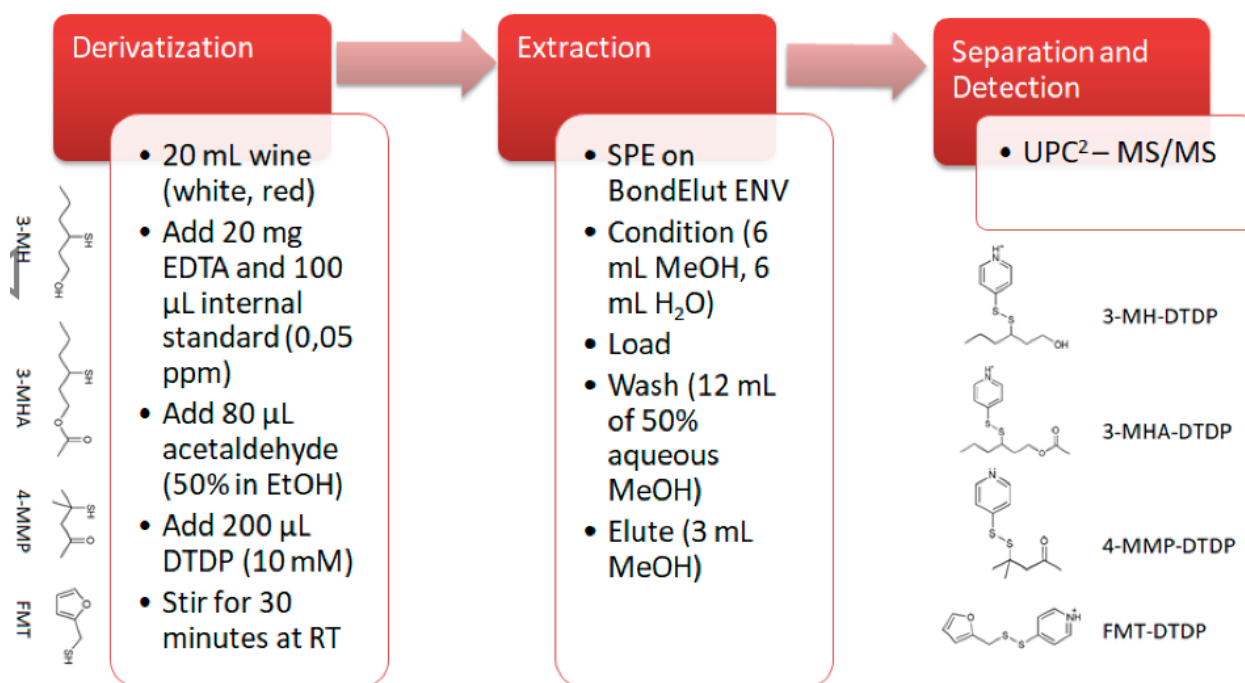
2018 – Foods

Keywords: thiols; wine; derivatization; DTDP; convergence chromatography; supercritical fluid chromatography (SFC); UPC2-MS/MS; SPE

#### Abstract

Wine varietal thiols are important contributors to wine aroma. The chemical nature of thiols makes them difficult to measure due to low concentrations, high sensitivity to oxidation, and low ionization. Methods for the measurement of thiols usually consist of multiple steps of sample preparation followed by instrumental measurement. Studies have collected large datasets of thiols in white wine but not in red wine, due to the lack of availability of suitable methods. In this study, for the first

time, convergence chromatography was used to measure thiols in red wine at ultratrace levels with improved sensitivity compared to previous methods. Performance parameters (selectivity, linearity, limits of detection, precision, accuracy) were tested to demonstrate the suitability of the method for the proposed application. Red wine thiols were measured in South African Pinotage, Shiraz, and Cabernet Sauvignon wines (n = 16 each). Cultivar differentiation using the thiol profile was demonstrated.



<https://doi.org/10.3390/foods7090138>

#### 64. Unmatched Kinetic Performance in Enantioselective Supercritical Fluid Chromatography by Combining Latest Generation Whelk-O1 Chiral Stationary Phases with a Low-Dispersion in-House Modified Equipment

Omar H. Ismail, Gioacchino L. Losacco, Giulia Mazzocanti, Alessia Ciogli, Claudio Villani, Martina Catani, Luisa Pasti, Scott Anderson, Alberto Cavazzini and Francesco Gasparrini

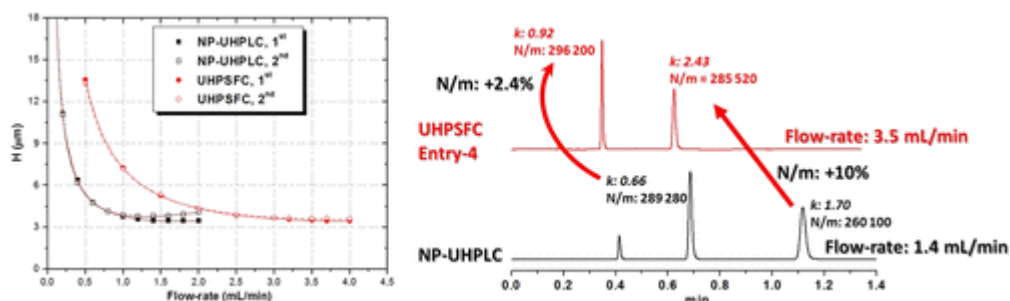
2018 – Analytical Chemistry

Keywords:

Abstract

This proof-of-concept work investigates the ultimate kinetic limits reachable in chiral supercritical fluid chromatography (SFC) with modern columns and advanced technological solutions. A commercial equipment (Waters Acquity UPC2) has been in-house modified to minimize its overall extra-column variance through a series of technical adjustments including low-volume connecting tubings, reduced-volume flow cell, an in-house made external column oven, external low-dispersion injection system, and electronic temperature controller. Compared to the original (as-shipped) configuration, the extra-column variance on the low-dispersion equipment was reduced by more than 97%, from about 85 to slightly more than 2  $\mu$ L<sup>2</sup> (measured at 2.0 mL/min). This was mainly achieved thanks to the occurrence of fully developed turbulent regime with a proper selection of capillary i.d. at significantly smaller flow rates (1.5–4 mL/min; CO<sub>2</sub>/methanol 80/20, v/v; 35 °C; back pressure regulator (BPR), 105 bar) than in entry-1 configuration. Ultrahigh efficiency columns of different geometries in-house packed with latest generation sub-2  $\mu$ m UHPC-FPP-Whelk-O1 Chiral Stationary Phase (CSP) have been employed under sub- and supercritical fluid conditions. By carefully modulating the length and the internal diameter of connecting tubings in the function of column geometry, state of the art efficiencies (estimated in roughly 300 000 theoretical plates/m with reduced HETP of roughly 1.85) have been obtained on 4.6 mm i.d. chiral columns. Remarkably, for 3.0 mm  $\times$  100 mm (i.d.  $\times$  length) columns, the efficiency gain on the fully modified SFC system

(compared to an instrumental configuration where only the standard injector was replaced by the low-dispersion one) was greater than 90% for compounds with a retention factor of 1 and as large as 25% for retention factors of 2.5.



<https://doi.org/10.1021/acs.analchem.8b01907>

## 65. Synergistic interactions of sulfamethoxazole and azole antifungal drugs against emerging multidrug-resistant *Candida auris*

Hassan E. Eldesouky, Xiaoyan Li, Nader S. Abutaleb, Haroon Mohammad, Mohamed N. Seleem  
2018 - International Journal of Antimicrobial Agents

Keywords: *Candida auris*; Antifungal; Azole resistance; Sulfamethoxazole; *Caenorhabditis elegans*; ERG11p

### Abstract

*Candida auris* is an emerging multidrug-resistant pathogen that has been implicated in numerous outbreaks worldwide, with a notably high rate of mortality (~60%). A significant challenge with treatment of these infections is *C. auris* is resistant to most antifungal drugs used clinically. Thus, finding co-drugs capable of overcoming resistance to frontline antifungal drugs is of prime clinical importance. Herein, we evaluated the ability of the combination of different sulfa drugs with azole antifungal drugs to inhibit the growth of azole-resistant *C. auris*. Among the active sulfa drugs, sulfamethoxazole exhibited the most potent in vitro synergistic interactions with voriconazole and itraconazole. The sulfamethoxazole-voriconazole combination restored voriconazole's fungistatic activity against three out of eight voriconazole-resistant clinical isolates. Similarly, the sulfamethoxazole-itraconazole combination restored itraconazole's fungistatic activity against three out of four itraconazole-resistant clinical isolates. This activity was further confirmed in vivo in a *Caenorhabditis elegans* model of *C. auris* infection. The sulfamethoxazole-voriconazole combination enhanced survival of nematodes infected with *C. auris* by nearly 70%. Notably, our data indicate that the efficacy of this novel combination is dependent on the underlying mechanisms of azole resistance. Mutant strains which demonstrated azole resistance by either overproduction of/or decreased affinity for the azole target (ERG11p) were found highly susceptible to the sulfamethoxazole-azole combination. However, this synergistic interaction was ineffective against mutant strains which demonstrated azole resistance via hyperactivity of efflux pumps. In conclusion, sulfamethoxazole represents a promising co-drug that can restore the efficacy of certain azole antifungal drugs against some azole-resistant isolates of *Candida auris*.

<https://doi.org/10.1016/j.ijantimicag.2018.08.016>

## 66. Detection of tris (2,3-dibromopropyl) phosphate and other organophosphorous compounds in Arctic rivers

Ian J. Allan, Øyvind A. Garmo, Jan Thomas Rundberget, Petr Terentjev, Guttorm Christensen, Nikolay A. Kashulin

2018 – Environmental Science and Pollution Research

Keywords: Organophosphorus flame retardants, Passive sampling, Silicone rubber, Arctic, TDBrPP, Rivers, Organic contaminants

### Abstract

The flame-retardant tris(2,3-dibromopropyl) phosphate (TDBrPP) was in the 1970s banned for uses in textiles that may be in contact with the skin, owing to strong suspicions that the substance was a human carcinogen. The substance is looked for but rarely detected in samples from the built and

natural environments, but there are indications that TDBrPP is still in use. Here, we report the measurement of a polymer-water partition coefficient ( $K_{pw}$ ) for two types of silicone rubber (SR), allowing quantitative estimation of freely dissolved concentrations of TDBrPP by passive sampling in water. We found levels of 100 to 200 pg/L in two Arctic rivers that were sampled during a 2014–2015 survey of contamination using passive samplers in Norwegian and Russian rivers draining into the Barents Sea. We also report the widespread presence of other organophosphorus flame retardants in this survey of eight rivers that drain into the Barents Sea.

<https://doi.org/10.1007/s11356-018-2947-5>

## 67. Residue and Dietary Risk Assessment of Chiral Cyflumetofen in Apple

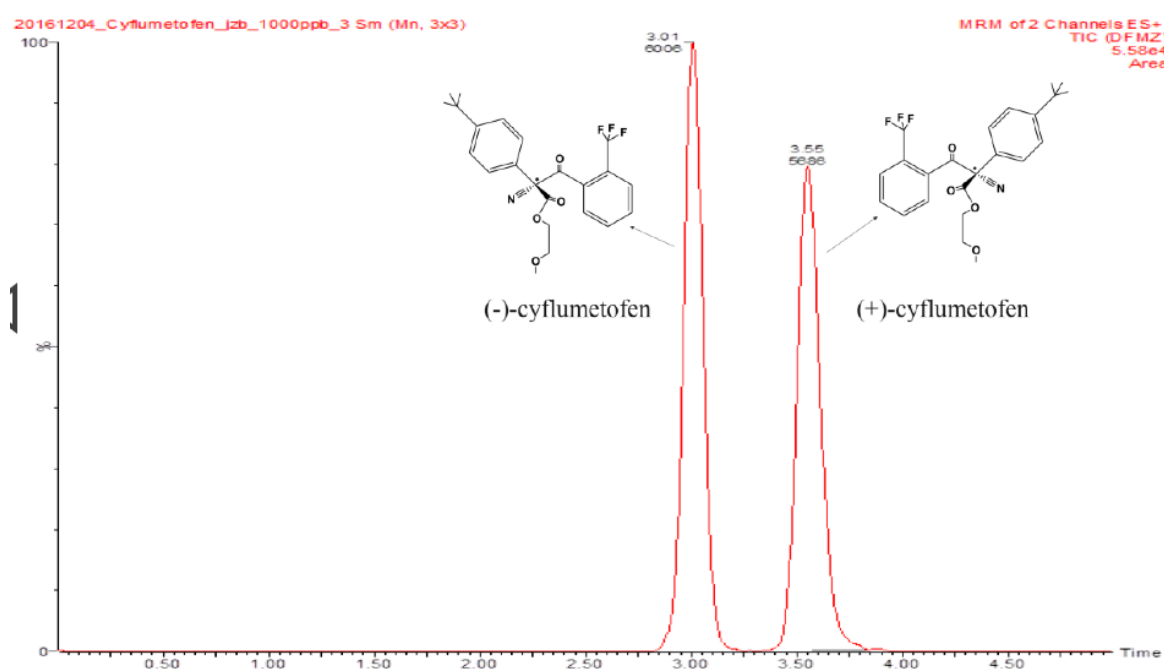
Jing Guo, Minmin Li, Yongguo Liu, Fengzhong Wang, Zhiqiang Kong 1, Yufeng Sun, Jia Lu, Nuo Jin, Yatao Huang, Jiameng Liu, Frédéric Francis and Bei Fan

2018 – Molecules

Keywords: chiral cyflumetofen; enantioselective degradation; distribution; ultra-performance convergence chromatography; dietary risk assessment

### Abstract

Ultra-performance convergence chromatography is an environmentally-friendly analytical method that uses dramatically reduced amounts of organic solvents. In addition, a robust and highly sensitive chiral separation method was developed for the novel chiral acaricide cyflumetofen by using ultra-performance convergence chromatography coupled with tandem mass spectrometry, which shows that stereoisomer recoveries determined for various apple parts ranged from 78.3% to 119.9%, with the relative standard deviations being lower than 14.0%. The half-lives of (–)-cyflumetofen and (+)-cyflumetofen obtained under 5-fold applied dosage equal to 22.13 and 22.23 days, respectively. For 1.5-fold applied dosage, the respective values were determined as 22.42 and 23.64 days, i.e., the degradation of (–)-cyflumetofen was insignificantly favored over that of its enantiomer. Importantly, cyflumetofen was unevenly distributed in apples, with its relative contents in apple peel, peduncle, and pomace equal to 50%, 22%, and 16%, respectively. The proposed method can be used to efficiently separate and quantify chiral pesticide with advantages of a shorter analysis time, greater sensitivity, and better environmental compatibility. Additionally, the consumption of apples with residue of cyflumetofen did not pose a health risk to the population if the cyflumetofen applied under satisfactory agricultural practices after the long-term dietary risk assessment.



<https://doi.org/10.3390/molecules23051060>



## 68. Supercritical Fluid Chromatography with Photodiode Array Detection in the Determination of Fat-Soluble Vitamins in Hemp Seed Oil and Waste Fish Oil

Katarzyna Tyćkiewicz, Roman Gieysztor, Izabela Maziarczyk, Paweł Hodurek, Edward Rój and Krystyna Skalicka-Woźniak

2018 – Molecules

Keywords: fat-soluble vitamins; hemp seed oil; purification; supercritical fluid chromatography; waste fish oil

### Abstract

In the presented study for the first time a new, optimized, fast SFC (supercritical fluid chromatography) method was applied to separate in one run fat-soluble vitamins from waste fish oil, including cis- and trans-retinyl palmitate, cis- and trans-retinyl acetate, retinol,  $\alpha$ -tocopherol,  $\beta$ -tocopherol,  $\gamma$ -tocopherol,  $\delta$ -tocopherol, ergocalciferol (D2), cholecalciferol (D3), cis- and trans-phyloquinone (K1) and menaquinone-4 (K2-MK4). Vitamins were baseline separated on an Acquity UPC2 (ultra performance convergence chromatography) HSS C18 SB (highly strength chemically modified silica) column within 13 min. The influence of the stationary phase, such as Torus 1-AA (1-aminoanthracene), Torus Diol (high density diol), Torus DEA (diethylamine), BEH (silica with no bonding), BEH-2EP (2-ethylpyridine), CSH Fluoro-Phenyl (silica with fluoro-phenyl groups), column temperature, flow rate and back pressure on the separation of the compounds was described. The application of the modified saponification procedure allowed us to increase concentration in the sample prepared for the analysis of  $\gamma$ -tocopherol from less than 1% (wt %) to 14% for the first time. In addition,  $\alpha$ -tocopherol,  $\gamma$ -tocopherol,  $\delta$ -tocopherol and retinol were identified in waste fish oil. Vitamin purification and analysis in waste fish oil are reported for the first time here. Due to the short time and effectiveness of the proposed method, it can be easily applied in industrial processes.

<https://doi.org/10.3390/molecules23051131>

## 69. Ultra-performance convergence chromatography method for the determination of four chromones and quality control of *Saposhnikovia divaricata* (Turcz.) Schischk.

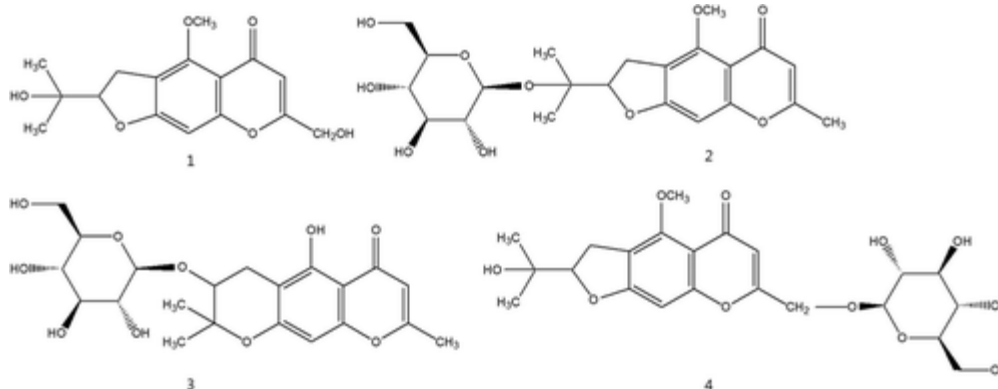
Hyo Seon Kim, Goya Choi, A. Yeong Lee

2018 - Journal of Separation Science

Keywords: Chromone, quality control, *saposhnikovia divaricata*, Schischk, UPC2

### Abstract

Ultra - performance convergence chromatography is an environmentally friendly analytical technique that employs dramatically reduced amounts of organic solvents compared to conventional chromatographic methods. In this study, a rapid, sensitive, and environmentally friendly method based on ultra - performance convergence chromatography was developed for the quantification of four major chromones present in the roots of *Saposhnikovia divaricata* (Turcz.) Schischk. Using this method, the analysis time was significantly shortened compared to conventional high - performance liquid chromatography techniques. In addition, the influence of cosolvent type, cosolvent ratio, column temperature, system pressure, and flow rate on the peak resolution was investigated. The proposed method was validated in terms of its limits of detection, limits of quantitation, linearity, precision, and accuracy. More specifically, the limits of detection of the four chromones ranged from 0.006 to 0.033  $\mu\text{g/mL}$ , while the limits of quantitation ranged from 0.019 to 0.101  $\mu\text{g/mL}$ . Our method also exhibited a good regression ( $r^2 > 0.999$ ), excellent precision (RSD < 0.60%), and acceptable recoveries (99.48–102.89%). Finally, the quantities of these four chromones present in 20 commercial samples from Korea and China were successfully evaluated using the developed method, indicating that the proposed method is suitable for the rapid and accurate quality control of *Saposhnikovia divaricata*.



<https://doi.org/10.1002/jssc.201701281>

## 70. Fast determination of betaine in Lycii Fructus by ultra-performance convergence chromatography-tandem mass spectrometry

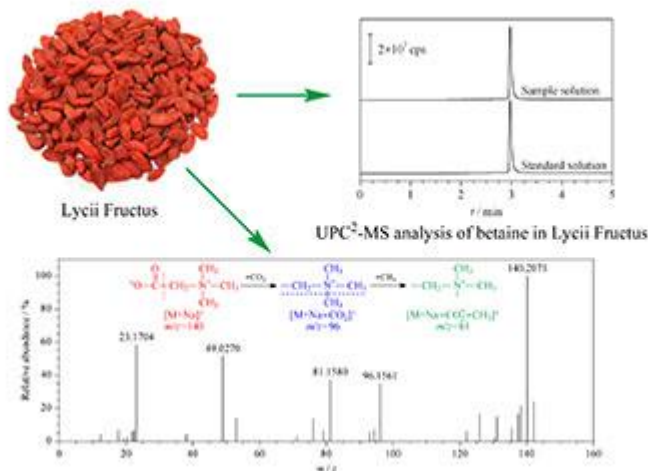
ZHANG Xianfei, YANG Junli, CHEN Juan, SHI Yanping

2018 – Chinese Journal of Chromatography

Keywords: ultra-performance convergence chromatography-tandem mass spectrometry (UPC2-MS), betaine, Lycii Fructus, quality control

### Abstract

Over the past 2500 years, Lycii Fructus has been widely used as a functional food and tonic in Chinese herbal medicine. It can nourish the liver and kidneys, moisten the lungs, and improve eyesight. In this study, a new rapid and sensitive method has been developed for the quantitative determination of betaine (index compound) in Lycii Fructus by using ultra-performance convergence chromatography-tandem mass spectrometry (UPC2-MS). The separation of betaine was successfully achieved on an ACQUITY UPC2 BEH 2-EP column (150 mm×2.1 mm, 1.7 μm), with isocratic elution by a CO<sub>2</sub>-methanol (80:20, v/v) solvent at a flow rate of 0.7 mL/min. The conditions used in the separation process were as follows: modifier, 0.1% (v/v) formic acid in methanol; column temperature, 40°C; backpressure, 1.31 × 10<sup>7</sup> Pa; injection volume, 1 μL; and retention time, 3 min. The MS system was equipped with an electrospray ionization (ESI) ion source and operated in the selected ion recording (SIR) and positive ion mode. Under the abovementioned conditions, the calibration curve was obtained. The linear range of detection was 0.5-50.0 μg/mL, with a correlation coefficient of 0.9992, and the limit of detection (LOD) was found to be 0.013 μg/mL. The validity of the method was tested by analyses of precision, repeatability, stability, and accuracy (average recovery: 96.3%). Finally, the developed method was applied to analyze 11 batches of samples. The results indicated that this method was suitable for evaluating the quality of Lycii Fructus.



<http://www.chrom-china.com/EN/abstract/abstract14480.shtml>

## 71. Simultaneous determination of six zearanols in milk samples by immunoaffinity solid phase extraction coupled with ultra-performance convergence chromatography-tandem mass spectrometry

Zhang L, Sun J, Wang Y, Wu H, Yu S.

2018 – Chinese Journal of Chromatography

Keywords: ultra-performance convergence chromatography-tandem spectrometry (UPC2-MS/MS), solid phase extraction (SPE), immunoaffinity column (IAC), zearanols, milk

### Abstract

A method was developed for the simultaneous determination of  $\alpha$ -zearalanol,  $\beta$ -zearalanol,  $\alpha$ -zearalenol,  $\beta$ -zearalenol, zearalenone and zearalanone residues in milk samples by ultra-performance convergence chromatography-tandem mass spectrometry (UPC2-MS/MS) after immunoaffinity column-solid phase extraction (IAC-SPE). The sample was diluted with deionized water and cleaned with IAC-SPE. The chromatographic separation was performed on an ACQUITY UPC2 Torus 2-PIC column (50 mm $\times$ 3.0 mm, 1.7  $\mu$ m) using the mobile phases of supercritical carbon dioxide and methanol containing 0.1% (v/v) formic acid with gradient elution. The separated compounds were detected in negative electrospray ionization (ESI-) mode. The results showed no significant matrix effect after cleaning by IAC-SPE. The calibration curves of the six compounds were linear in the range of 1-200 ng/mL (correlation coefficients ( $r^2$ )  $\geq$  0.9957). The recoveries were 75.9%-106.5% in the three spiked levels, and the intra-day and inter-day precisions were no more than 11.4%. The method is specific, environment friendly, and is suitable for the rapid determination of  $\alpha$ -zearalanol,  $\beta$ -zearalanol,  $\alpha$ -zearalenol,  $\beta$ -zearalenol, zearalenone and zearalanone residues in milk samples.

<http://www.chrom-china.com/CN/10.3724/SP.J.1123.2018.02008>

## 72. Simultaneous determination of 22 phthalate esters in polystyrene food-contact materials by ultra-performance convergence chromatography with tandem mass spectrometry

Ying - Li Fan, Ming Ma, He - Zhen Cui, Shu Liu, Min - Li Yang, Xiu - Feng Hou

2018 – Journal of Separation Science

Keywords: dissolution-precipitation; mass spectrometry; phthalate esters; polystyrene food-contact material; ultraperformance convergence chromatography

### Abstract

A method for the determination of 22 phthalate esters in polystyrene food - contact materials has been established using ultraperformance convergence chromatography with tandem mass spectrometry. In this method, 22 phthalate esters were analyzed in <3.5 min on an ACQUITY Tours 1 - AA column by gradient elution. The mobile phase, the compensation solvent, the flow rate of mobile phase, column temperature, and automatic back pressure regulator pressure were optimized, respectively. There was a good linearity of 20 phthalate esters with a range of 0.05-10 mg/L, diisodecyl phthalate and diisononyl phthalate were 0.25-10 mg/L, and the correlation coefficients of all phthalates were higher than 0.99 and those of 16 phthalates were higher than 0.999. The limits of detection and the limits of quantification of 15 phthalates were 0.02 and 0.05 mg/kg, meanwhile diallyl phthalate, diisobutyl phthalate, dimethyl phthalate, di - n - butyl phthalate, and di(2 - ethylhexyl) phthalate were 0.05 and 0.10 mg/kg, and diisodecyl phthalate and diisononyl phthalate were 0.10 and 0.25 mg/kg. The spiked recoveries were in the range of 76.26-107.76%, and the relative standard deviations were in the range of 1.78-12.10%. Results support this method as an efficient alternative to apply for the simultaneous determination of 22 phthalate esters in common polystyrene food - contact materials.

<https://doi.org/10.1002/jssc.201800094>

## 73. Current trends in the analysis and quality control of food supplements based on plant extracts

Jakub Fibigr, Dalibor Šatínský, Petr Solich

2018 - Analytica Chimica Acta

Keywords: Food/dietary supplements; Analytical methods; Sample preparation; Bioactive substances; Plant extracts; Contaminants; Adulterants

### Abstract

Food (dietary) supplements include a wide range of products that are designed to be taken because of their added nutrients and presumed health benefits. Global food supplement sales are experiencing rapid growth and supplements that based on botanicals are among the most popular. The meteoric rise in sales coupled with the general lack of a commitment to pass effective regulation make this market more vulnerable to dishonest producers, increase the likelihood that supplements containing adulterants are sold on the market, and a greater prevalence of safety and quality issues (contamination by pesticides and mycotoxins). In this paper, we present an overview of various sample preparation and analytical techniques that can be used for the determination of bioactive substances in food supplements based on plant extracts and for making purity assessments of plant extracts in these preparations. The analysis looks at data collected from 2012 to 2017. The work is divided according to the different approaches taken when analysing food supplements and groups of bioactive substances found in plant extracts (purity assessments and the determination of bioactive substances).



<https://doi.org/10.1016/j.aca.2018.08.017>

## 74. Rapid analysis of tristyrylphenol ethoxylates in cucumber-field system using supercritical fluid chromatography–tandem mass spectrometry

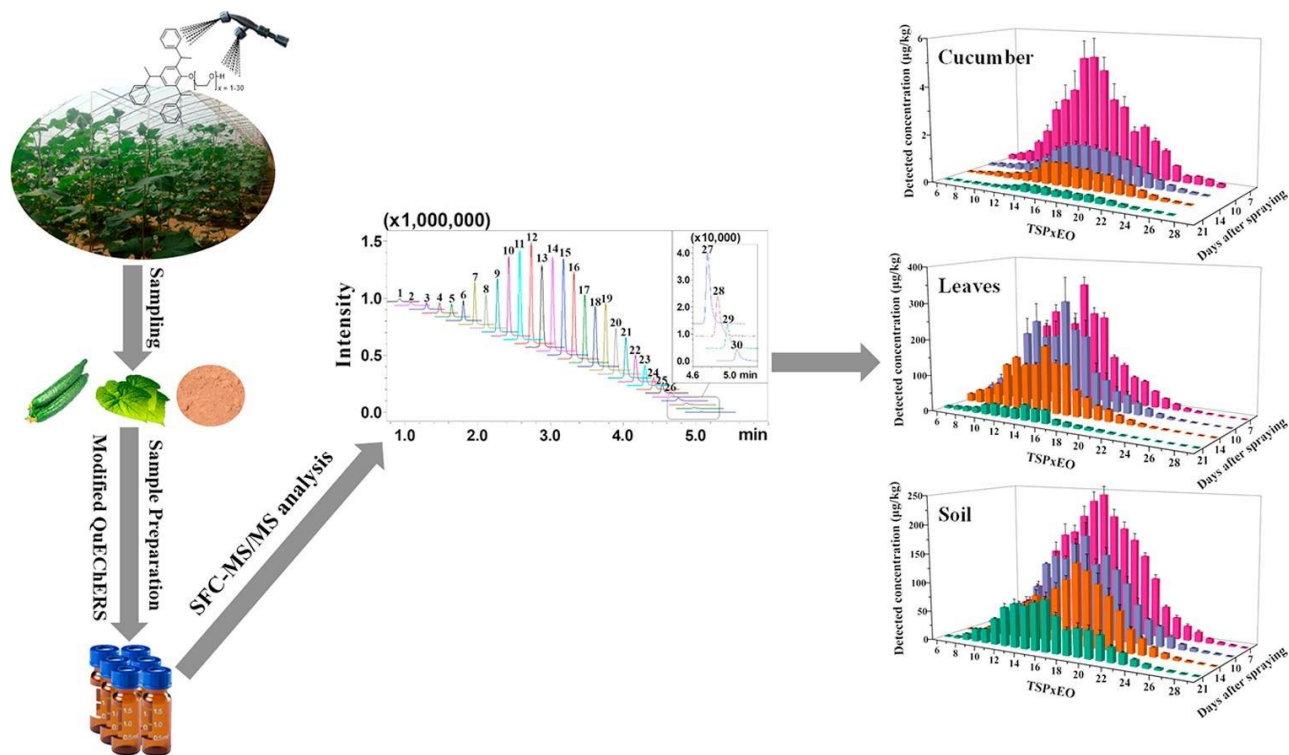
Zejun Jiang, Xiaolin Cao, Hui Li, Chan Zhang, A.M. Abd El-Aty, Ji Hoon Jeong, Yong Shao, Hua Shao, Maojun Jin, Fen Jin, Jing Wang

2018 - Food Chemistry

### Abstract

Tristyrylphenol ethoxylates (TSPxEOs), nonionic surfactant adjuvants, are widely used to replace alkylphenols in many agricultural formulations. Herein, a rapid and sensitive method based on a modified quick, easy, cheap, effective, rugged, and safe “QuEChERS” and supercritical fluid chromatography–tandem mass spectrometry (SFC–MS/MS) method was developed to quantify TSPxEOs in cucumber, leaves, and soil. Following optimization, the tested oligomers were fully separated within 8 min. The matrix-matched calibration standards showed satisfactory linearity with coefficients of determination ( $R^2$ )  $\geq 0.991$ . The limits of quantification (LOQs: 0.001–0.048  $\mu\text{g kg}^{-1}$ )

were excellent for TSPxEOs ( $x = 6-29$ ). The average recoveries at three (low, medium, and high) fortification levels were ranged between 62.5% and 112.9% with relative standard deviations (RSDs)  $\leq 20.0\%$  for TSPxEOs ( $x = 6-29$ ) in various matrices. The method was successfully applied to determine TSPxEOs residual levels in field-incurred samples. Conclusively, the developed method is versatile and could be used for monitoring TSPxEOs in food and environmental samples.



<https://doi.org/10.1016/j.foodchem.2018.05.122>

## 75. Systematic evaluation of matrix effects in supercritical fluid chromatography versus liquid chromatography coupled to mass spectrometry for biological samples

Vincent Desfontaine, Francesca Capetti, Raul Nicoli, Tiia Kuuranne, Jean-Luc Veuthey, Davy Guillarme

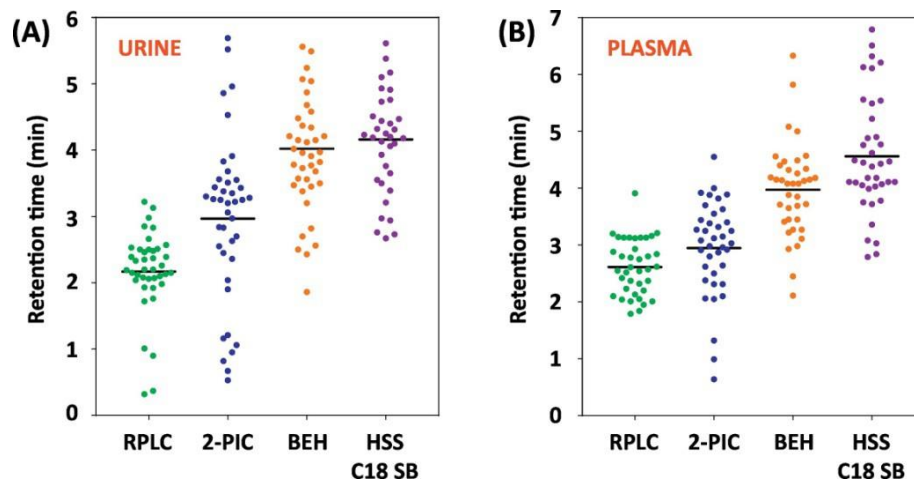
2018 – Journal of Chromatography

Keywords: Matrix effects, LC-MS, SFC-MS, Urine, Plasma

### Abstract

Matrix effects (ME) is acknowledged as being one of the major drawbacks of quantitative bioanalytical methods, involving the use of liquid chromatography coupled to mass spectrometry (LC-MS). In the present study, the incidence of ME in SFC-MS/MS and LC-MS/MS in the positive mode electrospray ionization (ESI+) was systematically compared for the analysis of urine and plasma samples using two representative sets of 40 doping agents and 38 pharmaceutical compounds, respectively. Three different SFC stationary phase chemistries were employed, to highlight the importance of the column in terms of selectivity. Biological samples were prepared using two different sample treatments, including a non-selective sample clean-up procedure (dilute and shoot (DS) and protein precipitation (PP) for urine and plasma samples, respectively) and a selective sample preparation, namely solid phase extraction (SPE) for both matrices. The lower susceptibility to ME in SFC vs. reversed phase LC (RPLC) was verified in all the experiments performed on urine, and especially when a simple DS procedure was applied. Also, with the latter, the performance strongly varied according to the selected SFC stationary phase, whereas the results were quite similar with the three SFC columns, in the case of SPE clean-up. The same

trend was observed with plasma samples. Indeed, with the PP procedure, the occurrence of ME was different on the three SFC columns, and only the 2-picolyamine stationary phase chemistry displayed lower incidence of ME compared to LC-MS/MS. On the contrary, when a SPE clean-up was carried out, the results were similar to the urine samples, with higher performance of SFC vs. LC and limited discrepancies between the three SFC columns. The type of ME observed in LC-MS/MS was generally a signal enhancement and an ion suppression for urine and plasma samples, respectively. In the case of SFC-MS/MS, the type of ME randomly varied according to the analyzed matrix, selected column and sample treatment.



<https://doi.org/10.1016/j.jchromb.2018.01.037>

## 76. Screening of stationary phase selectivities for global lipid profiling by ultrahigh performance supercritical fluid chromatography

Said Al Hamimi, Margareta Sandahl, Marina Armeni, Charlotta Turner, Peter Spéjel

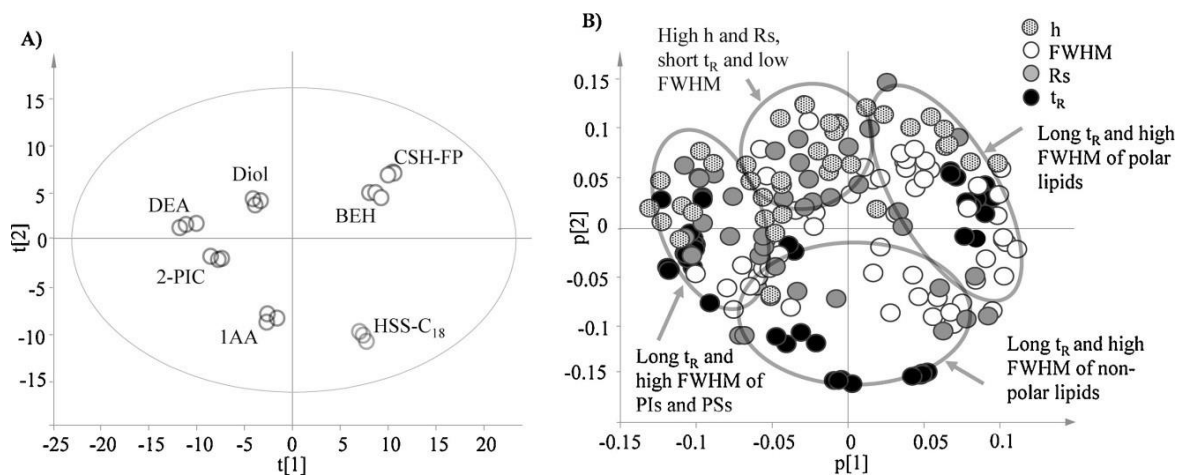
2018 – Journal of Chromatography A

Keywords: Mass spectrometry, Lipidomics, Design of experiments, Blood serum

**Abstract**



The performance of seven sub-2- $\mu\text{m}$  particle packed columns (2-picolylamine, 2-PIC; charged surface hybrid fluoro-phenyl, CSH-FP; high strength silica C18 SB, HSS-C<sub>18</sub>; diethylamine, DEA; 1-aminoanthracene, 1-AA; high density diol and ethylene bridged hybrid; BEH) was examined for lipid separation in ultra-high performance supercritical fluid chromatography (UHPSFC) coupled to quadrupole time-of-flight mass spectrometry. Based on the results of the column screening a method for profiling of multiple lipid species from the major lipid classes was developed. Stationary phases containing  $\beta$ -hydroxy amines, *i.e.* 1-AA, DEA and 2-PIC, yielded strong retention and poor peak shapes of zwitterionic lipids with primary amine groups, such as phosphatidylserines, phosphatidylethanolamines and its lyso forms. The BEH and HSS-C<sub>18</sub> columns showed strong retention of polar and nonpolar lipids, respectively. The Diol column retained the majority of major lipid classes and also produced symmetric peaks. In addition, this column also produced the highest resolution within and between major lipid classes. An injection solvent composed of methanol:chloroform (1:2, v:v) and the addition of 20 mM ammonium formate in the mobile phase improved chromatographic separation and mass spectrometry detection in comparison to ammonium acetate or absence of additive. Finally, chromatographic and mass spectrometric parameters were optimized for the Diol column using a design of experiments approach. The separation mechanism on the Diol column depended on the lipid functionality and the length and degree of unsaturation of the acyl groups. The developed method could resolve 18 lipid classes and multiple lipids within each class, from blood serum and brain tissue in 11 min.



<https://doi.org/10.1016/j.chroma.2018.03.024>

## 77. Forensic applications of supercritical fluid chromatography – mass spectrometry

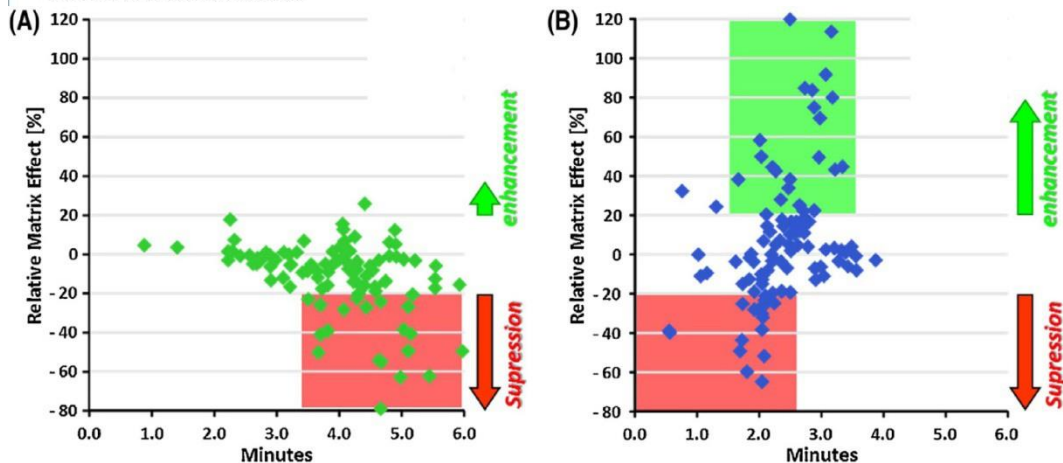
Volodymyr Pauk, Karel Lemr

2018 – Journal of Chromatography B

Keywords: Drug of abuse, New psychoactive substance, Doping control, Food authenticity, Adulteration

### Abstract

Achievements of supercritical fluid chromatography with mass spectrometric detection made in the field of forensic science during the last decade are reviewed. The main topics include analysis of traditional drugs of abuse (e.g. cannabis, methamphetamine) as well as new psychoactive substances (synthetic cannabinoids, cathinones and phenethylamines), doping agents (anabolic steroids, stimulants, diuretics, analgesics etc.) and chemical warfare agents. Control of food authenticity, detection of adulteration and identification of toxic substances in food are also pointed out. Main aspects of an analytical workflow, such as sample preparation, separation and detection are discussed. A special attention is paid to the performance characteristics and validation parameters of supercritical fluid chromatography-mass spectrometric methods in comparison with other separation techniques.



<https://doi.org/10.1016/j.jchromb.2018.04.015>

## 78. Comparison between liquid chromatography and supercritical fluid chromatography coupled to mass spectrometry for beta-agonists screening in feeding stuff

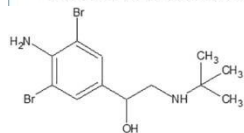
L. Herpin, E. Bichon, L. Rambaud, F. Monteau, B. Le Bizec

2018 – Journal of Chromatography B

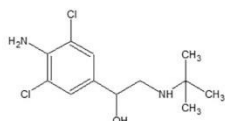
Keywords:  $\beta$ -agonists, UHPLC-MS/MS, SFC-MS/MS, Feeding stuff, Growth promoters monitoring

### Abstract

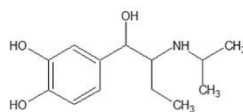
$\beta$ -agonistic drugs have been forbidden as growth promoters in rearing animals in Europe since the late 1980s (Dir 96/22/EC). Specific and sensitive analytical methods based on UHPLC-MS/MS allow to monitor a large set of these substances. However, optimal performances are not observed for all the target analytes, especially for those exhibiting the highest polarities. We developed an SFC-MS/MS approach to cover the huge elution window of  $\beta$ -agonists, from the most polar which are usually eluted in the void volume when using reversed phase chromatography in conventional HPLC to the most apolar ones. The objective was to reach performances in accordance with the European Union recommended level in feeding stuff, i.e.  $50 \mu\text{g kg}^{-1}$ . LC/MS and SFC/MS performances were thoroughly compared in terms of analytical validation data (linearity, selectivity, recovery rates, reproducibility, compounds identification, trueness, decision limit (CC $\alpha$ ) and detection capability (CC $\beta$ )) for 6  $\beta$ -agonistic drugs, namely brombuterol, clenbuterol, isoxsuprine, ractopamine, salbutamol and zilpaterol. As a result, the SFC approach appeared complementary to the LC one because the elution order of compounds was totally different from the one obtained with a classical C18 stationary phase. Moreover, the UPLC-MS/MS approach gave a better response linearity and more accurate values, whereas SFC-MS/MS provided greater data for identification purposes, reproducibility and sensitivity. Both analytical approaches enabled the detection of targeted  $\beta$ -agonists at a lower concentration than the recommended one ( $50 \mu\text{g kg}^{-1}$ ).



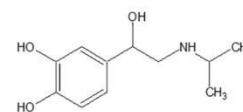
Bromobuterol



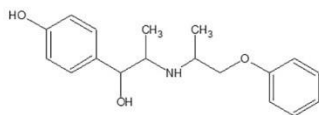
Clenbuterol



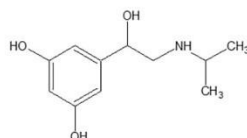
Isoetharine



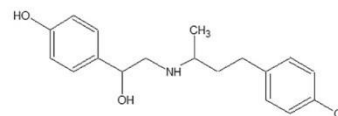
Isoproterenol



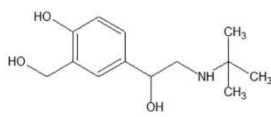
Isoxuprine



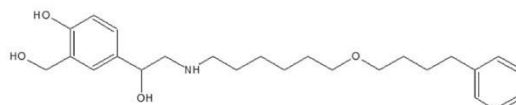
Metaproterenol



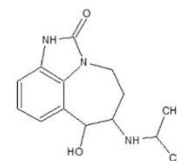
Ractopamine



Salbutamol



Salmeterol



Zilpaterol

<https://doi.org/10.1016/j.jchromb.2018.04.023>

## 79. Analysis of multiple vitamin D metabolites by ultra-performance supercritical fluid chromatography-tandem mass spectrometry (UPSFC-MS/MS)

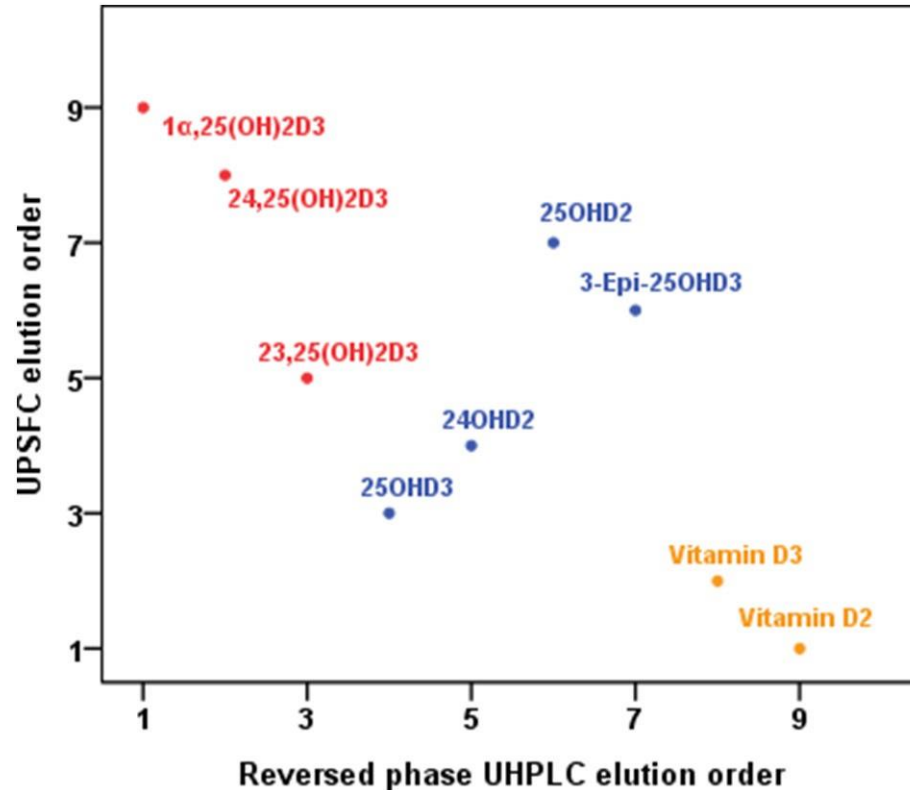
Carl Jenkinson, Angela Taylor, Karl-Heinz Storbeck, Martin Hewison

2018 – Journal of Chromatography B

Keywords: Vitamin D, UPSFC-MS/MS, Supercritical fluid chromatography-tandem mass spectrometry

### Abstract

In recent years, increased interest in the human health benefits of vitamin D has led to demand for improved analysis of patient vitamin D 'status'. Studies to date have focused primarily on a single vitamin D metabolite, 25-hydroxyvitamin D, despite the existence of a broad range of vitamin D metabolites, referred to as the vitamin D metabolome. This study reports on the development of a rapid UPSFC-MS/MS method for the analysis of nine vitamin D metabolites in human serum. Optimum separation was obtained with a Lux-Cellulose chiral column. We observed an orthogonal elution order when compared with ultra-high performance liquid chromatography (UHPLC). The order of elution was reversed based on hydroxyl- group number, however elution order did not differ between isomeric changes in hydroxyl- group position or epimers. Although UPSFC yielded superior resolution and selectivity over previously developed UHPLC-MS/MS methods, improvements in sensitivity could not be achieved owing to the lower injection volume required for UPSFC relative to UHPLC. Method validation was performed on the developed UPSFC-MS/MS method and found to be within acceptable limits. Applying the method to the analysis of human serum samples showed a significant correlation with serum concentrations of metabolites measured by UHPLC-MS/MS (25OHD3  $r = 0.997$ ,  $P < 0.001$ , and 3-epi-25OHD3  $r = 0.996$ ,  $P \leq 0.001$ ). These data indicate that UPSFC provides an efficient analytical platform for rapid analysis of multiple vitamin D metabolites from serum.



<https://doi.org/10.1016/j.ichromb.2018.04.025>

## 80. Novel and rare prenyllipids – Occurrence and biological activity

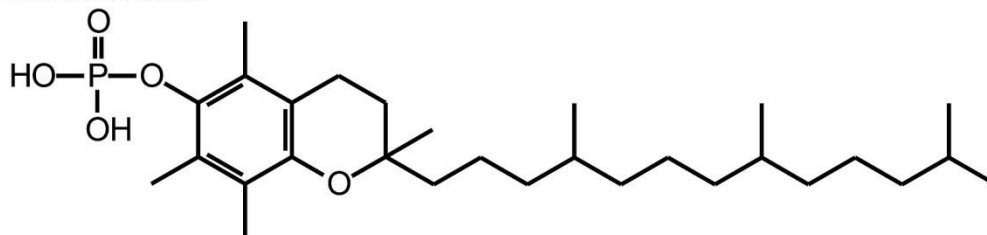
Renata Szymańska, Jerzy Kruk

2018 – Plant Physiology and Biochemistry

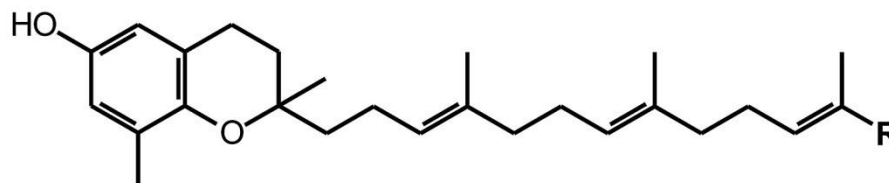
Keywords: Prenyllipids, Tocochromanols, Plastoquinones, Ubiquinones, Vitamin E, Antioxidants

### Abstract

The data presented indicate that there is a variety of unique prenyllipids, often of very limited taxonomic distribution, whose origin, biosynthesis, metabolism and biological function deserves to be elucidated. These compounds include tocoenols, tocochromanol esters, tocochromanol acids, plastoquinones and ubiquinones. Additionally, based on the available data, it can be assumed that there are still unrecognized prenyllipids, like prenylquinols fatty acid esters of the hydroquinone ring, including prenylquinol phosphates, and others, whose biological function might be of great importance. Our knowledge of these compounds is not only important from the scientific point of view, but may also be of practical significance to medicine, pharmacy or cosmetics.



$\alpha$ -tocopherol phosphate



Compound	R
$\delta$ -Tocotrienol	CH <sub>3</sub>
Garcinoic acid ( $\delta$ -Tocotrienolic acid)	COOH
Garcinal	CHO
$\delta$ -Tocotrienolic alcohol	CH <sub>2</sub> OH
$\delta$ -Tocotrienol methyl ester	COOCH <sub>3</sub>
$\delta$ -Tocotetraenol	(CH <sub>2</sub> ) <sub>2</sub> CH=C(CH <sub>3</sub> ) <sub>2</sub>

<https://doi.org/10.1016/j.plaphy.2017.11.008>

## 81. Continuous multicomponent quantification during supercritical fluid extraction applied to microalgae using in-line UV/Vis absorption spectroscopy and on-line evaporative light scattering detection

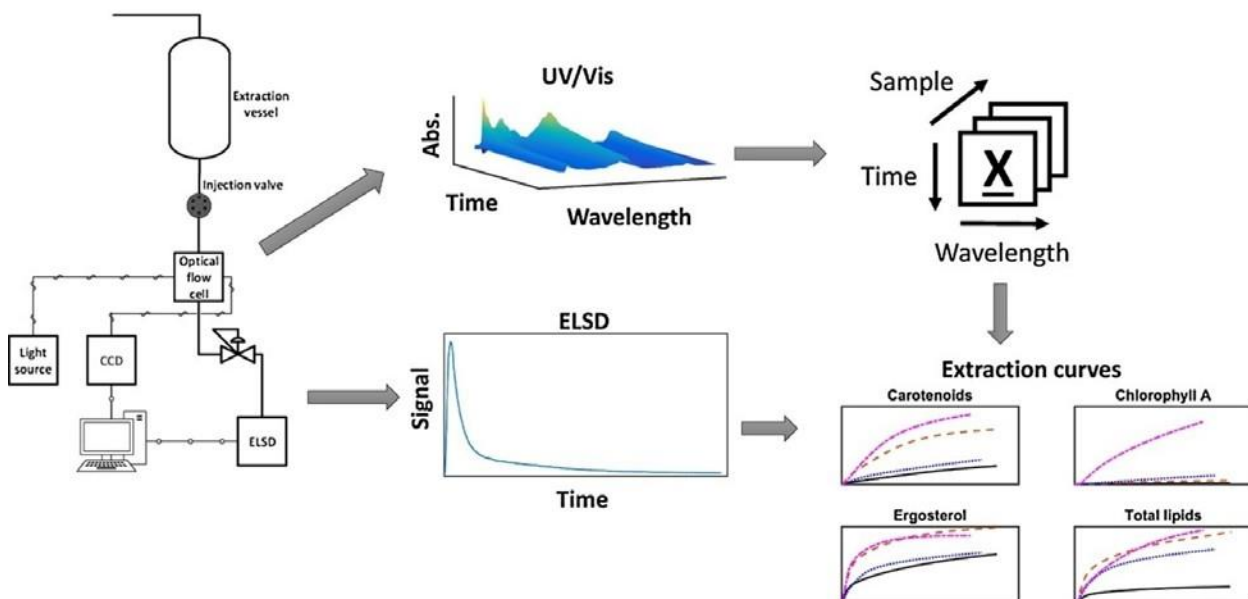
Victor Abrahamsson, Firas Jumaah, Charlotta Turner

2018 – The Journal of Supercritical Fluids

Keywords: Carotenoids, Chromatography, Microalgae, SFC, SFE, Analytical method

### Abstract

A quantitative methodology based on in-line UV/Vis absorption spectroscopy and on-line evaporative light scattering detection for supercritical fluid extraction is proposed. The method was applied to the extraction of carotenoids, chlorophyll A, ergosterol and total lipids from microalgae. One regression technique and two curve resolution techniques were applied on the absorption spectroscopy data and evaluated, namely classical least squares, multivariate curve resolution by alternating least squares and parallel factor analysis (PARAFAC2). The two former both generated useful models, furthermore multivariate curve resolution also successfully enabled estimation of both spectra and concentration profiles of the analytes. The integrated extraction profiles of each analyte were compared with analysis of the collected fractions using reference analysis methods. Precision, in regards to quantification of the analytes in the eluent, was better using in-line measurements compared to off-line measurements by UV/Vis absorption spectroscopy, supercritical fluid chromatography with mass spectrometry and liquid chromatography with UV/Vis detection.



<https://doi.org/10.1016/j.supflu.2017.09.014>

## 82. Interest of achiral-achiral tandem columns for impurity profiling of synthetic drugs with supercritical fluid chromatography

Caroline West, Ise Lemasson, Sophie Bertin, Philippe Hennig, Eric Lesellier

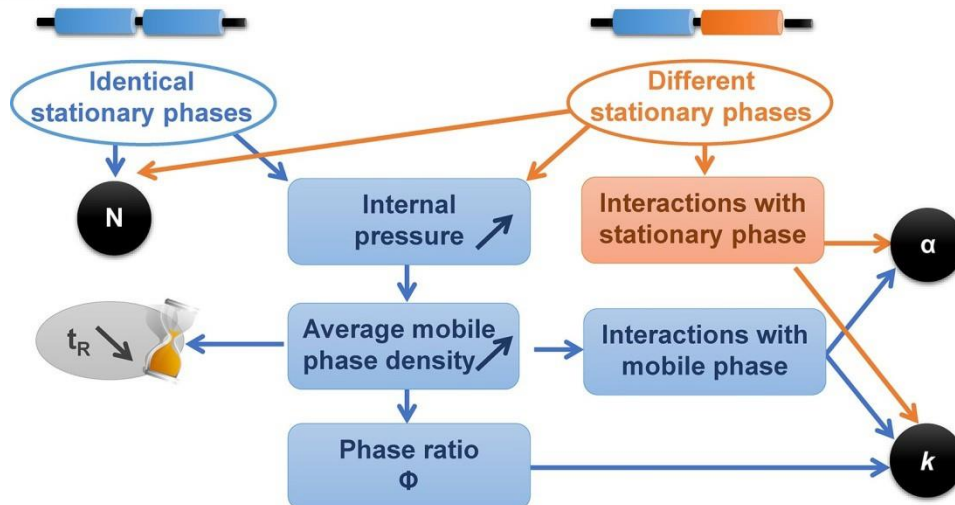
2018 – Journal of Chromatography A

Keywords: High-resolution separations, Impurity profiling, Orthogonal methods, Performance comparison, Pharmaceutical ingredients, Tandem columns

### Abstract

To achieve the most complete impurity profiling of synthetic drugs with a single chromatographic technique, high resolution is required, which may be gained with a combination of high efficiency and versatile selectivity, allowing to separate most similar analytes. Compared to a single-column chromatographic method, coupling complementary stationary phases promises both an increase in efficiency and an increase in selectivity possibilities. With supercritical fluid chromatography (SFC), the use of long columns is facilitated by the low viscosity of the mobile phase. In this paper, we investigate the interest of coupling two achiral stationary phases (Acquity UPC<sup>2</sup> HSS C18 SB and Nucleoshell HILIC) that were previously observed to have excellent complementarity in SFC to carry out impurity profiling on 25 individual drug substances containing varied numbers and amounts of impurities. The single-column gradient methods are compared to tandem-column gradient methods with the two possible ordering of columns (C18 phase in first or second position) based on selectivity, peak capacity, sensitivity, UV-estimated purity of the active pharmaceutical ingredient and number of impurities detected with UV-estimated concentration >0.04%. It appears that it could be more beneficial to have two columns coupled in a single analysis than two consecutive methods with the single columns. The overall analysis time are nearly the same, but with more informative chromatograms in about 35% cases.





<https://doi.org/10.1016/j.chroma.2017.12.061>

### 83. Inefficient UGT-conjugation of adrenal 11 $\beta$ -hydroxyandrostenedione metabolites highlights C11-oxy C<sub>19</sub> steroids as the predominant androgens in prostate cancer

Therina du Toit, Amanda C. Swart

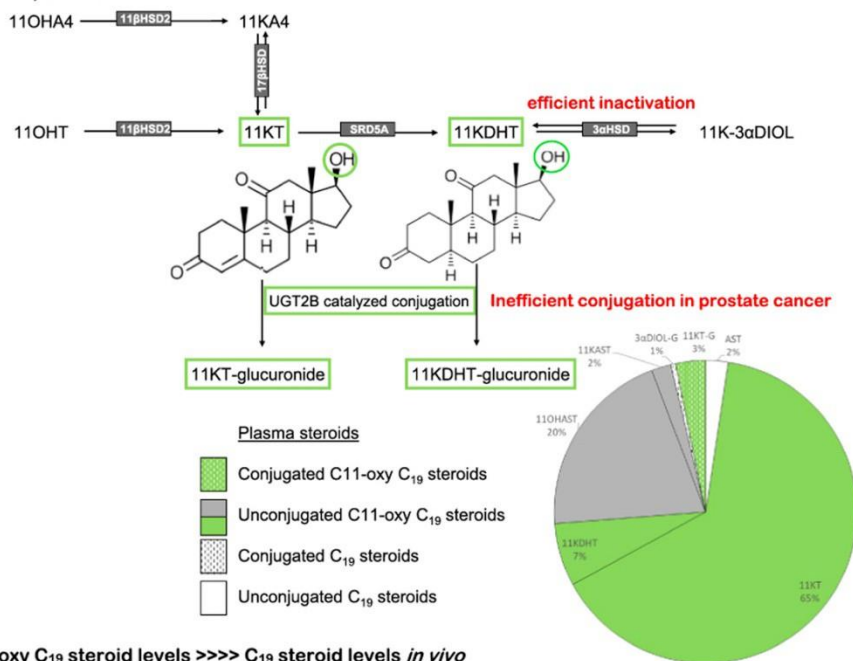
2018 – Molecular and Cellular Engineering

Keywords: 11keto-dihydrotestosterone (11KDHT) is readily inactivated *in vitro*; Dihydrotestosterone (DHT) is fully conjugated while 11KDHT remains unconjugated; C11-oxy C<sub>19</sub> steroid levels are significantly higher than C<sub>19</sub> steroid levels *in vivo*; Conjugated 11KDHT and 11ketotestosterone (11KT) levels are negligible in plasma; 11 $\beta$ HSD2 catalyses 11KDHT and 11KT biosynthesis in C4-2B and VCaP cells.

#### Abstract

Although the adrenal C<sub>19</sub> steroids, androstenedione and testosterone, contribute to prostate cancer (PCa) progression the full complement of adrenal androgens, including the C11-oxy C<sub>19</sub> steroids, 11 $\beta$ -hydroxyandrostenedione (11OHA4) and 11 $\beta$ -hydroxytestosterone (11OHT) and their androgenic metabolites, 11keto-testosterone (11KT) and 11keto-dihydrotestosterone (11KDHT) have, to date, not been considered. This study investigated the contribution of 11OHA4 and 11OHT to the pool of active androgens in the prostate. Steroid profiles were determined in LNCaP, C4-2B and VCaP cell models, in PCa tissue, and in plasma focussing on the inactivation, reactivation and glucuronidation of 11OHA4, 11OHT and their downstream products using ultra-performance convergence chromatography tandem mass spectrometry (UPC<sup>2</sup>-MS/MS). The C11-oxy C<sub>19</sub> steroids were the predominant steroids with the production of 11KT and 11KDHT in prostate cell models identifying 11 $\beta$ -hydroxysteroid dehydrogenase type 2 activity. Active:inactive steroid ratios indicated efficient inactivation of dihydrotestosterone (DHT) and 11KDHT by 3 $\alpha$ -hydroxysteroid dehydrogenases, while the reactivation of DHT by retinol-like dehydrogenases was greater than the reactivation of 11KDHT. In PCa tissue, inactive C11-oxy C<sub>19</sub> steroids ranged from 27 to 30 ng/g, whereas inactive C<sub>19</sub> steroids were below 1 ng/g. Steroid glucuronidation was impeded: in VCaP cells, the C11-oxy C<sub>19</sub> steroids were unconjugated and the C<sub>19</sub> steroids fully conjugated; in C4-2B cells, all steroids were unconjugated, except for DHT of which 50% was conjugated; in LNCaP cells only androsterone, 11KT and 11 $\beta$ -hydroxyandrosterone were unconjugated. In PCa patients' plasma 11KDHT was present only in the unconjugated form, with 11KT also predominantly unconjugated (90–95%). Even though plasma and tissue sample numbers were limited, this study serves to demonstrate the abundance of C11-oxy C<sub>19</sub> steroids, with notable differences in their metabolism, dictated by steroidogenic enzymes and hampered conjugation, affecting active androgen levels. Larger cohorts are required to analyse profiles in modulated metabolic pathways, in order to shed light on treatment outcomes. The C11-oxy C<sub>19</sub> steroids are involved in PCa, with impeded glucuronidation in PCa ascribing a dominant role to these steroids in disease progression.

In LNCaP, C4-2B and VCaP cells:



<https://doi.org/10.1016/j.mce.2017.09.026>

## 84. Ameliorating effects of D-47, a newly developed compound, on lipid metabolism in an animal model of familial hypercholesterolemia (WHHLMI rabbits)

Shohei Tamura, Yui Koike, Hiroaki Takeda, Tomonari Koike, Yoshihiro Izumi, Ryosuke Nagasaka, Tetsuto Tsunoda, Motoo Tori, Kazuo Ogawa, Takeshi Bamba, Masashi Shiomi

2018 – European Journal of Pharmacology

Keywords: Adipose tissue accumulation, Gene expression, D-47, Lipid-lowering effects, Lipidome analyses, Liver lipid contents

### Abstract

Improvements induced in lipid metabolism in the liver by D-47, a newly developed compound, were examined herein.

WHHLMI rabbits, an animal model of hypercholesterolemia and coronary atherosclerosis, was fed D-47-supplemented chow for 5 weeks at a dose of 30 mg/kg. Lipid concentration were assayed using enzymatic methods. Plasma lipoproteins were fractionated with an ultracentrifuge. mRNA expression was analyzed with real-time PCR. Lipidome analyses of lipoproteins were performed using supercritical fluid chromatography mass spectrometry. In the D-47-treated group, serum lipid levels decreased by 23% for total cholesterol and by 40% for triglycerides. These reductions were mainly attributed to decreases in the VLDL fraction. Compared with the control, in the D-47 group, lipid contents in the liver were decreased by 22% in cholesterol and by 69% in triglycerides, and fat accumulation was decreased by 57% in pericardial fat and by 17% in mesenteric fat. In lipidome analyses of VLDL fraction, lysophosphatidylcholine, phosphatidylcholine, phosphatidylethanolamine, phosphatidylinositol, phosphatidylethanolamine plasmalogen, sphingomyelin, and ceramide were decreased by the D-47 treatment. mRNA expression in the liver was 51% lower for FAS and 24% lower for MTP, but 5.9- and 5.1-fold higher for CYP7A1 and CPT-1, respectively, in the D-47 group than in the control. mRNA expression was 72%, 64%, and 36% higher for LPL, CTP-1, and PPAR $\gamma$ , respectively, in mesenteric fat in the D-47 group.

D-47 is a potent lipid-lowering compound that uses a different mechanism of action from that of statins. It has potential as a compound in the treatment of steatohepatitis and metabolic syndrome.

<https://doi.org/10.1016/j.ejphar.2018.01.013>

## 85. Supercritical fluid chromatographic-tandem mass spectrometry method for monitoring dissipation of thiacloprid in greenhouse vegetables and soil under different application modes

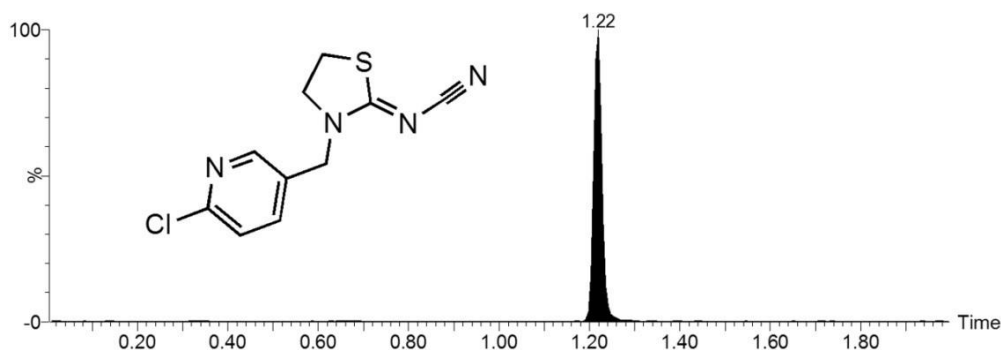
Runan Li, Zenglong Chen, Fengshou Dong, Jun Xu, Xingang Liu, Xiaohu Wu, Xinglu Pan, Yan Tao, Yongquan Zheng

2018 – Journal of Chromatography B

Keywords: Thiacloprid, Greenhouse vegetables, Application modes, Degradation rates, SFC-MS/MS

### Abstract

A rapid, sensitive and effective supercritical fluid chromatographic-tandem mass spectrometry (SFC-MS/MS) method was developed to analyze thiacloprid for the first time. The SFC-MS/MS conditions were optimized with the ultra-performance convergence chromatography (UPC<sup>2</sup>) BEH column (100 mm × 3.0 mm, 1.7 μm particle size) and thiacloprid was eluted at 1.22 min in gradient mode with CO<sub>2</sub>/methanol as mobile phase. The 0.1% formic acid in methanol (v/v) was used as postcolumn compensation solution to improve sensitivity. The ABPR pressure, flow rate of mobile phase and flow rate of compensation pump were set at 1800 psi, 1.8 mL/min, and 0.1 mL/min, respectively. The average recoveries of thiacloprid in soil at four spiking levels (5, 10, 100, 1000 μg/kg) ranged between 78.8% and 107.1% with relative standard deviations (RSDs) lower than 12.2% and the limit of quantitation (LOQ) was 5 μg/kg. The proposed method can distinctly improve the analysis efficiency by 2–12 times and reduce the solvent consumption by 5%–95% compared with reported methods. It was applied to investigate the dissipation rates of thiacloprid in greenhouse vegetables and soil under different application modes. The half-lives of thiacloprid in cucumber and soil were 9.55–20.44 days and 3.74–9.14 days separately under different application modes, 10.60 days in tomato under foliar spraying. The residues in vegetables under root irrigation were all less than that under foliar spraying. The results could offer useful data for risk assessment of thiacloprid in agricultural production.



<https://doi.org/10.1016/j.jchromb.2018.02.021>

## 86. Analytical challenges to determine emerging persistent organic pollutants in aquatic ecosystems

María Lorenzo, Julián Campo, Yolanda Picóac

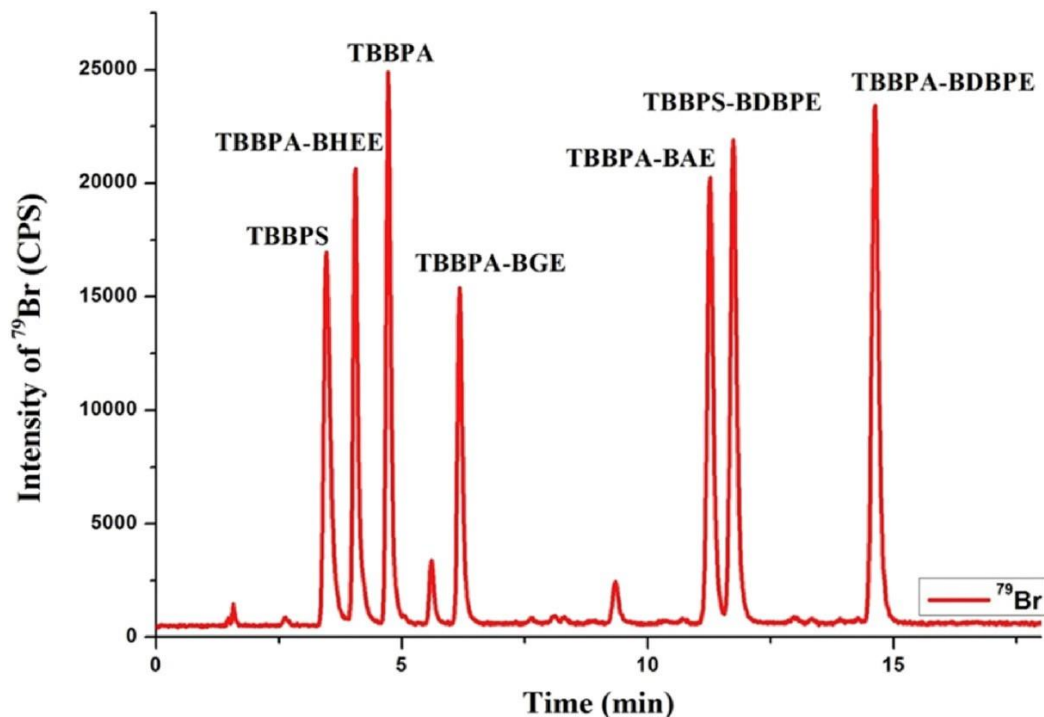
2018 – TrAC Trends in Analytical Chemistry

Keywords: Emerging persistent organic pollutants, Perfluoroalkyl substances, Novel brominated flame retardants, Organophosphorus flame retardants, Aquatic ecosystem, Sample treatment Extraction, Analytical determination

### Abstract

Emerging persistent organic pollutants (ePOPs) include polybrominated biphenyl (PBDEs) and perfluorooctane sulfonyl fluoride/perfluorooctane sulfonate (POSF/PFOS), which are newly listed in the Stockholm Convention. Other ePOPs, which have not been regulated, include organophosphate flame retardants (PFRs), novel brominated flame retardants (NBFRs) and other perfluoroalkyl substances (PFASs). Often ePOPs data related to occurrence, toxicity, impact or environmental behavior are insufficient or inadequate because of the lack of proper analytical methods to obtain them. Thus, a critical review of the analytical procedures proposed in the last six years (2011–2017) for determining ePOPs by chromatographic methods in the different compartments of the aquatic

ecosystems is presented. The overall analytical procedure, from sampling to final determination, is emphasized presenting recent developments in the extraction, pre-concentration, and instrumental detection needed for the accurate quantification of ePOPs in environmental samples. Finally, this review examines the basic challenges we face in order to anticipate future directions and urgent needs of this field.



<https://doi.org/10.1016/j.trac.2018.04.003>

## 87. Milk lipidomics: What we know and what we don't

Zhiqian Liu, Simone Rochfort, Ben Cocks

2018 – Progress in Lipid Research

Keywords: Milk, Lipidomics, Gas chromatography, Liquid chromatography, Mass spectrometry

### Abstract

Bovine milk contains 3–5% of fat, of which the dominant portion (about 98%) is in the form of triacylglycerols, whereas polar lipids such as glycerophospholipids and sphingolipids are minor components (0.5–1%) of milk fat. Milk fat is thought to contain several thousand lipid species, making it the most complex material in nature in terms of lipid composition. Significant progress has been made in the past two decades in the identification and quantification of lipid species of milk thanks to the advance in analytical tools especially high-resolution mass spectrometers (MS). Currently, milk lipids are characterized mainly in two ways, *i.e.* global fatty acid composition profiling by gas chromatography and lipid molecular species identification and quantification by liquid chromatography tandem MS; the former provides information related to the physicochemical properties and nutritive quality of milk fat, whereas the latter provides the detailed chemical structure of lipid species. Until now, only about 400 lipid species have been described in bovine milk, with many low-abundance species remaining to be discovered. The merits and limitations of various separation techniques and different MS methodologies applied to lipid structural elucidation and quantification are critically reviewed and the challenging problems to be solved in milk lipidomic analysis highlighted.

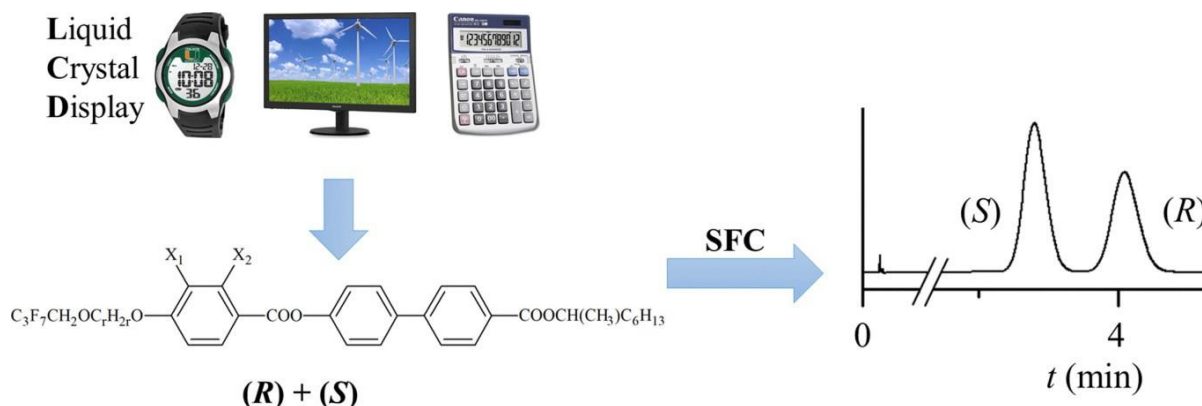
<https://doi.org/10.1016/j.plipres.2018.06.002>

## 88. Ultra-performance supercritical fluid chromatography: A powerful tool for the enantioseparation of thermotropic fluorinated liquid crystals

Keywords: Supercritical fluid chromatography, Enantioseparation, Liquid crystalline materials, Chiral fluorinated liquid crystals, Amylose

### Abstract

A fast and simple supercritical fluid chromatography method for the enantioseparation of twenty newly synthesized orthoconic antiferro electric liquid crystals is reported for the first time. The effects of alkoxy spacer length and fluorine atom presence and position in the phenyl ring on chromatographic behavior were investigated. Baseline enantioseparation of all compounds was achieved using simple mobile phases consisting of carbon dioxide and alcohol as cosolvent on (3,5-dimethylphenylcarbamate) derivative of amylose as chiral stationary phase. The analysis times ranged from 2 to 4 and from 4 to 7 min for most samples when using methanol and propane-2-ol, respectively. The significant effect of cosolvent type on the enantioseparation of these compounds was assessed and partial complementarity of methanol and propane-2-ol was observed.



<https://doi.org/10.1016/j.aca.2018.07.001>

## 89. Dedicated comparisons of diverse polysaccharide- and zwitterionic *Cinchona* alkaloid-based chiral stationary phases probed with basic and ampholytic indole analogs in liquid and subcritical fluid chromatography mode

Attila Bajtai, Gyula Lajkó, IstvánSzatmári, Ferenc Fülöp, Wolfgang Lindner, István Ilisz, Antal Pétera

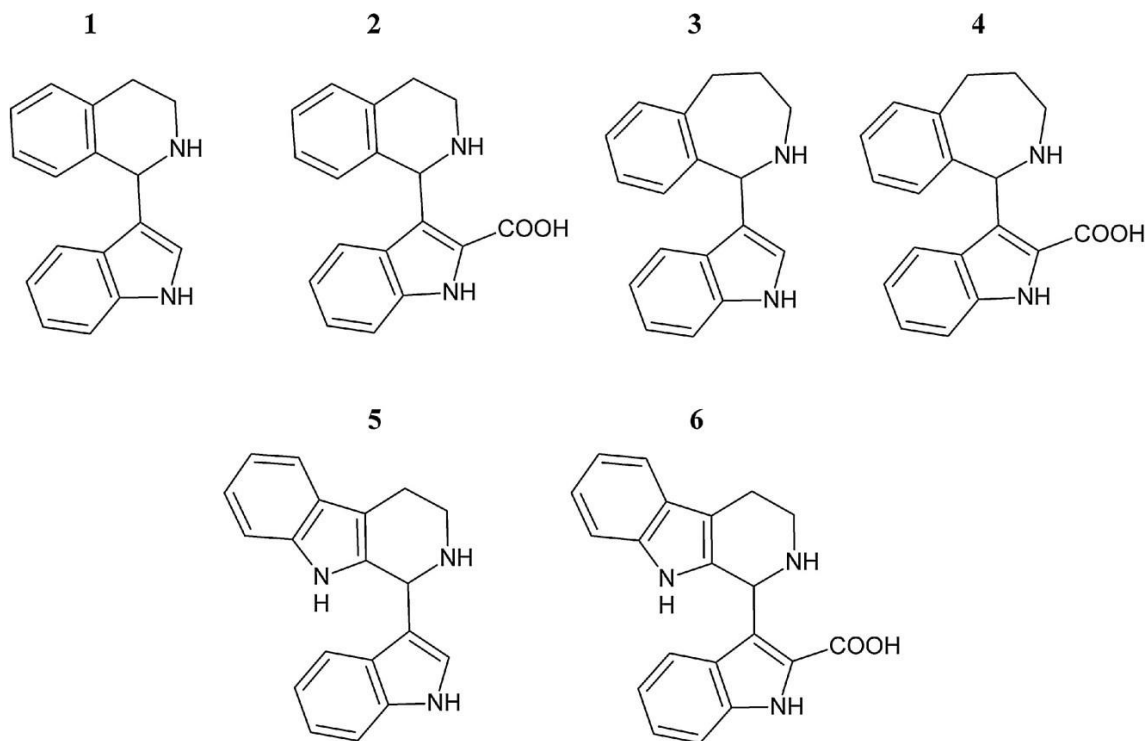
2018 – Journal of Chromatography A

Keywords: Enantiomer separation, Zwitterionic chiral stationary phases, Polysaccharide-based columns, Indole analogs, Comparative study

### Abstract

Normal phase (NP) high-performance liquid and sub- and supercritical fluid chromatographic (both acronymed as SFC) methods have been developed for the enantiomer separation of three basic and three ampholytic structurally related C-3-substituted indole analogs on seven non-ionic (neutral) polysaccharide-based and two chemically entirely different zwitterionic *Cinchona* alkaloid- and sulfonic acid-based chiral stationary phases (CSPs). In a systematic fashion the effect of the composition of the mobile phase, the nature of the alcohol and amine additives on the retention characteristics and enantioselectivity of the ionizable analytes were investigated. On all studied polysaccharide-based CSPs the three ampholytes remained unretained in NP-LC mode, while they were nicely retained and resolved in SFC mode. These unexpected results underline a specific property of liquid CO<sub>2</sub> as bulk solvent in combination with alcohols as co-solvents and amine additives thus creating an environment around the chiral selector sites which support the retention of ampholytes. The zwitterionic CSPs worked equally well for the resolution of the basic and ampholytic analytes using a polar ionic mobile phase in both LC and SFC modes. Results acquired by studying the effect of temperature were used to calculate the changes in standard enthalpy  $\Delta(\Delta H^\circ)$ , entropy  $\Delta(\Delta S^\circ)$ , and free energy  $\Delta(\Delta G^\circ)$  applying van't Hoff plots. The

values of the thermodynamic parameters depended on the nature of selectors, the structure of analytes and the properties of the mobile phases. On polysaccharide-based CSPs and columns operated in NP-LC mode enthalpically-, whereas in SFC mode both enthalpically- and entropically-driven enantiomer separations were observed.



<https://doi.org/10.1016/j.chroma.2018.05.064>

## 90. High-fast enantioselective determination of prothioconazole in different matrices by supercritical fluid chromatography and vibrational circular dichroism spectroscopic study

Ying Jiang, Jun Fan, Rujian He, Dong Guo, Tai Wang, Hui Zhang, Weiguang Zhang

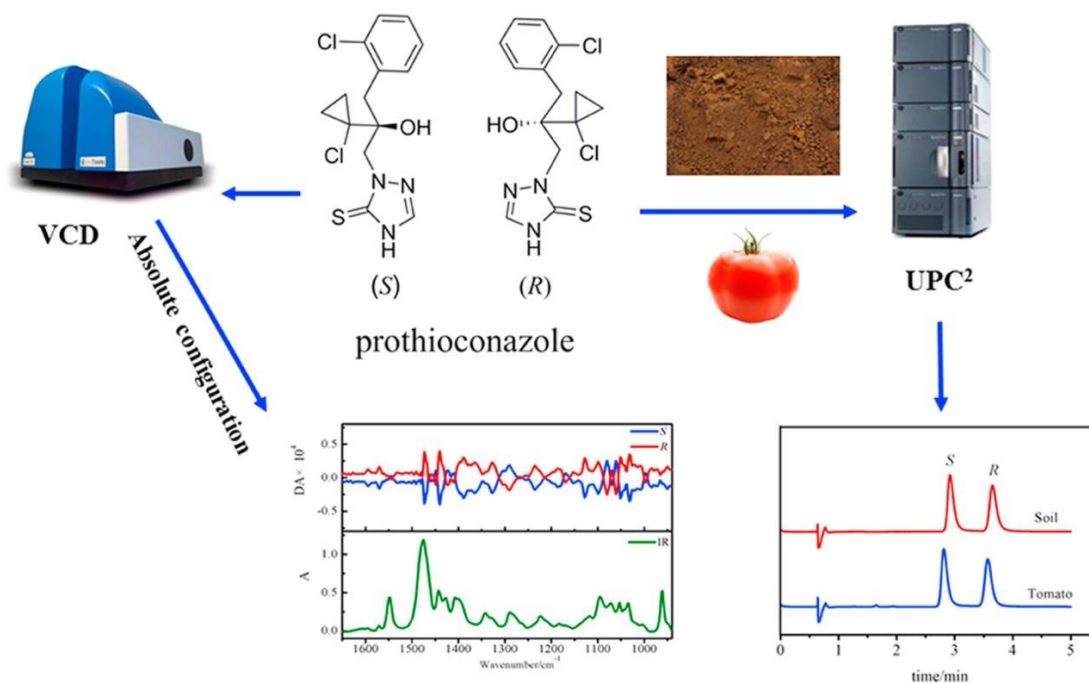
2018- Tanta

**Keywords:** Prothioconazole, Supercritical fluid chromatography, Stereoselective quantification, Vibrational circular dichroism spectroscopy, Absolute configuration; Fast separation and quantification for prothioconazole enantiomers by SFC; Absolute configurations of two enantiomers were confirmed through VCD spectroscopy; Enantioselective determination of prothioconazole in two matrices; Analysis time through SFC was five-fold shorter than traditional HPLC.

### Abstract

Herein, we developed a rapid supercritical fluid chromatography (SFC) method for chiral separation and enantioselective determination of prothioconazole in soil and tomatoes. The potential effects of chiral stationary phases, co-solvents, column temperature, and back pressure on enantioseparation of prothioconazole have been studied in detail. Two prothioconazole enantiomers were best separated on cellulose tris(3, 5- dimethylphenylcarbamate)-coated chiral stationary phase with CO<sub>2</sub>-2-propanol (80:20, v/v) as the mobile phase, and the run time through SFC (about 4 min) was five-fold shorter than HPLC. Then, through comparing the experimental vibrational circular dichroism spectrum of the later-eluted component with the calculated pattern based on the (*R*)-configuration, it should be (*R*)-(-)- prothioconazole. Moreover, the modified QuEChERS (quick, easy, cheap, effective, rugged and safe) extraction and cleanup procedures were applied in enantiomeric analysis of prothioconazole in two matrices. Good linearity ( $R^2 \geq 0.9992$ ) and recoveries (91.84–101.66%, RSD  $\leq 3.98\%$ ) for two enantiomers were achieved. This proposed method showed good accuracy and precision, and might be suitable for fast enantioselective determination and residual quantitative analysis of prothioconazole in food and environmental samples.





<https://doi.org/10.1016/j.talanta.2018.04.097>

## 91. C11-oxy C<sub>19</sub> and C11-oxy C<sub>21</sub> steroids in neonates: UPC<sup>2</sup>-MS/MS quantification of plasma 11 $\beta$ -hydroxyandrostenedione, 11-ketotestosterone and 11-ketoprogesterone

Therina du Toit<sup>a</sup>, Martijn J.J. Finken, Henrike M. Hamer, Annemieke C. Heijboer, Amanda C Swart

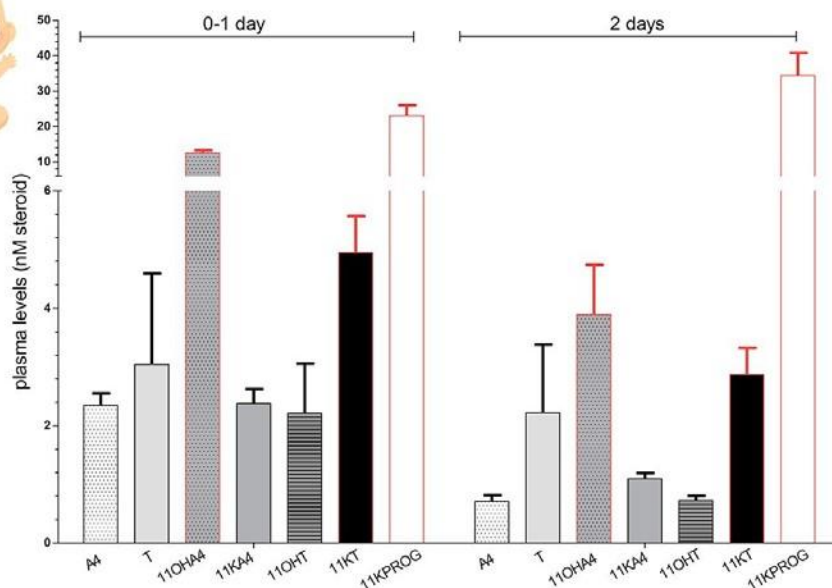
2018 – Steroids

Keywords: Disorders of sexual development (DSD), Congenital adrenal hyperplasia (CAH), 11keto-dihydrotestosterone (11KDHT), Congenital hypogonadotropic hypogonadism (CHH), Newborn care 11 $\beta$ -hydroxysteroid dehydrogenase (11 $\beta$ HSD)

### Abstract

The purpose of this study was to identify the C11-oxy C<sub>19</sub> and C11-oxy C<sub>21</sub>steroids in male and female neonate plasma. At birth, the most abundant C11-oxy steroids detected in neonatal plasma were 11 $\beta$ -hydroxyandrostenedione, ~13 nM, and 11-ketoprogesterone, ~23 nM. C11-oxy C<sub>19</sub> steroids were higher than C<sub>19</sub> steroids in neonatal plasma, 22.2 nM vs 5.4 nM. The inclusion of C11-oxy C<sub>19</sub> and C<sub>21</sub> steroid reference ranges in routine steroid analyses will assist the characterization of disorders associated with impaired steroidogenic enzyme expression and the identification of potential biomarkers.

**UPC<sup>2</sup>-MS/MS analyses of C<sub>19</sub> steroids, C<sub>11</sub>-oxy C<sub>19</sub> steroids  
 and C<sub>11</sub>-oxy C<sub>21</sub> steroids in neonates**



<https://doi.org/10.1016/j.steroids.2018.06.003>

## 92. Supercritical fluid chromatography coupled to mass spectrometry – A metabolomics perspective

Vladimir Shulaev, Giorgis Isaac

2018 – Journal of Chromatography B

Keywords: Supercritical fluid chromatography, Mass spectrometry, Metabolomics, Metabolite profiling, SFC-MS, HPSFC-MS, UPC<sup>2</sup>-MS

### Abstract

Metabolomics as a global analysis of a large number of cellular metabolites relies heavily on the new developments in separation science and technology. None of the existing analytical techniques can simultaneously separate and measure all the cellular metabolites due to complexity of cellular metabolome and, therefore, a combination of analytical techniques must be used. Currently NMR, GC-MS and LC-MS are most often used in metabolomics. Novel separation methods such as supercritical fluid chromatography (SFC), which can increase metabolome coverage while decreasing cost and analysis time, can provide alternative to other analytical techniques. As a result of major improvements in instrumentation and development of a new diverse column chemistries SFC-MS is increasingly used in a variety of biomedical applications and is becoming an attractive complement to other major analytical platforms in metabolomics. Despite its potential and advantages, SFC-MS application in metabolomics is limited. Here we provide a brief overview of the latest developments of SFC-MS for metabolomics applications.

<https://doi.org/10.1016/j.ichromb.2018.06.021>

## 93. Methods in endogenous steroid profiling – A comparison of gas chromatography mass spectrometry (GC-MS) with supercritical fluid chromatography tandem mass spectrometry (SFC-MS/MS)

Julian Teubel, Bernhard Wüst, Carola G. Schipke, Oliver Peters, Maria Kristina Parr

2018 – Journal of Chromatography A

Keywords: Successful separation of steroid isomers by SFC-ESI-MS/MS; Determination of 51 endogenous steroids and sulphates by SFC-ESI-MS/MS; Method development for determination of

neurosteroids in cerebrospinal fluid; Method comparison of SFC-ESI-MS/MS and GC-EI-MS for steroid profiling; Intact steroid sulfate determination by SFC-MS/MS

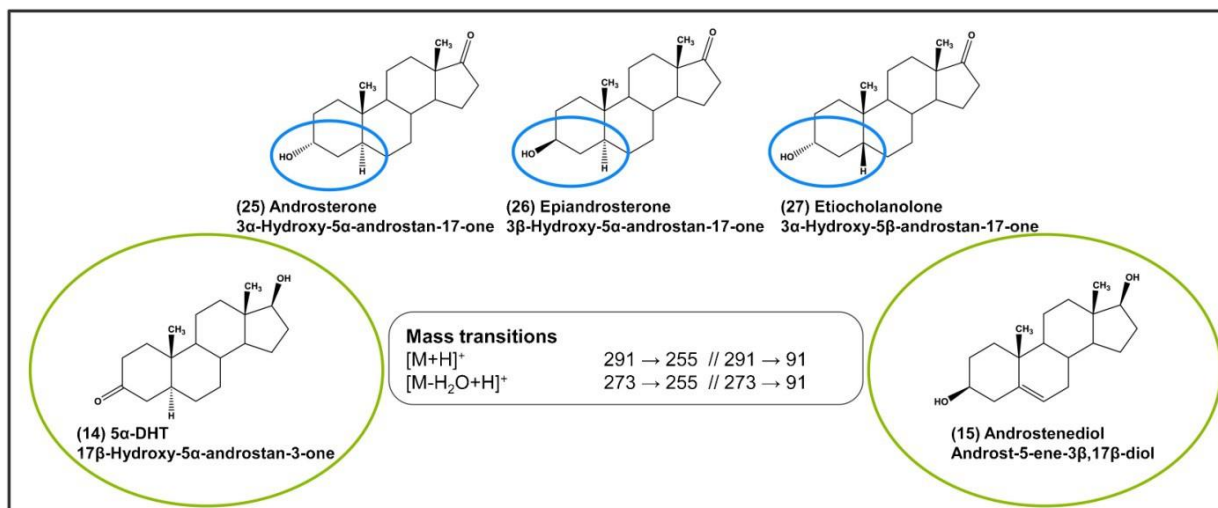
### Abstract

In various fields of endocrinology, the determination of steroid hormones synthesised by the human body plays an important role. Research on central neurosteroids has been intensified within the last years, as they are discussed as biomarkers for various cognitive disorders. Their concentrations in cerebrospinal fluid (CSF) are considered to be regulated independently from peripheral fluids. For that reason, the challenging matrix CSF becomes a very interesting specimen for analysis. Concentrations are expected to be very low and available amount of CSF is limited. Thus, a comprehensive method for very sensitive quantification of a set of analytes as large as possible in one analytical aliquot is desired.

However, high structural similarities of the selected panel of 51 steroids and steroid sulfates, including numerous isomers, challenges achievement of chromatographic selectivity.

Since decades the analysis of endogenous steroids in various body fluids is mainly performed by gas chromatography (GC) coupled to (tandem) mass spectrometry (MS(/MS)). Due to the structure of the steroids of interest, derivatisation is performed to meet the analytical requirements for GC-MS(/MS). Most of the laboratories use a two-step derivatisation in multi-analyte assays that was already published in the 1980s. However, for some steroids this elaborate procedure yields multiple isomeric derivatives. Thus, some laboratories utilize (ultra) high performance liquid chromatography ((U)HPLC)-MS/MS as alternative but, even UHPLC is not able to separate some of the isomeric pairs. Supercritical fluid chromatography (SFC) as an orthogonal separation technique to GC and (U)HPLC may help to overcome these issues.

Within this project the two most promising methods for endogenous steroid profiling were investigated and compared: the "gold standard" GC-MS and the orthogonal separation technique SFC-MS/MS. Different derivatisation procedures for gas chromatographic detection were explored and the formation of multiple derivatives described and confirmed. Taken together, none of the investigated derivatisation procedures provided acceptable results for further method development to meet the requirements of this project. SFC with its unique selectivity was able to overcome these issues and to distinguish all selected steroids, including (pro-)gestagens, androgens, corticoids, estrogens, and steroid sulfates with appropriate selectivity. Valued especially in the separation of enantiomeric analytes, SFC has shown its potential as alternative to GC. The successful separation of 51 steroids and steroid sulfates on different columns is presented to demonstrate the potential of SFC in endogenous steroid profiling.



<https://doi.org/10.1016/j.chroma.2018.04.035>

## 94. Development of an analytical method for separation of phenolic acids by ultra- performance convergence chromatography (UPC<sup>2</sup>) using a column packed with a sub-2- $\mu$ m particle

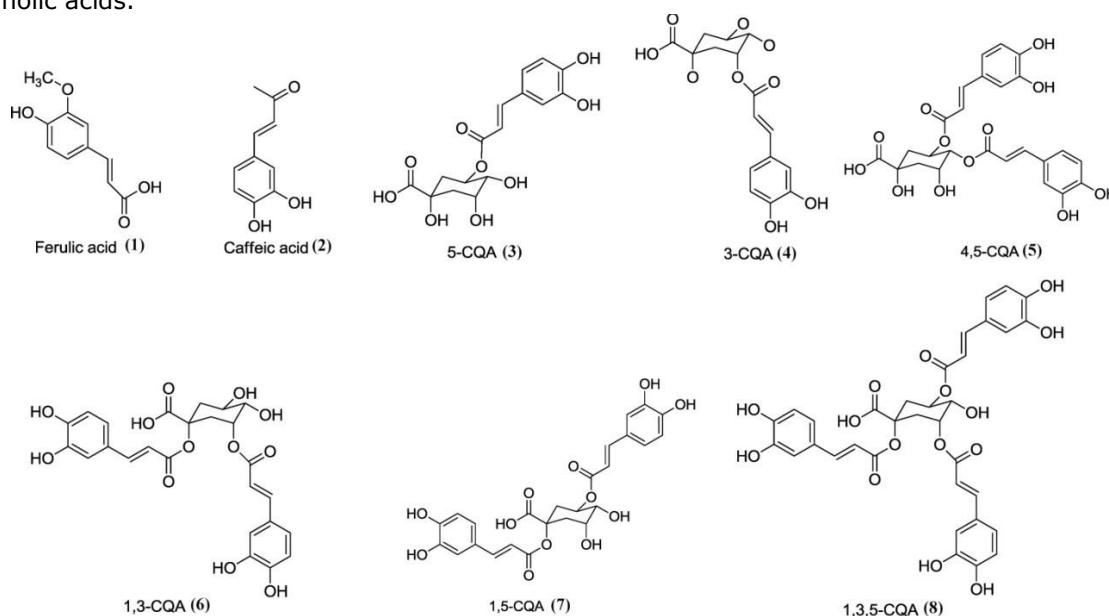
Hai Jiang, Liu Yang, Xudong Xing, Meiling Yan, Xinyue Guo, Bingyou Yang, Qiu-Hong Wang, Hai- Xue Kuanga

Keywords: A method for the analysis of phenolic acids by ultra-performance convergence chromatography is firstly proposed; The developed method was subsequently applied to the determination of eight phenolic acids in 10 batch of Xanthii Fructus by ultra-performance convergence chromatography; The newly method is beneficial for quality control and

standardization of herbal drugs using UPC<sup>2</sup>, providing an efficient, rapid and environmentally friendly scientific basis for future analysis of phenolic acids in TCM.

#### Abstract

Phenolic acids are important active components of certain Traditional Chinese Medicines (TCM) and have a wide range of biological effects. Separation and purification of phenolic acids remains challenging due to difficulties with quality control using existing chromatographic methods. The purpose of this study was to compare the effects of different chromatographic columns and conditions for the separation of phenolic acids. The BEH column was determined to be optimal, providing efficient separation in the shortest time (17.00 min) using gradient elution with carbon dioxide as the mobile phase, methanol/acetonitrile (70:30, v/v) with 1% TFA as the modifier, and a flow rate of 0.8 mL/min. Good peak shapes were obtained, and the peak asymmetry values were close to 1.00 for all phenolic acids. The resolution was more than 2.83 for all separated peaks. The developed method was subsequently applied to the determination of phenolic acids in *Xanthii Fructus*. These results are beneficial for quality control and standardization of herbal drugs using UPC<sup>2</sup>, providing an efficient, rapid and environmentally friendly scientific basis for future analysis of phenolic acids.



<https://doi.org/10.1016/j.jpba.2018.02.027>

## 95. A high-throughput UPC<sup>2</sup>-MS/MS method for the separation and quantification of C<sub>19</sub> and C<sub>21</sub> steroids and their C<sub>11</sub>-oxy steroid metabolites in the classical, alternative, backdoor and 11OHA4 steroid pathways

Therina du Toit, Maria A. Stander, Amanda C. Swart

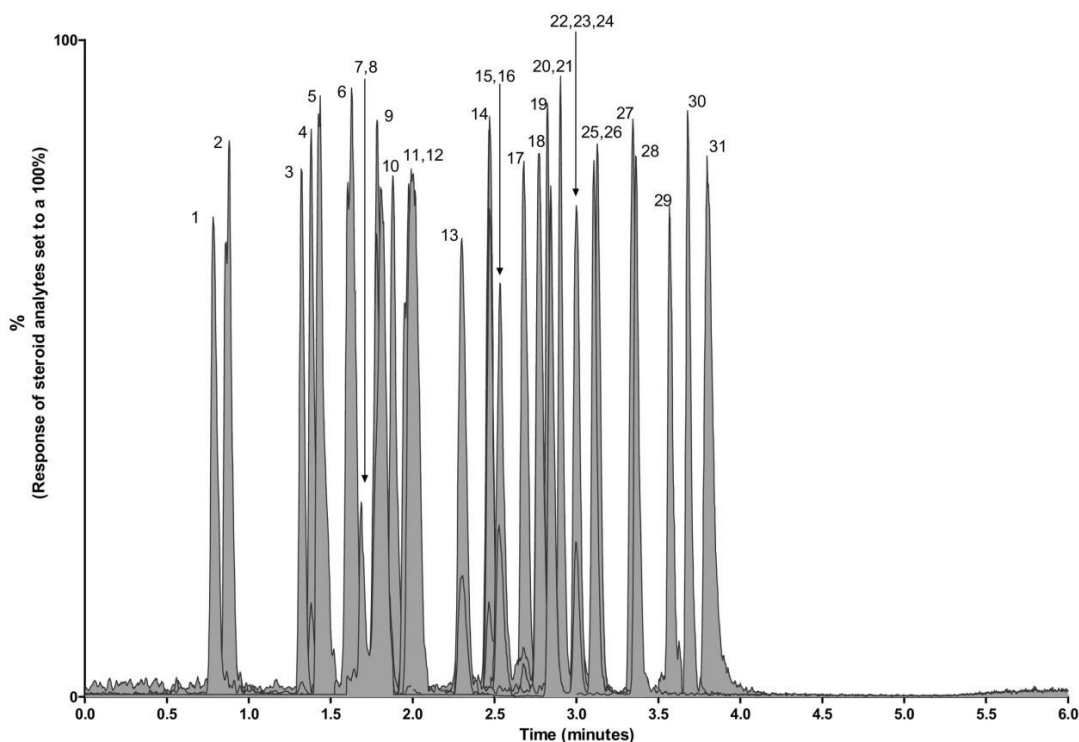
2018 – Journal of Chromatography B

Keywords: UPC<sup>2</sup>-MS/MS quantifies C<sub>19</sub> and C<sub>21</sub> steroids – including hydroxyl and keto steroids, UPC<sup>2</sup> separates 28 steroids in a serum matrix in a single 6 min chromatographic step, Sensitivity of the method: LOQs ranging from 0.01 to 20 ng/mL, Selectivity of the method separates stereoisomers and regioisomers.

#### Abstract

In the present study an ultra-performance convergence chromatography tandem mass spectrometry (UPC<sup>2</sup>-MS/MS) analytical method was developed and validated for the determination of 17 C<sub>19</sub> and 14 C<sub>21</sub> steroids, including C<sub>11</sub>-oxy C<sub>19</sub> and C<sub>11</sub>-oxy C<sub>21</sub> steroids. The limit of detection and limit of quantification ranged from 0.01 to 10 ng/mL and from 0.01 to 20 ng/mL, respectively, and the method shows the recovery, matrix effect and process efficiency of steroids isolated from a serum matrix to be within acceptable limits. Good accuracy, repeatability and

reproducibility were also shown and the method provided excellent sensitivity and selectivity as stereoisomers and regioisomers were also resolved and quantified accurately. Clinical conditions such as congenital adrenal hyperplasia, polycystic ovary syndrome in females and disorders of sex development in neonates and in children, amongst others, are characterized by abnormal steroid levels. Steroid profiling is essential to accurately diagnose steroid levels in the above settings as well as in androgen excess or deficiency in adrenal-linked endocrine diseases. Our method, separating C<sub>19</sub> and C<sub>21</sub> steroids in a single chromatographic step, offers a reduced sample turnover rate in the clinical setting, while providing comprehensive steroid profiles of *in vivo* steroids in the nmol/L range. This is, to our knowledge, the first method reported to simultaneously separate C<sub>19</sub> and C<sub>21</sub> steroids, together with their C11-hydroxy and C11- keto metabolites –one which may hold promise in the identification of new steroid markers in steroid-linked endocrine diseases, in addition to profiling steroid metabolism and abnormal enzyme activity in patients.



<https://doi.org/10.1016/j.ichromb.2018.02.023>

## 96. Exploring lipid markers of the quality of coix seeds with different geographical origins using supercritical fluid chromatography mass spectrometry and chemometrics

Jin-Jun Hou, Chun-Mei Cao, Yong-wei Xu, Shuai Yao, Lu-Ying Cai, Hua-li Long, Qi-Rui Bi, Yuan-Yuan Zhen, Wan-Ying Wu, De-an Guo

2018 – Phytomedicine

Keywords: Traditional Chinese medicine, Lipids, Coix seeds, metabolites, CCD test, markers

### Abstract

Background: Lipids, a group of primary metabolites, could be used as quality markers of Traditional Chinese medicine.

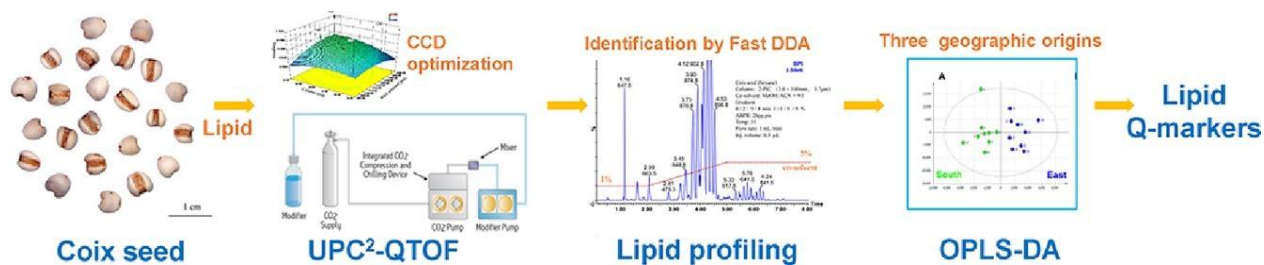
Purpose: The present study was designed to develop a research method to explore lipid markers of the quality of coix seeds with different geographical origins.

Study Design: The geographical origins of coix seeds were divided into three regions based on the latitude. A central composite design (CCD test) was used to optimize the chromatographic parameters of supercritical fluid chromatography to obtain optimal lipid profile of coix seed.

Methods: An untargeted method based on ultra-performance convergence chromatography - quadrupole/time-of-flight hybrid mass spectrometry (UPC2-QTOF) was developed. Four chromatographic parameters were optimized using CCD test, and a fusion index established by



Derringer function was used to evaluate. The lipid profile of 27 batches of coix seeds were acquired and processed by Progenesis QI software, and the MS/MS spectrums were obtained to identify, simultaneously. The difference lipids were explored by orthogonal partial least squares discriminant analysis (OPLS-DA). The lipids that showed differences depending on their seeds' geographical origin were selected as markers of the quality of coix seeds from the three regions. Results: A Torus 2-PIC (1.7  $\mu\text{m}$ , 100 mm  $\times$  3.0 mm) was selected as the optimal column of the untargeted method which the run time was only 8 minutes. From the CCD test, the interaction of chromatographic parameters between column temperature and backpressure was founded which the optimal parameters were 55  $^{\circ}\text{C}$  and 2600 psi, respectively. Thirty-two peaks in the lipid profile of coix seed were tentatively identified, of which 20 were triglyceride, and 12 were diglyceride. Nine features that could potentially be used to distinguish the coix seeds by their geographical origin were identified, most of which were diglycerides, such as OP. Conclusions: Our findings confirm that UPC2-QTOF combined with chemometrics could be used as an efficient method for exploring potential lipid markers of the quality of herbal medicine.



<https://doi.org/10.1016/j.phymed.2018.03.010>

## 97. Enantioselective behaviour of tetraconazole during strawberry wine-making process

Na Liu, Xinglu Pan, Shuang Zhang, Mingshan Ji, Zhihong Zhang

2018 – Chirality

Keywords: Chiral, Tetraconazole, wine making, strawberry

### Abstract

The fate of tetraconazole enantiomers in strawberries during wine-making process was studied. The residues were determined by ultra-performance convergence chromatography tandem triple quadrupole mass spectrometry after each process steps. Results indicated that there was significant enantioselective dissipation of tetraconazole enantiomers during the fermentation process. And (–)-tetraconazole degraded faster than (+)-tetraconazole. The half-lives of (–)-tetraconazole and (+)-tetraconazole were 3.12, 3.76 days with washing procedure and 3.18, 4.05 days without washing procedure. The processing factors of strawberry wine samples after each step were generally less than 1. In particular, the processing factors of the fermentation process were the lowest. The results could help facilitate more accurate risk assessments of tetraconazole during wine-making process.

<https://doi.org/10.1002/chir.22845>

## 98. Improved Analytical Method for Dichlorobenzaldehyde Impurity Detection in Lozenges by Convergence Chromatography

Nandan Kumar Dhir, Tulika Mishra, Varinder Kaur

2018 - Asian Journal of Pharmaceutical Research and Health

Keywords: 2,4 - dichlorobenzaldehyde, Di Benzyl Alcohol, Gas Chromatography, Lozenges, Ultra Performance Convergence Chromatography

### Abstract

Lozenges are the commonly used throat relieving pharmaceutical product that contains DBA and AMC as their active pharmaceutical ingredients. Reports have shown that during the longer storage conditions DBA converts to toxic 2, 4, dichlorobenzaldehyde (DCBZ). Present study reports the development of novel method for detection of DCBZ with UPC2 (Ultra performance convergence chromatography) instrument, that utilize the potential supercritical fluid chromatography, which is

sustainable, reduced cost and green technology reducing the use of organic solvent. In this simple and robust method to detect DCBZ, runtime reduced to 2 minutes as compared to 10 min by Gas Chromatography with higher precision. By utilizing conventional method of Gas Chromatography, 2, 4, dichlorobenzaldehyde is detectable but with very low response and interference with other ingredients use in Lozenges. Method has facilitated faster detection and more sensitivity for DCBZ detection. The improved method provides less flow rate during the process, making it highly cost-effective. Use of non-polar solvents, high to low gradient is some of the advantages of the improved method of present investigation when compared to traditional method. The improved process of present invention proves to be 27 times more cost-effective.

<https://doi.org/10.18311/ajprhc/2018/18109>

## 99. The utility of ultra-high performance supercritical fluid chromatography–tandem mass spectrometry (UHPSFC-MS/MS) for clinically relevant steroid analysis

Karl-Heinz Storbeck, Lorna Gilligan, Carl Jenkinson, Elizabeth S. Baranowski, Jonathan L. Quanson, Wiebke Art, Angela E. Taylor

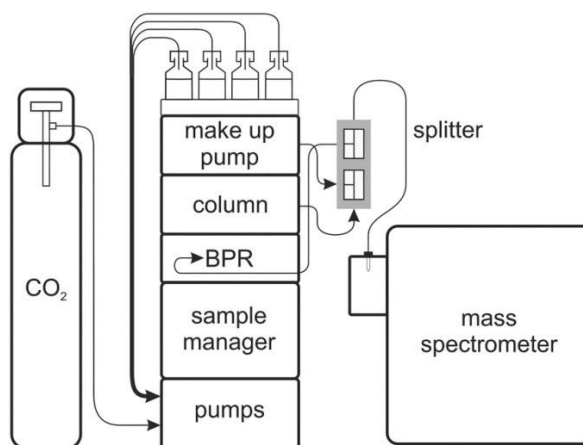
2018 - Journal of Chromatography B

Keywords: Ultra-high performance supercritical fluid chromatography–tandem mass spectrometry, Ultra-high performance liquid chromatography–tandem mass spectrometry, Gas chromatography–mass spectrometry, Steroid analysis

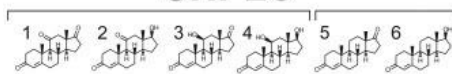
### Abstract

Liquid chromatography tandem mass spectrometry (LC-MS/MS) assays are considered the reference standard for serum steroid hormone analyses, while full urinary steroid profiles are only achievable by gas chromatography (GC-MS). Both LC-MS/MS and GC-MS have well documented strengths and limitations. Recently, commercial ultra-high performance supercritical fluid chromatography–tandem mass spectrometry (UHPSFC-MS/MS) systems have been developed.

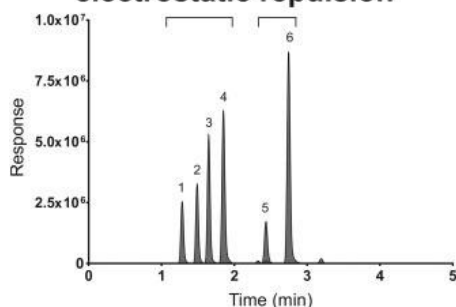
These systems combine the resolution of GC with the high-throughput capabilities of UHPLC. Uptake of this new technology into research and clinical labs has been slow, possibly due to the perceived increase in complexity. Here we therefore present fundamental principles of UHPSFC-MS/MS and the likely applications for this technology in the clinical research setting, while commenting on potential hurdles based on our experience to date.



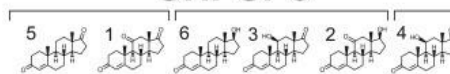
## UHPLC



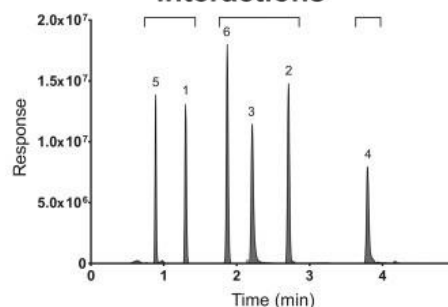
### Hydrophobic interactions and electrostatic repulsion



## UHPSFC



### H-bonding and dipole-dipole interactions



<https://doi.org/10.1016/j.ichromb.2018.03.033>

## 100. A study on the onset of turbulent conditions with SFC mobile-phases

2017 – Journal of Chromatography A

Keywords: SFC, Turbulent, Laminar, Pressure-drop, Extra-column, Tubing

### Abstract

Following a recent publication, the topic of turbulent flow in SFC has generated both interest and questions. Liquid-like density, coupled with significantly low viscosity of CO<sub>2</sub>-based mobile-phases may result in high Reynolds number (*Re*) – higher than what represents laminar flow conditions, reaching the so-called turbulent regions. Although such turbulent flows can form only in the connecting tubings, thus not directly affecting the chromatographic process, it is important to know under many situations, whether the flow inside the tubing is laminar or turbulent.

In this report a comprehensive guideline to identify the possibilities of turbulent flow conditions is provided through a series of charts. Flow properties depend on state conditions (composition, pressure and temperature) and also on the tubing material and geometry. Here guidelines to detect the onset of turbulent conditions is provided for cylindrical stainless-steel tubings of different internal diameters (i.d.) under a wide range of SFC mobile-phase conditions.

### Highlights

- Turbulent flow strongly depends on set method conditions.
- Possibilities of turbulence higher in lower pressure and higher temperatures.
- Flow can be turbulent even with high percent of co-solvent.
- Charts, summarizing comprehensive effects of method conditions are presented.

<https://doi.org/10.1016/j.chroma.2017.11.056>

## 101. Characterization of five chemistries and three particle sizes of stationary phases used in supercritical fluid chromatography

2017 – Journal of Chromatography A

Keywords: Linear solvation energy relationships (LSER), Solvation parameter model, Stationary phase characterization, Sub-2 microns particles, Supercritical fluid chromatography, Ultra-performance convergence chromatography

### Abstract

Sub-2-microns particles employed as supporting phases are known to favor column efficiency. Recently a set of columns based on sub-2-microns particles for use with supercritical fluid mobile phases have been introduced by Waters. Five different stationary phase chemistries are available: BEH silica, BEH Ethyl-pyridine, XSelect CSH Fluorophenyl, HSS C18 SB and BEH Shield RP18. This paper describes the characterization of 15 stationary phases, the five different chemistries, and three particle sizes, 1.7 (or 1.8), 3.5 and 5 microns, with the same carbon dioxide-methanol mobile phase and a set of more than a hundred compounds. The interactions established in the 15 different chromatographic systems used in supercritical fluid chromatography (SFC) are assessed with linear solvation energy relationships (LSERs). The results show the good complementarity of the five column chemistries, and their comparative location inside a classification map containing today around 70 different commercial phases. Among the five different chemistries, the HSS C18 SB phase displays a rather unusual behavior in regards of classical C18 phases, as it displays significant hydrogen-bonding interactions. Besides, it appears, as expected, that the BEH Ethyl-pyridine phase has weak interactions with basic compounds. The effect of particle size was studied because smaller particles induce increased inlet and internal pressure. For compressible fluids, this pressure change modifies the fluid density, *i.e.* the apparent void volume and the eluting strength. These changes could modify the retention and the selectivity of compounds in the case of method transfer, by using different particle sizes, from 5 down to 1.7  $\mu\text{m}$ . A hierarchical cluster analysis shows that stationary phase clusters were based on the phase chemistry rather than on the particle size, meaning that method transfer from 5 to 1.7 microns can be achieved in the subcritical domain *i.e.* by using a weakly compressible fluid.

#### Highlights

- 5 different stationary phase chemistries were evaluated with 3 particle sizes.
- The systems were compared based on retention measured for over 100 analytes.
- Chemometric methods were used to assess the effects of changing particle size.
- Method transfer from 5 to 1.7  $\mu\text{m}$  particles is possible with weakly compressible fluids.

<https://doi.org/10.1016/j.chroma.2013.10.037>

## 102. Supercritical fluid chromatography-tandem mass spectrometry-assisted methodology for rapid enantiomeric analysis of fenbuconazole and its chiral metabolites in fruits, vegetables, cereals, and soil

2017 – Food Chemistry

Keywords: Chiral, Enantioseparation, Fenbuconazole, Metabolites, SFC-MS/MS

#### Abstract

Here, we developed a rapid and robust supercritical fluid chromatography-tandem mass spectrometry (SFC-MS/MS) method for simultaneous detection of fenbuconazole and its chiral metabolites in fruit, vegetable, cereal, and soil. Baseline separation of six stereoisomers was achieved on an amylose tris-(3,5-dimethylphenylcarbamate)-coated chiral column in 4.0 min using a mobile phase composed of CO<sub>2</sub>/ethanol (flow rate of 1.8 mL/min). Ionisation efficiency and sensitivity was optimized with a post-column compensation solvent (0.1% formic acid/methanol). Target analytes were extracted with acetonitrile and purified using dispersive solid phase extraction sorbents. Six stereoisomers at three concentrations (5, 50, and 250  $\mu\text{g}/\text{kg}$ ) achieved satisfactory recoveries (76.3–104.6%) with RSDs  $\leq$  11.5% Excellent linearities ( $R^2 \geq 0.9963$ ) and the limits of quantification (LOQs, 0.13–3.31  $\mu\text{g}/\text{kg}$ ) were established for all six stereoisomers. Results show that the proposed method is suitable for routine detection of six stereoisomers of fenbuconazole and its chiral metabolites in food and environmental samples.

#### Highlights

- SFC-MS/MS was initially developed to analyze fenbuconazole and its metabolites.
- The total six stereoisomers were successfully baseline separated within 4.0 min.
- 0.4 mL/min flow rate of the compensation solvent showed higher MS signal response

<https://doi.org/10.1016/j.foodchem.2017.08.038>

### 103. Lipidomic analysis of biological samples: Comparison of liquid chromatography, supercritical fluid chromatography and direct infusion mass spectrometry methods

2017 – Journal of Chromatography A

Keywords: Lipidomics, Lipidomic analysis, UHPLC, UHPSFC, Direct infusion, Mass spectrometry

#### Abstract

Lipidomic analysis of biological samples in a clinical research represents challenging task for analytical methods given by the large number of samples and their extreme complexity. In this work, we compare direct infusion (DI) and chromatography – mass spectrometry (MS) lipidomic approaches represented by three analytical methods in terms of comprehensiveness, sample throughput, and validation results for the lipidomic analysis of biological samples represented by tumor tissue, surrounding normal tissue, plasma, and erythrocytes of kidney cancer patients. Methods are compared in one laboratory using the identical analytical protocol to ensure comparable conditions. Ultrahigh-performance liquid chromatography/MS (UHPLC/MS) method in hydrophilic interaction liquid chromatography mode and DI-MS method are used for this comparison as the most widely used methods for the lipidomic analysis together with ultrahigh-performance supercritical fluid chromatography/MS (UHPSFC/MS) method showing promising results in metabolomics analyses. The nontargeted analysis of pooled samples is performed using all tested methods and 610 lipid species within 23 lipid classes are identified. DI method provides the most comprehensive results due to identification of some polar lipid classes, which are not identified by UHPLC and UHPSFC methods. On the other hand, UHPSFC method provides an excellent sensitivity for less polar lipid classes and the highest sample throughput within 10 min method time. The sample consumption of DI method is 125 times higher than for other methods, while only 40  $\mu$ L of organic solvent is used for one sample analysis compared to 3.5 mL and 4.9 mL in case of UHPLC and UHPSFC methods, respectively. Methods are validated for the quantitative lipidomic analysis of plasma samples with one internal standard for each lipid class. Results show applicability of all tested methods for the lipidomic analysis of biological samples depending on the analysis requirements.

#### Highlights

- UHPLC, UHPSFC and direct infusion MS methods are compared for the lipidomic analysis of biological samples.
- Methods are tested in one laboratory using the identical analytical protocol and instrumentation.
- Comprehensiveness, sample throughput and validation results of individual methods are demonstrated.
- Tested methods are applicable for the lipidomic analysis of biological samples with particular limitations for each method.

<https://doi.org/10.1016/j.chroma.2017.10.022>

### 104. A rapid method for the separation of vitamin D and its metabolites by ultra-high performance supercritical fluid chromatography–mass spectrometry

2017 – Journal of Chromatography A

Keywords: Ultra-high performance supercritical fluid chromatography, Vitamin D<sub>2</sub> and D<sub>3</sub> metabolites, Orthogonal column screening, Method development, Plasma, Mass spectrometry

#### Abstract

In this study, a new supercritical fluid chromatography–mass spectrometry (SFC–MS) method has been developed for the separation of nine vitamin D metabolites within less than eight minutes. This is the first study of analysis of vitamin D and its metabolites carried out by SFC–MS. Six columns of orthogonal selectivity were examined, and the best separation was obtained by using a 1-aminoanthracene (1-AA) column. The number and the position of hydroxyl groups in the structure of the studied compounds as well as the number of unsaturated bonds determine the physicochemical properties and, thus the separation of vitamin D metabolites that is achieved on this column. All D<sub>2</sub> and the D<sub>3</sub> forms were baseline separated with resolution values > 1.5. The effects of pressure, temperature, flow rate and different gradient modes were studied. Electrospray ionization (ESI) and atmospheric pressure chemical ionization (APCI) were compared

in positive mode, both by direct infusion and after SFC separation. The results showed that the sensitivity in APCI<sup>+</sup> was higher than in ESI<sup>+</sup> using direct infusion. In contrast, the sensitivity in APCI<sup>+</sup> was 6-fold lower than in ESI<sup>+</sup> after SFC separation. The SFC–MS method was validated between 10 and 500 ng/mL for all analytes with coefficient of determination ( $R^2$ )  $\geq$  0.999 for all calibration curves. The limits of detection (LOD) were found to range between 0.39 and 5.98 ng/mL for 24,25-dihydroxyvitamin D<sub>3</sub> (24,25(OH)<sub>2</sub>D<sub>3</sub>) and 1-hydroxyvitamin D<sub>2</sub>(1OHD<sub>2</sub>), respectively. To show its potential, the method was applied to human plasma samples from healthy individuals. Vitamin D<sub>3</sub> (D<sub>3</sub>), 25-hydroxyvitamin D<sub>3</sub> (25OHD<sub>3</sub>) and 24,25(OH)<sub>2</sub>D<sub>3</sub> were determined in plasma samples and the concentrations were  $6.6 \pm 3.0$  ng/mL,  $23.8 \pm 9.2$  ng/mL and  $5.4 \pm 2.7$  ng/mL, respectively.

#### Highlights

- Column screening on six orthogonal stationary phases for vitamin D analysis.
- Nine vitamin D metabolites (D<sub>2</sub> and D<sub>3</sub> forms) are baseline separated in 8 min.
- The effect of co-solvent, temperature, pressure and flow rate is studied.
- ESI<sup>+</sup> is 6-fold more sensitive than APCI<sup>+</sup> in SFC–MS.

<https://doi.org/10.1016/j.chroma.2016.02.043>

## 105. Evaluation of the quantitative performances of supercritical fluid chromatography: From method development to validation

2017 – Journal of Chromatography A

Keywords: Supercritical fluid chromatography (SFC), Ultra high performance supercritical fluid chromatography (UHPSFC), Ultra high performance liquid chromatography (UHPLC), Quantitative performances, Method validation, Total error approach

#### Abstract

Recently, the number of papers about SFC increased drastically but scientists did not truly focus their work on quantitative performances of this technique. In order to prove the potential of UHPSFC, the present work discussed about the different steps of the analytical life cycle of a method: from development to validation and application. Moreover, the UHPSFC quantitative performances were evaluated in comparison with UHPLC, which is the main technique used for quality control in the pharmaceutical industry and then could be considered as a reference. The methods were developed using Design Space strategy, leading to the optimization of robust method. In this context, when the Design Space optimization shows guarantee of quality, no more robustness study is required prior to the validation. Then, the methods were geometrically transferred in order to reduce the analysis time. The UHPSFC and UHPLC methods were validated based on the total error approach using accuracy profile. Even if UHPLC showed better precision and sensitivity, UHPSFC method is able to give accurate results in a dosing range larger than the 80–120% range required by the European Medicines Agency. Consequently, UHPSFC results are valid and could be used for the control of active substance in a finished pharmaceutical product. Finally, UHPSFC validated method was used to analyse real samples and gave similar results than the reference method (UHPLC).

#### Highlights

- UHPSFC method was successfully validated considering total error approach
- Quantitative performances of UHPSFC are compliant with the E.M.A. and ICH recommendations.
- UHPSFC can be used as a quantitative method for the quality control of medicines.
- Design Space strategy led to the optimization of a robust method as recommended by USP.

<https://doi.org/10.1016/j.chroma.2014.01.046>

## 106. Analysis of hydroxylated polybrominated diphenyl ethers (OH-BDEs) by supercritical fluid chromatography/mass spectrometry

2017 – Talanta

Keywords: Hydroxylated polybrominated diphenyl ethers (OH-BDEs), Supercritical fluid chromatography (SFC), Mass spectrometry (MS), Metabolism, Human serum

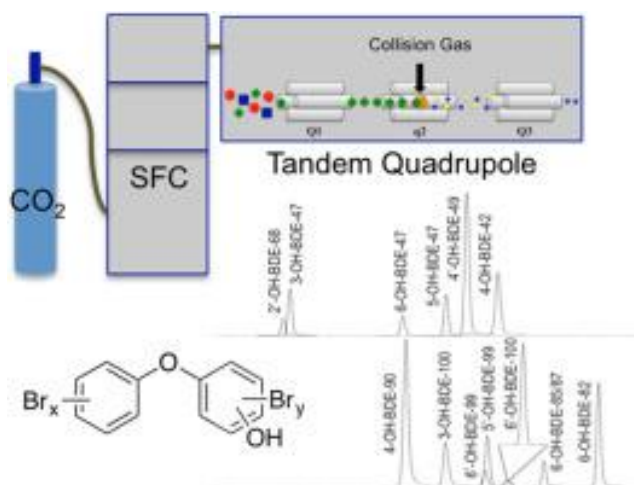
#### Abstract



Hydroxylated polybrominated diphenyl ethers (OH-BDEs), which have anthropogenic and natural origins, have exhibited neurotoxic and endocrine disrupting effects in humans and wildlife. Therefore, there is an increased interest in the analysis of these compounds in biological matrices in order to assess their potential toxicological risks. Analysis of OH-BDEs is conventionally completed using liquid chromatography/mass spectrometry (LC/MS), or by gas chromatography/mass spectrometry (GC/MS) after derivatization. Issues with resolution in separating congeners have limited the analysis of OH-BDEs *via* LC/MS, with published methods only able to include 13 congeners in the analysis. On the other hand, while GC/MS analysis can analyze more OH-BDE congeners, derivatization of OH-BDEs to convert them to GC amenable compounds adds to sample preparation time and limits the column lifetime due to trace residues of highly reactive derivatization agents entering the column. Herein we report the development of a supercritical fluid chromatography/mass spectrometry (SFC/MS) method for the analysis of 22 OH-BDE congeners. Instrument limits of detection for the developed method ranged from 2 to 106 fg injected on column, which is lower than previously optimized LC/MS and GC/MS methods. The developed SFC/MS method was successfully applied towards the analysis of *in vitro* metabolism samples and human serum samples to demonstrate its applicability with different biological matrices.

#### Highlights

- The development of an SFC/MS/MS method for the analysis of OH-BDEs.
- Calculated iLODs ranged from 2 to 106 fg injected on column.
- Successfully applied towards *in vitro* metabolism and human serum samples.



<https://doi.org/10.1016/j.talanta.2016.08.013>

## 107. Coupling state-of-the-art supercritical fluid chromatography and mass spectrometry: From hyphenation interface optimization to high-sensitivity analysis of pharmaceutical compounds

2017 – Journal of Chromatography A

Keywords: SFC–MS, UHPSFC–MS, Interfacing approach, Detection sensitivity, Pharmaceutical application

#### Abstract

The recent market release of a new generation of supercritical fluid chromatography (SFC) instruments compatible with state-of-the-art columns packed with sub-2  $\mu\text{m}$  particles (UHPSFC) has contributed to the reemergence of interest in this technology at the analytical scale. However, to ensure performance competitiveness of this technique with modern analytical standards, a

robust hyphenation of UHPSFC to mass spectrometry (MS) is mandatory. UHPSFC–MS hyphenation interface should be able to manage the compressibility of the SFC mobile phase and to preserve as much as possible the chromatographic separation integrity. Although several interfaces can be envisioned, each will have noticeable effects on chromatographic fidelity, flexibility and user-friendliness. In the present study, various interface configurations were evaluated in terms of their impact on chromatographic efficiency and MS detection sensitivity. An interface including a splitter and a make-up solvent inlet was found to be the best compromise and exhibited good detection sensitivity while maintaining more than 75% of the chromatographic efficiency. This interface was also the most versatile in terms of applicable analytical conditions. In addition, an accurate model of the fluidics behavior of this interface was created for a better understanding of the influence of chromatographic settings on its mode of operation. In the second part, the most influential experimental factors affecting MS detection sensitivity were identified and optimized using a design-of-experiment approach. The application of low capillary voltage and high desolvation temperature and drying gas flow rate were required for optimal ESI ionization and nebulization processes. The detection sensitivity achieved using the maximized UHPSFC–ESI-MS/MS conditions for a mixture of basic pharmaceutical compounds showed 4- to 10-fold improvements in peak intensity compared to the best performance achieved by UHPLC–ESI-MS/MS with the same MS detector.

#### Highlights

- Several UHPSFC–MS hyphenation interfaces were critically evaluated.
- The interface including a splitter and a make-up solvent inlet was found to be the most versatile.
- High desolvation temperature and drying gas flow rate were mandatory for optimal ESI process.
- UHPSFC–ESI-MS/MS was, on average, 10 times more sensitive than UHPLC–ESI-MS/MS.
- UHPSFC–ESI-MS/MS appears to be a competitive analytical approach.

<https://doi.org/10.1016/j.chroma.2014.03.006>

## 108. Comparison of ultra-high performance supercritical fluid chromatography and ultra-high performance liquid chromatography for the separation of spirostanol saponins

2017 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: Spirostanol saponins, Ultra-high performance supercritical fluid chromatography, Ultra-high performance liquid chromatography, Chromatographic behavior, Natural products

#### Abstract

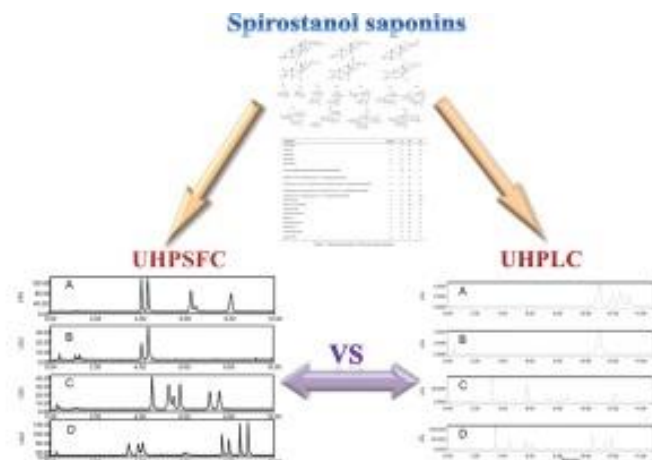
Spirostanol saponins are important active components of some herb medicines, and their isolation and purification are crucial for the research and development of traditional Chinese medicines. We aimed to compare the separation of spirostanol saponins by ultra-high performance supercritical fluid chromatography (UHPSFC) and ultra-high performance liquid chromatography (UHPLC). Four groups of spirostanol saponins were separated respectively by UHPSFC and UHPLC. After optimization, UHPSFC was performed with a HSS C18 SB column or a Diol column and with methanol as the co-solvent. A BEH C18 column and mobile phase containing water (with 0.1% formic acid) and acetonitrile were used in UHPLC. We found that UHPSFC could be performed automatically and quickly. It is effective in separating the spirostanol saponins which share the same aglycone and vary in sugar chains, and is very sensitive to the number and the position of hydroxyl groups in aglycones. However, the resolution of spirostanol saponins with different aglycones and the same sugar moiety by UHPSFC was not ideal and could be resolved by UHPLC instead. UHPLC is good at differentiating the variation in aglycones, and is influenced by double bonds in aglycones. Therefore, UHPLC and UHPSFC are complementary in separating spirostanol saponins. Considering the naturally produced spirostanol saponins in herb medicines are different both in aglycones and in sugar chains, a better separation can be achieved by combination of UHPLC and UHPSFC. UHPSFC is a powerful technique for improving the resolution when UHPLC cannot resolve a mixture of spirostanol saponins and vice versa.

#### Highlights

- UHPSFC is a good automatic chromatographic technique and has little in common with normal phase HPLC.

- UHPSFC separates spirostanol saponins varying only in sugar chains or in hydroxyls of aglycones well.
- UHPLC with C18 column separates spirostanol saponins varying only in aglycones well, especially with different double bonds.
- UHPSFC and UHPLC are complementary and could be applied together in separating spirostanol saponins.
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<https://doi.org/10.1016/j.ipba.2015.12.002>



## 109. Analysis of ultra-short chain perfluoroalkyl substances in Swedish environmental waters

2017 - Örebro universitet publication

### Summary

The purpose of this study was to investigate the environmental occurrence of ultra-short chain perfluoroalkyl substances (PFASs) in Swedish water samples. So far established protocols have focused on measuring PFASs with a carbon chain length of four or more carbons. In this study, perfluoroalkyl sulfonates of chain lengths of two, perfluoroethane sulfonate (PFEtS), and three, perfluoropropane sulfonate (PFPrS), carbons have been measured using a newly established instrumental method employing supercritical fluid separation (SFC) coupled to tandem mass spectrometry detection. A total of 26 samples were analysed, including ground water, surface water, rain water and snow. The sample locations included military and civilian airports, a former hard chromium plating facility, the vicinity of a hazardous waste management facility and background areas (lake surface water, rain and snow). Results show that both PFPrS and PFEtS could be detected in environmental samples using SFC separation coupled to triple quadrupole detection. Out of the 26 samples analysed, the ultra-shortchain PFPrS could be detected and quantified in 22 samples. The concentrations for PFPrS in all the samples ranged between 0.93 ng/l to 39 000 ng/l. The ultra-short-chain PFPEtS could be quantified in all of the 26 samples, with a concentration range between 0.07 and 5 700 ng/l. The highest concentrations represents highly contaminated ground water samples collected from a military airport. In the samples, PFPrS had a relative contribution to total PFAS concentration of 6 and 10 %, indicating the importance of measuring these compounds in environmental samples.

[PDF] [Analysis of ultra-short chain perfluoroalkyl substances in Swedish environmental waters](#)

## 110. A rapid and sensitive supercritical fluid chromatography/tandem mass spectrometry method for detection of ezetimibe in dog plasma and its application in pharmacokinetic studies

2017 – Journal of Chromatography B

Keywords: ezetimibe, SFC-MS/MS, beagle dog, pharmacokinetics

### Abstract

The aim of this study is to develop and validate a rapid, high-selective and sensitive supercritical fluid chromatography/tandem mass spectrometry (SFC-MS/MS) with a multiple reactions monitoring (MRM) mode method for the detection of ezetimibe in dog plasma. Several conditions were optimized systematically as follows: lipid-lipid extraction (LLE) performances were used to extract analytes from dog plasma; an ACQUITY HSS C<sub>18</sub> SB (1.8 μm, 3.0 × 100 mm) column was employed to separate the target compounds; the triple-quadrupole mass spectrometry equipped with electrospray ionization (ESI) source was applied to detect ezetimibe. The method, which required a relatively small volume of plasma (100 μL), was obtained at concentration ranging from 1.0 to 100 ng/mL ( $r^2 > 0.99$ ). The lower limit of quantification (LLOQ) for ezetimibe was found to be as low as 1.0 ng/mL. In addition, the validations of the methodology including sensitivity, recovery, matrix effect, intra- and inter-day precision, accuracy and stability were all within acceptable limits. The  $C_{max}$ ,  $AUC_{0-inf}$  and  $T_{max}$  values obtained in our study were  $52.2 \pm 6.3$ ,  $820.6 \pm 4.3$  and  $1.25 \pm 0.35$  for reference formulation;  $61.8 \pm 12.6$ ,  $924.2 \pm 4.7$  and  $2.00 \pm 0$  for test formulation. In conclusion, the method developed in this study can be successfully applied to pharmacokinetic studies after oral administration of ezetimibe in dogs.

### Highlights

- We determined ezetimibe in dog plasma by a rapid, high-selective and sensitive SFC-MS/MS.
- Ezetimibe-glucuronide should be hydrolyzed to the original drug by the β-Glucuronidase.
- The total free ezetimibe will be detected by MS after liquid-liquid extraction.
- 

<https://doi.org/10.1016/j.jchromb.2017.10.053>

## 111. Lipidomic analysis of biological samples: Comparison of liquid chromatography, supercritical fluid chromatography and direct infusion mass spectrometry methods

2017 – Journal of Chromatography A

Keywords: Lipidomics, Lipidomic analysis, UHPLC, UHPSFC, Direct infusion, Mass spectrometry

### Abstract

Lipidomic analysis of biological samples in a clinical research represents challenging task for analytical methods given by the large number of samples and their extreme complexity. In this work, we compare direct infusion (DI) and chromatography – mass spectrometry (MS) lipidomic approaches represented by three analytical methods in terms of comprehensiveness, sample throughput, and validation results for the lipidomic analysis of biological samples represented by tumor tissue, surrounding normal tissue, plasma, and erythrocytes of kidney cancer patients. Methods are compared in one laboratory using the identical analytical protocol to ensure comparable conditions. Ultrahigh-performance liquid chromatography/MS (UHPLC/MS) method in hydrophilic interaction liquid chromatography mode and DI-MS method are used for this comparison as the most widely used methods for the lipidomic analysis together with ultrahigh-performance supercritical fluid chromatography/MS (UHPSFC/MS) method showing promising results in metabolomics analyses. The nontargeted analysis of pooled samples is performed using all tested methods and 610 lipid species within 23 lipid classes are identified. DI method provides the most comprehensive results due to identification of some polar lipid classes, which are not identified by UHPLC and UHPSFC methods. On the other hand, UHPSFC method provides an excellent sensitivity for less polar lipid classes and the highest sample throughput within 10 min method time. The sample consumption of DI method is 125 times higher than for other methods, while only 40 μL of organic solvent is used for one sample analysis compared to 3.5 mL and 4.9 mL in case of UHPLC and UHPSFC methods, respectively. Methods are validated for the quantitative lipidomic analysis of plasma samples with one internal standard for each lipid class. Results show applicability of all tested methods for the lipidomic analysis of biological samples depending on the analysis requirements.

### Highlights

- UHPLC, UHPSFC and direct infusion MS methods are compared for the lipidomic analysis of biological samples.

- Methods are tested in one laboratory using the identical analytical protocol and instrumentation.
- Comprehensiveness, sample throughput and validation results of individual methods are demonstrated.
- Tested methods are applicable for the lipidomic analysis of biological samples with particular limitations for each method.

<https://doi.org/10.1016/j.chroma.2017.10.022>

## 112. Ultra-high-performance supercritical fluid chromatography with quadrupole-time-of-flight mass spectrometry (UHPSFC/QTOF-MS) for analysis of lignin-derived monomeric compounds in processed lignin samples

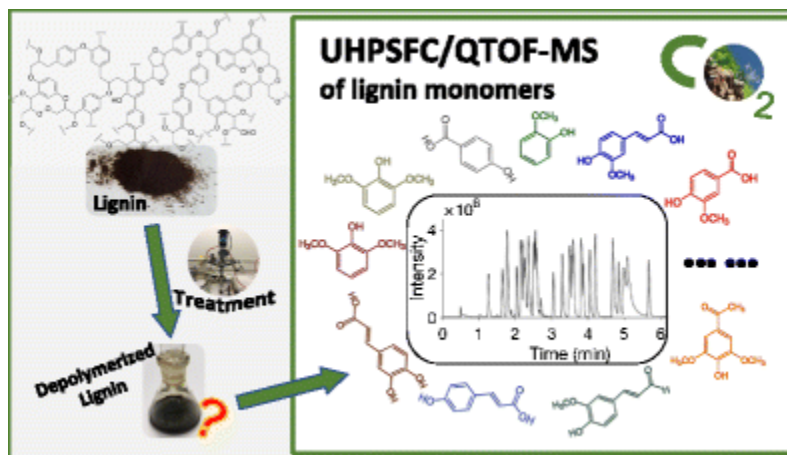
2017 – Analytical and Bioanalytical Chemistry

Keywords: Column selectivity, Design of experiment, Ionisation efficiency, Lignin, Supercritical fluid chromatography

### Abstract

The conversion of lignin to potentially high-value low molecular weight compounds often results in complex mixtures of monomeric and oligomeric compounds. In this study, a method for the quantitative and qualitative analysis of 40 lignin-derived compounds using ultra-high-performance supercritical fluid chromatography coupled to quadrupole-time-of-flight mass spectrometry (UHPSFC/QTOF-MS) has been developed. Seven different columns were explored for maximum selectivity. Makeup solvent composition and ion source settings were optimised using a D-optimal design of experiment (DoE). Differently processed lignin samples were analysed and used for the method validation. The new UHPSFC/QTOF-MS method showed good separation of the 40 compounds within only 6-min retention time, and out of these, 36 showed high ionisation efficiency in negative electrospray ionisation mode.

<https://doi.org/10.1007/s00216-017-0663-5>



**Graphical abstract**

A rapid and selective method for the quantitative and qualitative analysis of 40 lignin-derived compounds using ultra-high-performance supercritical fluid chromatography coupled to quadrupole-time-of-flight mass spectrometry (UHPSFC/QTOF-MS)

## 113. Method optimization for drug impurity profiling in supercritical fluid chromatography: Application to a pharmaceutical mixture

2017 – Journal of Chromatography A

Keywords: Supercritical fluid chromatography, Separation optimization, Experimental design, Chromatographic response modeling, Chromatogram simulation

### Abstract

A supercritical chromatographic method for the separation of a drug and its impurities has been developed and optimized applying an experimental design approach and chromatogram simulations. Stationary phase screening was followed by optimization of the modifier and injection solvent composition. A design-of-experiment (DoE) approach was then used to optimize column temperature, back-pressure and the gradient slope simultaneously. Regression models for the retention times and peak widths of all mixture components were built. The factor levels for different grid points were then used to predict the retention times and peak widths of the mixture components using the regression models and the best separation for the worst separated peak pair in the experimental domain was identified.

A plot of the minimal resolutions was used to help identifying the factor levels leading to the highest resolution between consecutive peaks. The effects of the DoE factors were visualized in a way that is familiar to the analytical chemist, i.e. by simulating the resulting chromatogram. The mixture of an active ingredient and seven impurities was separated in less than eight minutes. The approach discussed in this paper demonstrates how SFC methods can be developed and optimized efficiently using simple concepts and tools.

#### Highlights

- Effect of different modifier and injection solvent compositions on retention and peak shape.
- Optimization of temperature, back-pressure and gradient time with a response surface design approach.
- Modelling retention as a function of temperature, back-pressure and gradient time.
- Chromatogram simulation of the predicted optimal separation.

<https://doi.org/10.1016/j.chroma.2017.10.036>

### 114. Separation of achiral analytes using supercritical fluid chromatography with chiral stationary phases

2017 - TrAC Trends in Analytical Chemistry

Keywords: Achiral separation, Chiral stationary phase, Chiral supercritical fluid chromatography, Closely-related species, Complex mixture, Method development, Supercritical fluid chromatography, Ultra high performance liquid chromatography

#### Abstract

In recent years, chiral supercritical fluid chromatography (SFC) has emerged as the preferred technique for analytical, semi-preparative and preparative separation of enantiomers in the pharmaceutical industry, due to advantages in speed, high column efficiency and significantly lower mobile-phase consumption than conventional liquid chromatography (LC) techniques. We illustrate the benefits of SFC using chiral stationary phases (CSPs) in method development for separating multicomponent mixtures of closely-related achiral analytes, including hydroxylation isomers, halogen-containing molecules, drug metabolites and analogs, methylation and demethylation species, constitutional isomers, and diastereomers. We present several case studies to illustrate the advantage of using SFC with CSPs for achiral separations, where conventional achiral LC and achiral SFC methods fail or deliver sub-optimal chromatographic performance.

#### Highlights

- Solving multicomponent achiral separation challenges *via* SFC with chiral stationary phases (CSPs).
- Challenging mixtures of achiral drug metabolites and analogs can often be resolved by CSPs in SFC mode.
- Achiral UHPLC and SFC vs chiral SFC for separation of closely related achiral analytes.
- Separation of complex non-enantiomeric mixtures often require alternative approaches such as chiral SFC.

<https://doi.org/10.1016/j.trac.2015.01.004>

### 115. Simultaneous determination of topiramate, carbamazepine, oxcarbazepine and its major metabolite in human plasma by SFC-ESI-MS/MS with polarity switching: Application to therapeutic drug monitoring



Keywords: Antiepileptic drugs, Antiepileptic drugs, SFC-ESI-MS/MS, Human plasma, Therapeutic drug monitoring, UPC2

**Abstract**

Antiepileptic drugs are the first choice for epilepsy treatment. Monitoring antiepileptic drugs is important to minimize their adverse side effects by choosing the optimum drug dosage. An accurate and high throughput supercritical fluid chromatography-tandem mass spectrometry method has been developed for the simultaneous quantification of several antiepileptic drugs in human plasma. Plasma samples were extracted with ethyl acetate and the upper organic layer was directly injected into the supercritical fluid chromatography/mass spectrometry (SFC-MS/MS) system without further nitrogen evaporation and subsequent reconstitution. The analytes were eluted on a UPC<sup>2</sup>™ BEH, 2-EP column (100 × 3 mm, 1.7 μm) at a flow rate of 1.0 mL/min and multi-reaction monitoring (MRM) was performed for determination of the analytes and internal standard (IS) in polarity switching mode. Calibration curves were linear over the concentration ranges of 0.08–40, 0.01–15, 0.01–8 and 0.5–50 μg/mL with lower limit of quantifications of 0.08, 0.01, 0.01 and 0.50 μg/mL for topiramate, carbamazepine, oxcarbazepine and monohydroxycarbamazepine, respectively. This sensitive, accurate, novel method will be very useful for monitoring the above antiepileptic drugs and for pharmacokinetic studies.

<https://doi.org/10.1016/j.arabic.2016.09.016>

### 116. Development and optimization of ultra-high performance supercritical fluid chromatography mass spectrometry method for high-throughput determination of tocopherols and tocotrienols in human serum

2017 – Analytica Chimica Acta

Keywords: Ultra-high performance supercritical fluid chromatography, Mass spectrometry, Liquid liquid extraction, Tocopherols, Tocotrienols, Human serum

**Abstract**

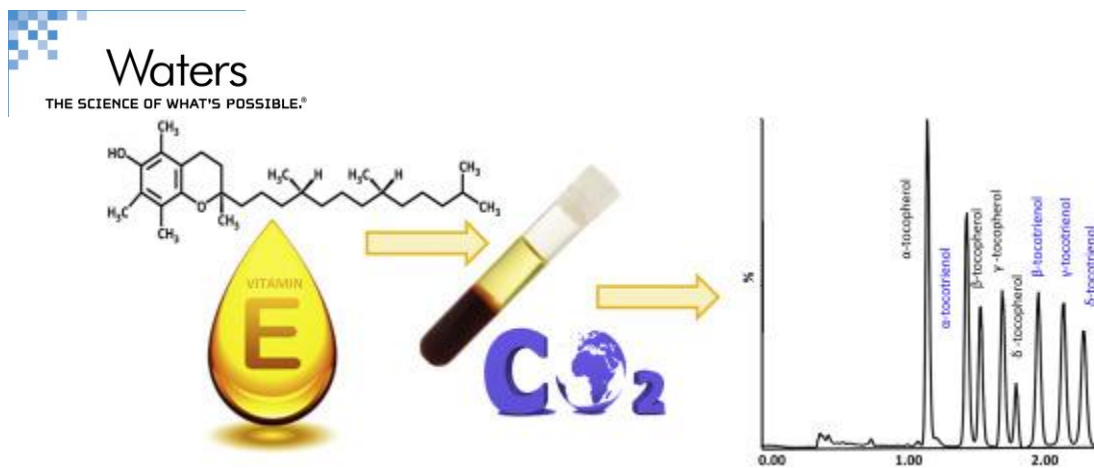
The goal of this study was to develop an effective supercritical fluid chromatography method using single quadrupole MS for analysis of all isomeric forms of vitamin E. Finally, two fast and effective methods, the high resolution one and the high speed one, for the determination of 8 vitamin E isomers in human serum were developed.

Rapid high-throughput liquid-liquid extraction was selected as a sample preparation step. Sample pretreatment of 100 μL human serum was consisted of protein precipitation with 200 μL ethanol and liquid-liquid extraction by 400 μL hexane/dichloromethane (80/20, v/v). The separation was performed on BEH 2-EP (3.0 × 100 mm, 1.7 μm) stationary phase, using isocratic elution with carbon dioxide and 10 mM ammonium formate in methanol in the ratio 98:2 for high resolution method with run time 4.5 min and in the ratio 95:5 for high speed method, where the run time was 2.5 min. The method development included optimization of key parameters: the choice of the suitable stationary phase and the composition of mobile phase, where an influence of various modifiers, their ratio and additives were tested, and optimization of fine tuning parameters including BPR pressure, flow-rate and column temperature. Quantification of all isomeric forms was performed using SIM (single ion monitoring) experiments in ESI positive ion mode. Both high speed and high resolution chromatographic methods were validated in terms of precision, accuracy, range, linearity, LOD, LOQ and matrix effects using the same LLE procedure. The high resolution method provided more sensitive results (LOD: 0.017–0.083 μg mL<sup>-1</sup>) and better linearity ( $r^2 > 0.9930$ ) than the high speed one (LOD: 0.083–0.25 μg mL<sup>-1</sup>,  $r^2 > 0.9877$ ) at the cost of double time of analysis.

Highlights

- Two fast, selective and sensitive UHPSFC-MS methods were developed and validated.
- Eight isomeric forms of vitamin E were fully separated in less than 4.5 min.
- The influence of individual SFC parameters was evaluated in detail.
- High-throughput LLE was used for sample preparation with sufficient selectivity and sensitivity.

<https://doi.org/10.1016/j.aca.2016.06.008>



### 117. Characterization of carotenoids in *Rhodothermus marinus*

2017 – MicrobiologyOpen

Keywords: ACQUITY UPC2, Xevo G2-QToF,

#### Abstract

*Rhodothermus marinus*, a marine aerobic thermophile, was first isolated from an intertidal hot spring in Iceland. In recent years, the *R. marinus* strain PRI 493 has been genetically modified, which opens up possibilities for targeted metabolic engineering of the species, such as of the carotenoid biosynthetic pathway. In this study, the carotenoids of the *R. marinus* type-strain DSM 4252<sup>T</sup>, strain DSM 4253, and strain PRI 493 were characterized. Bioreactor cultivations were used for pressurized liquid extraction and analyzed by ultra-high performance supercritical fluid chromatography with diode array and quadropole time-of-flight mass spectrometry detection (UHPSFC-DAD-QTOF/MS). Salinixanthin, a carotenoid originally found in *Salinibacter ruber* and previously detected in strain DSM 4253, was identified in all three *R. marinus* strains, both in the hydroxylated and nonhydroxylated form. Furthermore, an additional and structurally distinct carotenoid was detected in the three strains. MS/MS fragmentation implied that the mass difference between salinixanthin and the novel carotenoid structure corresponded to the absence of a 4-keto group on the β-ionone ring. The study confirmed the lack of carotenoids for the strain SB-71 ( $\Delta trpB\Delta purAcrtBI::trpB$ ) in which genes encoding two enzymes of the proposed pathway are partially deleted. Moreover, antioxidant capacity was detected in extracts of all the examined *R. marinus* strains and found to be 2–4 times lower for the knock-out strain SB-71. A gene cluster with 11 genes in two operons in the *R. marinus* DSM 4252<sup>T</sup> genome was identified and analyzed, in which several genes were matched with carotenoid biosynthetic pathway genes in other organisms.

<https://doi.org/10.1002/mbo3.536>

### 118. The differences in matrix effect between supercritical fluid chromatography and reversed phase liquid chromatography coupled to ESI/MS

2017 – Analytica Chimica Acta

Keywords: Matrix effects, Supercritical fluid chromatography, Electrospray ionization, Liquid chromatography, Ion enhancement, Ion suppression

#### Abstract

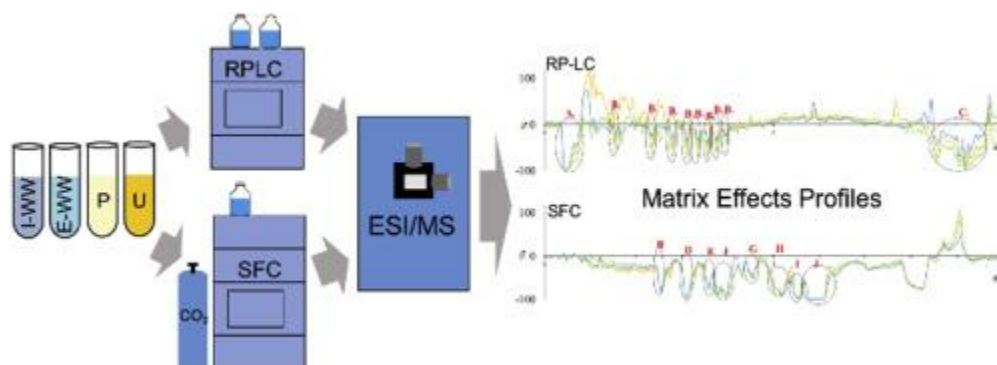
For many sample matrices, matrix effects are a troublesome phenomenon using the [electrospray ionization](#) source. The increasing use of [supercritical fluid chromatography](#) with CO<sub>2</sub> in combination with the electrospray ionization source for MS detection is therefore raising questions: is the matrix effect behaving differently using SFC in comparison with reversed phase LC? This was investigated using urine, plasma, influent- and effluent-wastewater as sample matrices. The matrix effect was evaluated using the post-extraction addition method and through post-column infusions. Matrix effect profiles generated from the post-column infusions in combination with time of flight-MS detection provided the most valuable information for the study. The combination of both qualitative and semi-quantitative information with the ability to use HRMS-data for identifying interfering compounds from the same experiment was very useful, and has to the

authors' knowledge not been used this way before. The results showed that both LC and SFC are affected by matrix effects, however differently depending on sample matrix. Generally, both suppressions and enhancements were seen, with a higher amount of enhancements for LC, where 65% of all compounds and all sample matrices were enhanced, compared to only 7% for SFC. Several interferences were tentatively identified, with [phospholipids](#), [creatinine](#), and metal ion clusters as examples of important interferences, with different impact depending on [chromatographic](#) technique. SFC needs a different strategy for limiting matrix interferences, owing to its almost reverse retention order compared to RPLC.

Highlights;

- Matrix effects were compared using screening methods with SFC/ESI-MS and RPLC/ESI-MS.
- Blood plasma, horse urine and influent/effluent wastewater were investigated.
- Through the use of post-column infusions, matrix effect profiles were generated.
- Quantitative and qualitative information was compared, interferences tentatively identified.
- Ion suppressions were generally more common for SFC, and enhancements for LC.

<https://doi.org/10.1016/j.aca.2017.10.014>



## 119. Quantitative Profiling Of Endogenous Fat-Soluble Vitamins And Carotenoids In Human Plasma Using An Improved UHPSFC-ESI-MS Interface

2017 – Analytical Chemistry

Keywords: UPC2, Mass Spec interface

### Abstract

Analytical solutions enabling the quantification of circulating levels of liposoluble micronutrients such as vitamins and carotenoids are currently limited to either single or a reduced panel of analytes. The requirement to use multiple approaches hampers the investigation of the biological variability on a large number of samples in a time and cost efficient manner. With the goal to develop high-throughput and robust quantitative methods for the profiling of micronutrients in human plasma, we introduce a novel, validated workflow for the determination of 14 fat-soluble vitamins and carotenoids in a single run. Automated workflow supported liquid extraction was optimized and implemented to simultaneously parallelize 48 samples in 1 h, and the analytes were measured using ultrahigh-performance supercritical fluid chromatography coupled to tandem mass spectrometry in less than 8 min. An improved mass spectrometry interface hardware was built up to minimize the post-decompression volume and to allow better control of the chromatographic effluent density on its route toward and into the ion source. In addition, a specific make-up solvent condition was developed to ensure both analytes and matrix constituents solubility after mobile phase decompression. The optimized interface resulted in improved spray plume stability and conserved matrix compounds solubility leading to enhanced hyphenation robustness while ensuring both suitable analytical repeatability and improved the detection sensitivity. The overall

developed methodology gives recoveries within 85–115%, as well as within and between-day coefficient of variation of 2 and 14%, respectively.

<http://pubs.acs.org/doi/abs/10.1021/acs.analchem.7b01476>

## 120. Maternal And Female Fetal Testosterone Levels Are Associated With Maternal Age And Gestational Weight Gain

2017 - European Journal of Endocrinology

Keywords: UPC2, Testosterone, Cortisol

### Abstract

**OBJECTIVE:** Prenatal androgen exposure has been suggested to play a role in polycystic ovary syndrome. Given the limited information on what maternal characteristics influence maternal testosterone levels, and the even less explored routes by which female fetus androgen exposure would occur, the aim of this study was to investigate the impact of maternal age, BMI, weight gain, depressed mood and aromatase SNPs on testosterone levels in maternal serum and amniotic fluid of female fetuses.

**METHODS:** Blood samples from pregnant women ( $n = 216$ ) obtained in gestational weeks 35-39, and pre-labor amniotic fluid samples from female fetuses ( $n = 56$ ), taken at planned Caesarean section or in conjunction with amniotomy for induction of labor, were analyzed. Maternal serum testosterone and amniotic fluid testosterone and cortisol were measured by tandem mass spectrometry.

**RESULTS:** Multiparity ( $\beta = -0.28, P < 0.001$ ), self-rated depression ( $\beta = 0.26, P < 0.001$ ) and weight gain ( $\beta = 0.18, P < 0.05$ ) were independent explanatory factors for the maternal total testosterone levels. Maternal age ( $\beta = -0.34, P < 0.001$ ), weight gain ( $\beta = 0.19, P < 0.05$ ) and amniotic fluid cortisol levels ( $\beta = 0.44, P < 0.001$ ) were independent explanatory factors of amniotic fluid testosterone in female fetuses, explaining 64.3% of the variability in amniotic fluid testosterone.

**WIDER IMPLICATIONS OF THE FINDINGS:** Young maternal age and excessive maternal weight gain may increase the prenatal androgen exposure of female fetuses. Further studies are needed to explore this finding.

<https://www.ncbi.nlm.nih.gov/pubmed/28705923>

## 121. QTL Mapping Of Stress Related Gene Expression In A Cross Between Domesticated Chickens And Ancestral Red Junglefowl.

2017 – Molecular and Cellular Endocrinology

Keywords: Hormonal analysis, UPC2

### Abstract

Domestication of animals is associated with numerous alterations in physiology, morphology, and behavior. Lower reactivity of the hypothalamic-pituitary-adrenal (HPA) axis and reduced fearfulness is seen in most studied domesticates, including chickens. Previously we have shown that the physiological stress response as well as expression levels of hundreds of genes in the hypothalamus and adrenal glands are different between domesticated White Leghorn and the progenitor of modern chickens, the Red Junglefowl. To map genetic loci associated with the transcription levels of genes involved in the physiological stress response, we conducted an eQTL analysis in the  $F_{12}$  generation of an inter-cross between White Leghorn and Red Junglefowl. We selected genes for further studies based on their known function in the regulation of the HPA axis or sympathoadrenal (SA) system, and measured their expression levels in the hypothalamus and the adrenal glands after a brief stress exposure (physical restraint). The expression values were treated as quantitative traits for the eQTL mapping. The plasma levels of corticosterone were also assessed. We analyzed the correlation between gene expression and corticosterone levels and mapped eQTL and their potential effects on corticosterone levels. The effects on gene transcription of a previously found QTL for corticosterone response were also investigated. The expression levels of the glucocorticoid receptor (GR) in the hypothalamus and several genes in the adrenal glands were correlated with the post-stress levels of corticosterone in plasma. We found several cis- and trans-acting eQTL for stress-related genes in both hypothalamus and adrenal. In the hypothalamus, one eQTL for c-FOS and one QTL for expression of GR were found. In the adrenal tissue, we identified eQTL for the genes NR0B1, RGS4, DBH, MAOA, GRIN1, GABRB2, GABRB3,

and HSF1. None of the found eQTL were significant predictors of corticosterone levels. The previously found QTL for corticosterone was associated with GR expression in hypothalamus. Our data suggests that domestication related modification in the stress response is driven by changes in the transcription levels of several modulators of the HPA and SA systems in hypothalamus and adrenal glands and not by changes in the expression of the steroidogenic genes. The presence of eQTL for GR in hypothalamus combined with the negative correlation between GR expression and corticosterone response suggests GR as a candidate for further functional studies regarding modification of stress response during chicken domestication.

<https://www.ncbi.nlm.nih.gov/pubmed/28189567>

## 122. Tandem Mass Spectrometry Determined Maternal Cortisone To Cortisol Ratio And Psychiatric Morbidity During Pregnancy-Interaction With Birth Weight.

2017 – Scientific Reports

Keywords: steroids, cortisol, cortisone, UPC2

### Abstract

Maternal serum cortisol has been suggested to be influenced by psychiatric morbidity, and may also influence fetal growth. However, several studies found equal cortisol levels in depressed and healthy pregnant women. Placental 11- $\beta$ -hydroxysteroid dehydrogenase type 2 (11 $\beta$ -HSD2) shields the fetus from maternal cortisol by conversion to cortisone, a function that may be compromised by maternal stress. We aimed to compare the serum ratio of cortisone to cortisol, in women with and without psychiatric morbidity during pregnancy. A secondary aim was to investigate whether fetal growth, approximated by infant birth weight, was associated with the cortisone to cortisol ratio. We performed tandem mass spectrometry analysis of serum cortisol and cortisone in late pregnancy in 94 women with antenatal psychiatric morbidity and 122 controls (cohort 1). We also compared the placental gene expression of HSD11B1 and 2 in another group of 69 women with psychiatric morbidity and 47 controls (cohort 2). There were no group differences in cortisol to cortisone ratio, absolute levels of cortisone and cortisol (cohort 1), or expression of HSD11B1 or 2 (cohort 2). However, cortisone to cortisol ratio was positively associated with birth weight in women with psychiatric morbidity, also after adjustment for gestational length, fetal sex, maternal height, smoking, SSRI use, and time of blood sampling (standardized  $\beta=0.35$ ,  $p<0.001$ ), with no association in the healthy controls. Thus, the maternal serum cortisone to cortisol ratio does not seem to be affected by psychiatric morbidity, but psychiatric morbidity may increase fetal exposure to cortisol or other metabolic factors influencing fetal growth.

<https://www.ncbi.nlm.nih.gov/pubmed/27088373>

## 123. Domestication Effects On Stress Induced Steroid Secretion And Adrenal Gene Expression In Chickens

2017 – Scientific Reports

Keywords: Steroids, UPC2

### Abstract

Understanding the genetic basis of phenotypic diversity is a challenge in contemporary biology. Domestication provides a model for unravelling aspects of the genetic basis of stress sensitivity. The ancestral Red Junglefowl (RJF) exhibits greater fear-related behaviour and a more pronounced HPA-axis reactivity than its domesticated counterpart, the White Leghorn (WL). By comparing hormones (plasmatic) and adrenal global gene transcription profiles between WL and RJF in response to an acute stress event, we investigated the molecular basis for the altered physiological stress responsiveness in domesticated chickens. Basal levels of pregnenolone and dehydroepiandrosterone as well as corticosterone response were lower in WL. Microarray analysis of gene expression in adrenal glands showed a significant breed effect in a large number of transcripts with over-representation of genes in the channel activity pathway. The expression of the best-known steroidogenesis genes were similar across the breeds used. Transcription levels of acute stress response genes such as *StAR*, *CH25* and *POMC* were upregulated in response to acute stress. Dampened HPA reactivity in domesticated chickens was associated with changes in the



expression of several genes that presents potentially minor regulatory effects rather than by means of change in expression of critical steroidogenic genes in the adrenal.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4608001/>

## 124. The Utility Of Ultra High Performance Supercritical Fluid Chromatography For The Analysis Of Seized Drugs: Application To Synthetic Cannabinoids And Bath Salts

2017 - U.S. Department of Justice Report

### Project Purpose

The purpose of this project is to investigate the role of ultra high performance supercritical fluid chromatography (UHPSFC) as a separation technique for forensic drug analysis. For this reason the challenging separation of emerging drugs such as synthetic cannabinoids and bath salts will be investigated. Emerging drugs contain similar solutes such as analogues, homologues, positional isomers, and stereoisomers. The latter two classes of compounds can present particularly difficult separation challenges for which UHPSFC appears well suited. An additional goal of this study is to establish UHPSFC as a viable separation technique (recognized as a Category B test by SWGDRUG) comparable to already established techniques for the separation of emerging drugs. For UHPSFC, validated methods for the determination of synthetic cannabinoids and synthetic cathinones (bath salts) in seized exhibits using UV-PDA detection and single-quad MS detection will be developed.

Project Design Experiments were designed to answer the question whether UHPSFC is a viable technique for forensic drug analysis, and whether as expected it is particularly well suited, compared to conventional techniques, for the separation of closely related substances (analogues, homologues, positional isomers, and diastereomers), which are present in emerging drug exhibits. The study consisted of three phases. For the first phase, using a UHPSFC instrument equipped with a PDA-UV detector and a single-quad mass spectrometric detector, optimum chromatographic and detector conditions were established for the separation of selected synthetic cannabinoids and substituted cathinones.

<https://www.ncjrs.gov/pdffiles1/nij/grants/250512.pdf>

## 125. Comparison Of Ultra High Performance Supercritical Fluid Chromatography, Ultra High Performance Liquid Chromatography, And Gas Chromatography For The Separation Of Synthetic Cathinones

2017 – Journal of Separation Science

### Abstract

A comparison of ultra high performance supercritical fluid chromatography, ultra high performance liquid chromatography, and gas chromatography for the separation of synthetic cathinones has been conducted. Nine different mixtures of bath salts were analyzed in this study. The three different chromatographic techniques were examined using a general set of controlled synthetic cathinones as well as a variety of other synthetic cathinones that exist as positional isomers. Overall 35 different synthetic cathinones were analyzed. A variety of column types and chromatographic modes were examined for developing each separation. For the ultra high performance supercritical fluid chromatography separations, analyses were performed using a series of Torus and Trefoil columns with either ammonium formate or ammonium hydroxide as additives, and methanol, ethanol or isopropanol organic solvents as modifiers. Ultra high performance liquid chromatographic separations were performed in both reversed phase and hydrophilic interaction chromatographic modes using SPP C18 and SPP HILIC columns. Gas chromatography separations were performed using an Elite-5MS capillary column. The orthogonality of ultra high performance supercritical fluid chromatography, ultra high performance liquid chromatography, and gas chromatography was examined using principal component analysis. For the best overall separation of synthetic cathinones, the use of ultra high performance supercritical fluid chromatography in combination with gas chromatography is recommended.

<https://doi.org/10.1002/jssc.201700349>



## 126. Ultra - High Performance Supercritical Fluid Chromatography Of Lignin - Derived Phenols From Alkaline Cupric Oxide Oxidation

2017 – Journal of Separation Science

Keywords: CuO oxidation, Humic acid, Lignin, Phenolic compounds, Ultra-high performance supercritical fluid chromatography

### Abstract

Traditional chromatographic methods for the analysis of lignin-derived phenolic compounds in environmental samples are generally time consuming. In this work, an ultra-high performance supercritical fluid chromatography method with a diode array detector for the analysis of major lignin-derived phenolic compounds produced by alkaline cupric oxide oxidation was developed. In an analysis of a collection of 11 representative monomeric lignin phenolic compounds, all compounds were clearly separated within 6 min with excellent peak shapes, with a limit of detection of 0.5–2.5  $\mu\text{M}$ , a limit of quantification of 2.5–5.0  $\mu\text{M}$ , and a dynamic range of 5.0–2.0 mM ( $R^2 > 0.997$ ). The new ultra-high performance supercritical fluid chromatography method was also applied for the qualitative and quantitative analysis of lignin-derived phenolic compounds obtained upon alkaline cupric oxide oxidation of a commercial humic acid. Ten out of the previous eleven model compounds could be quantified in the oxidized humic acid sample. The high separation power and short analysis time obtained demonstrate for the first time that supercritical fluid chromatography is a fast and reliable technique for the analysis of lignin-derived phenols in complex environmental samples.

<https://doi.org/10.1002/jssc.201600169>

## 127. Ultra-High-Performance Supercritical Fluid Chromatography As A Separation Tool For *Fusarium* mycotoxins And Their Modified Forms

2017 - Journal of AOAC International

Keywords: Beer, NIV, DON, 3-ADON, 15-ADON, DON-3G, NEO, DAS, T-2, HT-2, T-2-3G, ZEN, a-ZEL, and b-ZEL, UPC2, multi-mycotoxin analysis

### Abstract

A simple, reliable method for the detection of free and modified *Fusarium* mycotoxins in beer using state-of-the-art ultra-high-performance supercritical fluid chromatography (UHPSFC) with low-resolution tandem MS (MS/MS) is presented in this paper. The UHPSFC-MS/MS method was developed for nivalenol, deoxynivalenol, 15-acetyl-deoxynivalenol, 3-acetyl-deoxynivalenol, deoxynivalenol-3-glucoside, HT-2 toxin, T-2 toxin, T-2 toxin-3-glucoside, neosolaniol, diacetoxyscirpenol, zearalenone,  $\alpha$ -zearalenol, and  $\beta$ -zearalenol and their internal standards deepoxy-deoxynivalenol and zearalanone. Due to the broad range of the physicochemical properties of the aforementioned, the sample preparation step was minimized to avoid analyte losses. Extraction with acetonitrile–water–acetic acid (79 + 20 + 1, v/v/v) and hexane in combination with solid-phase extraction (C18) was followed by a filtration step. After filtration, the extract was evaporated, and the remaining residue was redissolved in a mobile phase for injection (methanol–water; 90 + 10, v/v). A mobile phase consisting of supercritical CO<sub>2</sub> and a small portion of methanol was used. The developed multimycotoxin method permits the simultaneous determination of multiple fusariotoxins in a one-step chromatographic run using UHPSFC-MS/MS. SFC is a promising strategy; however, the retention mechanism is complex, leading to the unpredictable nature of elution and to some mycotoxins not being retained on the column. This restricts the applicability of UHPSFC in multimycotoxin analyses. The present study is the first report on the use of UHPSFC for the analysis of free and modified *Fusarium* mycotoxins.

<https://doi.org/10.5740/jaoacint.17-0336>

## 128. Enantioseparation Of Nornicotine In Tobacco By Ultraperformance Convergence Chromatography With Tandem Mass Spectrometry

2017 – Journal of Separation Science

Keywords: Tobacco, UPC2

### Abstract

Nornicotine, an alkaloid constituent of tobacco, is a precursor to the carcinogen *N*-nitrosornicotine that is produced during the curing and processing of tobacco. Accumulating evidence reveals that nornicotine enantiomers have different neurochemical and behavioral

effects. In the present study, an accurate and rapid method was developed for the enantioseparation of (*R*)-(+)-nornicotine and (*S*)-(–)-nornicotine enantiomers in tobacco by ultraperformance convergence chromatography with tandem mass spectrometry. Chromatographic conditions were investigated to achieve the optimal resolution of two enantiomers. Results indicated that (*R*)-(+)-nornicotine and (*S*)-(–)-nornicotine could be separated within 5 min when ammonium hydroxide was added into the co-solvent, and the best resolution ( $R_s = 4.76$ ) was achieved on a immobilized cellulose tri(*S*)-(3,5-dichlorophenylcarbamate) chiral stationary phase. The proposed method was validated and was finally applied to analyze the compositions of (*R*)-(+)-nornicotine and (*S*)-(–)-nornicotine in three typical types of tobaccos (flue-cured, burley, and oriental). It was found that, enantiomer fraction of nornicotine (the proportion of (*S*)-(–)-nornicotine in the nornicotine pool) in burley tobacco samples was relatively high and constant compared with flue-cured and oriental tobaccos. The effective and rapid enantioseparation of nornicotine may help the understanding of alkaloids metabolites in different tobacco varieties and may also benefit pharmacological studies of alkaloid enantiomers.

<https://doi.org/10.1002/jssc.201700759>

### 129. Simultaneous Analysis Of Perfluoroalkyl And Polyfluoroalkyl Substances Including Ultrashort-Chain C2 And C3 Compounds In Rain And River Water Samples By Ultra Performance Convergence Chromatography

2017 - Journal of Chromatography A

Keywords: PFAS, Short-chain, Chromatography, Supercritical fluid chromatography (SFC), Trifluoroacetate (TFA)

#### Abstract

An analytical method using ultra performance convergence chromatography (UPC<sup>2</sup>) coupled to a tandem mass spectrometer operated in negative electrospray mode was developed to measure perfluoroalkyl and polyfluoroalkyl substances (PFASs) including the ultrashort-chain PFASs (C2-C3). Compared to the existing liquid chromatography tandem mass spectrometry method using an ion exchange column, the new method has a lower detection limit (0.4 pg trifluoroacetate (TFA) on-column), narrower peak width (3–6 s), and a shorter run time (8 min). Using the same method, different classes of PFASs (e.g., perfluoroalkyl sulfonates (PFASs) and perfluorinated carboxylates (PFCAs), perfluorinated phosphonates (PFPA) and phosphinates (PFPIAs), polyfluoroalkyl phosphate diesters (diPAPs)) can be measured in a single analysis. Rain ( $n = 2$ ) and river water ( $n = 2$ ) samples collected in Toronto, ON, were used for method validation and application. Results showed that short-chain PFAS (C2-C7 PFCAs and C4 PFSA) contributed to over 80% of the detectable PFASs in rain samples and the C2-C3 PFASs alone accounted for over 40% of the total. Reports on environmental levels of these ultrashort-chain PFASs are relatively scarce. Relatively large contribution of these ultrashort-chain PFASs to the total PFASs indicate the need to include the measurement of short-chain PFASs, especially C2 and C3 PFASs, in environmental monitoring. The sources of TFA and other short-chain PFASs in the environment are not entirely clear. The newly developed analytical method may help further investigation on the sources and the environmental levels of these ultrashort-chain PFASs.

<https://doi.org/10.1016/j.chroma.2017.09.049>

### 130. Step Economy Strategy For The Synthesis Of Amphoteric Aminoaldehydes, Key Intermediates For Reduced Hydantoins

2017 – Pure and Applied Chemistry

Keywords: amphoteric aminoaldehydes, aziridination, hydantoin, ICGC-6, organocatalysis, step economy

#### Abstract

Despite of the orthogonal reactivity of the N–H aziridines aldehyde, these compounds exist as an equilibrium of three different forms – whereas the dimeric one is mostly observed in a variety of solvents. In this work, we have developed an alternative protocol for the aminoaldehyde dimers synthesis in two steps starting with an organocatalyzed aziridination between  $\alpha,\beta$ -unsaturated aldehydes and a protected amine to afford known isolable and stable *N*-protected aziridine aldehydes. After Boc-deprotection, dimeric species were immediately formed from monomeric N–H

aziridine aldehydes. From this building-block new reduced hydantoins were prepared via [3+2]-annulation with isocyanates.

<https://doi.org/10.1515/pac-2017-0705>

### 131. Supercritical Fluid Chromatography In Traditional Chinese Medicine Analysis

2017 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: Supercritical fluid chromatography, Traditional chinese medicines, Achiral separations  
**Abstract**

Traditional Chinese medicines (TCMs) are gaining increasing popularity throughout the world due to their long historical clinical practices. Highly efficient analytical separation tools are essential for investigating the mysterious properties of TCMs and their quality control. Supercritical fluid chromatography (SFC) showed a great potential in TCM analysis for both nonpolar and polar components. In this paper, an overview of the experimental conditions (i.e. detection mode, stationary phase, mobile phase composition, pressure and temperature) used in SFC for achiral separations of TCM components is presented and recent applications to the analysis of different classes of compounds extracted from TCMs, such as lipids, terpene and terpenoids, phenolic compounds, flavonoids, alkaloids, saponins and carbohydrates, will be briefly described.

<https://doi.org/10.1016/j.jpba.2017.08.021>

### 132. Consequences Of Transition From Liquid Chromatography To Supercritical Fluid Chromatography On The Overall Performance Of A Chiral Zwitterionic Ion-Exchanger

2017 - Journal of Chromatography A

Keywords: Enantioseparation, Supercritical fluid chromatography, High performance liquid chromatography, Enhanced-fluidity mobile phase, Amino acids, Transient acid

#### **Abstract**

Major differences in the chromatographic performance of a zwitterion ion-exchange type (ZWIX) chiral stationary phase (CSP) in supercritical fluid chromatography (SFC) and high-performance liquid chromatography (HPLC) have been observed. To explain these differences, transition from HPLC to SFC conditions has been performed. The amount of a protic organic modifier in supercritical carbon dioxide (scCO<sub>2</sub>) was stepwise increased and the effect of this change studied using acidic, basic and ampholytic analytes. At the same time, the effect of various basic additives to the mobile phase and transient acidic buffer species, formed by the reaction of scCO<sub>2</sub> with the organic modifier and additives, was assessed. Evidence is provided that a transient acid together with the intrinsic counter-ions present in the ZWIX selector structure drive the elution of analytes even when no buffer is employed. We show that the tested analytes can be enantioseparated under both SFC and HPLC conditions; the best conditions for the resolution of ampholytes are in the so-called enhanced-fluidity mobile phase region. As a consequence, subcritical fluid and enhanced-fluidity mobile phase regions seem to be chromatographic modes with a high potential for operating ZWIX CSPs.

<https://doi.org/10.1016/j.chroma.2017.08.022>

### 133. Recent Advances On HPLC/MS In Medicinal Plant Analysis—An Update Covering 2011–2016

2017 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: Liquid chromatography, SFC, Mass spectrometry, LC–MS, Medicinal plants, Natural products, Analysis

#### **Abstract**

The separation, identification and quantification of constituents in complex plant extracts always has been, and most likely will be, a challenging task. Nevertheless, today a multiplicity of different separation techniques, specific stationary phases and detectors are available, helping to achieve the desired selectivity, sensitivity and speed for nearly any separation problem. The most prominent and popular technique in this area of research is definitely the combination of liquid chromatography and mass spectrometry. More than 40 years after its beginning LC–MS can be

considered a well-established routine technique, however there is a steady advancement in terms of instrumentation (ultra-high-performance LC, ion mobility MS, etc.), the hyphenation of different techniques (supercritical fluid chromatography – mass spectrometry, two-dimensional techniques, etc.), or the type of analyzed compounds (novel applications). The here presented review aims to consider all of these aspects, focusing on natural products/medicinal plants related LC–MS papers published within the years 2011–2016. It gives a short overview of recent technical trends as well summarizes the most relevant applications ordered by the type of natural products assessed (e.g. acids, alkaloids, flavonoids, terpenes). The respective reports are also differentiated according to the studies purpose (analysis of plant material or pharmacological investigation) and a special chapter is devoted to Traditional Chinese Medicine. For selected reports relevant methodological details are provided and limitations or advantages discussed, so that the current status of LC–MS for natural products analysis is reflected comprehensively.

<https://doi.org/10.1016/j.jpba.2017.07.038>



### 134. Investigation Of The Effect Of Column Temperature And Back-Pressure In Achiral Supercritical Fluid Chromatography Within The Context Of Drug Impurity Profiling

2017 - Journal of Chromatography A

Keywords: Dissimilar stationary phases, Response surface design, Retention prediction, Separation optimization, Chromatographic efficiency

#### Abstract

Twenty commercially available stationary phases were characterized in supercritical fluid chromatography (SFC) using a diverse set of pharmaceutical compounds. Six dissimilar phases were selected, and a benzodiazepine and a trimethoprim impurity mixture were screened on these phases. Two stationary phases were then selected for each mixture to study the effect of temperature and back-pressure on retention, separation and chromatographic efficiency using a response surface design approach. The maximal feasible domain for each phase was examined and column performance was monitored for stability during the duration of the study. Chromatographic responses of the individual mixture components, such as retention time, peak width and apparent plate count, were modeled as a function of temperature and back-pressure. The use of high temperatures led to improved separations and higher efficiencies while high back-pressures resulted in reduced retention. For the two mixtures, the response surface plots of the resolution of the worst-separated peak pair over the experimental domain allowed the identification of the temperature and back-pressure leading to the maximal resolution for the worst-separated peak pair. For the mixtures investigated, the use of high temperatures led to improved separations and high efficiencies, while high back-pressures resulted in reduced retention. These factors are fine-tuning parameters in SFC, and similarly to the modifier composition, they lead to local, rather than global selectivity differences.

<https://doi.org/10.1016/j.chroma.2017.08.008>

### 135. Determination Of Fat- And Water-Soluble Vitamins By Supercritical Fluid Chromatography: A Review

2017 – Journal of Separation Science

Keywords: **LSER**, linear solvation energy relationships, **SMB**, simulated moving bed, **UPC<sup>2</sup>**, ultra-performance convergence chromatography

#### Abstract

Vitamins are compounds that take part in all basic functions of an organism but also are subject of number of studies performed by different researchers. Two groups of vitamins are distinguished taking into consideration their solubility. Chromatography with supercritical CO<sub>2</sub> has found application in the determination, separation, and quantitative analyses of both fat- and water-soluble vitamins. The methods of vitamins separation have developed and improved throughout the years. Both groups of compounds were separated using supercritical fluid chromatography with different detection on different stationary phases. The main aim of this review is to provide an overview of the studies of vitamins separation that have been determined so far.

<https://doi.org/10.1002/jssc.201700598>

### 136. Is Supercritical Fluid Chromatography Hyphenated To Mass Spectrometry Suitable For The Quality Control Of Vitamin D3 Oily Formulations?

2017 - Journal of Chromatography A

Keywords: SFC-MS, Green analytical chemistry, Vitamin D3, Method validation, Accuracy profile

#### Abstract

Nowadays, many efforts are devoted to improve analytical methods regarding efficiency, analysis time and greenness. In this context, Supercritical Fluid Chromatography (SFC) is often regarded as a good alternative over Normal Phase Liquid Chromatography (NPLC). Indeed, modern SFC separations are fast, efficient with suitable quantitative performances. Moreover, the hyphenation of SFC to mass spectrometry (MS) provides additional gains in specificity and sensitivity. The present work aims at the determination of vitamin D3 by SFC-MS for routine Quality Control (QC) of medicines specifically. Based on the chromatographic parameters previously defined in SFC-UV by Design of Experiments (DoE) and Design Space methodology, the method was adapted to work under isopycnic conditions ensuring a baseline separation of the compounds. Afterwards, the response provided by the MS detector was optimized by means of DoE methodology associated to desirability functions. Using these optimal MS parameters, quantitative performances of the SFC-MS method were challenged by means of total error approach method validation. The resulting accuracy profile demonstrated the full validity of the SFC-MS method. It was indeed possible to meet the specification established by the European Medicines Agency (EMA) (i.e. 95.0 – 105.0% of the API content) for a dosing range corresponding to at least 70.0-130.0% of the API content. These results highlight the possibility to use SFC-MS for the QC of medicine and obviously support the switch to greener analytical methods.

<https://doi.org/10.1016/j.chroma.2017.07.057>

### 137. Ultra-High Performance Supercritical Fluid Chromatography-Mass Spectrometry Procedure For Analysis Of Monosaccharides From Plant Gum Binders

2017 - Analytica Chimica Acta

Keywords: Supercritical fluid chromatography, Mass spectrometry, Microwave-assisted hydrolysis, Monosaccharide, Plant gum, Watercolor

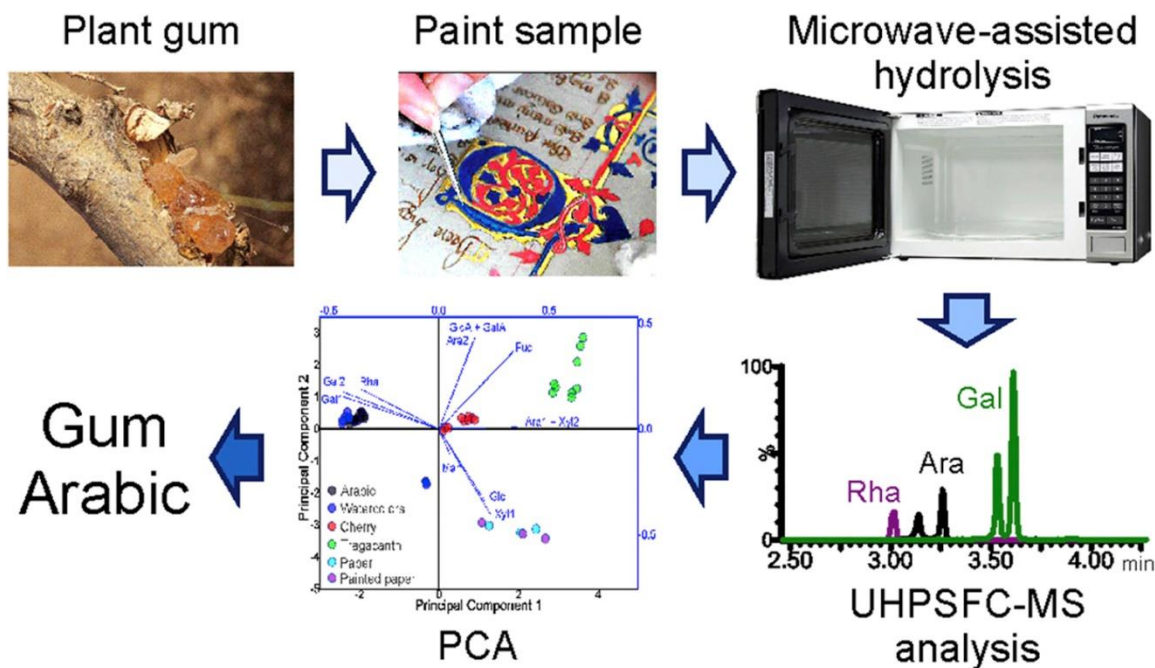
#### Abstract

The ultra-high performance supercritical fluid chromatography-mass spectrometry (UHPSFC/MS) procedure for analysis of native monosaccharides was developed. Chromatographic conditions were investigated to separate a mixture of four hexoses, three pentoses, two deoxyhexoses and two uronic acids. Increasing water content in methanol modifier to 5% and formic acid to 4% improved peak shapes of neutral monosaccharides and allowed complete elution of highly polar uronic acids in a single run. An Acquity HSS C18SB column outperformed other three tested stationary phases (BEH (silica), BEH 2-ethylpyridine, CSH Fluoro-Phenyl) in terms of separation of isomers and analysis time (4.5 min). Limits of detection were in the range 0.01–0.12 ng μL<sup>-1</sup>.



Owing to separation of anomers, identification of critical pairs (arabinose-xylose and glucose-galactose) was possible. Feasibility of the new method was demonstrated on plant-derived polysaccharide binders. Samples of watercolor paints, painted paper and three plant gums widely encountered in painting media (Arabic, cherry and tragacanth) were decomposed prior the analysis by microwave-assisted hydrolysis at 40 bar initial pressure using 2 mol L<sup>-1</sup> trifluoroacetic acid. Among tested temperatures, 120 °C ensured appropriate hydrolysis efficiency for different types of gum and avoided excessive degradation of labile monosaccharides. Procedure recovery tested on gum Arabic was 101% with an RSD below 8%. Aqueous hydrolysates containing monosaccharides in different ratios specific to each type of plant gum were diluted or analyzed directly. Filtration of samples before hydrolysis reduced interferences from a paper support and identification of gum Arabic in watercolor-painted paper samples was demonstrated. Successful identification of pure gum Arabic was confirmed for sample quantities as little as 1 µg. Two classification approaches were compared and principal component analysis was superior to analysis based on peak area ratios of monosaccharides. The proposed procedure using UHPSFC/MS represents an interesting alternative which can compete with other chromatographic methods in the field of saccharide analysis in terms of speed, sensitivity and simplicity of workflow.

<https://doi.org/10.1016/j.aca.2017.07.036>



### 138. Development And Comparison Of Quantitative Methods Using Orthogonal Chromatographic Techniques For The Analysis Of Potential Mutagenic Impurities

2017 – Chromatography Today Article

#### Introduction

There are many steps during the manufacturing process of an active pharmaceutical ingredient (API) where impurities can be introduced, whether as reagents, byproducts, intermediates, etc. Some of these impurities may be mutagenic, or have the potential to interact with DNA and ultimately cause carcinogenicity. Methodologies associated with monitoring API purity levels are often HPLC-UV based, which frequently do not provide the sensitivity levels needed to detect potentially mutagenic impurities (PMIs) at the levels required by regulatory agencies. For example, ondansetron is a pharmaceutical used in the prevention of nausea and vomiting and may contain one potential mutagenic impurity, 2-methylimidazole, as well as a second impurity very closely related in structure, imidazole.



Similar to 2-methylimidazole and imidazole, many mutagenic impurities are small, highly polar compounds that are poorly retained under typical reversed phase liquid chromatography (RPLC) conditions. Alternate forms of chromatography, such as hydrophilic interaction chromatography (HILIC), or the use of ion-pairing reagents can be employed, but these often result in tedious method development or non-MS friendly mobile phases. Supercritical fluid chromatography (SFC) is known to be orthogonal to RPLC, and employs reagents which are suitable for MS detection. In this study, methods for the analysis of ondansetron and five organic impurities were developed using both liquid and supercritical fluid chromatographic methods. Both chromatographic techniques generated high sensitivity methods that met the required limits of detection and both techniques showed good accuracy and reproducibility.

<https://www.chromatographytoday.com/article/bioanalytical/40/waters-corporation/development-and-comparison-of-quantitative-methods-using-orthogonal-chromatographic-techniques-for-the-analysis-of-potential-mutagenic-impurities/2203>

### 139. Enantiomeric Separation And Quantification Of Citalopram In Serum By Ultra-High Performance Supercritical Fluid Chromatography-Tandem Mass Spectrometry

2017 – Journal of Chromatography B

Keywords: UHPSFC-MS/MS, Citalopram, Enantiomeric, Serum, Therapeutic drug monitoring

#### Abstract

A method for enantiomeric separation and quantification of R/S-citalopram in serum was developed and validated using ultra-high performance supercritical fluid chromatography-tandem mass spectrometry (UHPSFC-MS/MS). Sample preparation prior to UHPSFC-MS/MS analysis consisted of protein precipitation with acidic acetonitrile and filtration through a phospholipid removal plate. The UHPSFC-MS/MS method used an UPC<sup>2</sup> Trefoil CEL2 column with a mobile phase consisting of CO<sub>2</sub> and methanol/acetonitrile (70:30, v/v) with 10 mM ammonium acetate. The injection volume was 1 µL and run time was 4 min. MS/MS detection was performed with positive electrospray ionization and two multiple reaction monitoring transitions ( $m/z$  325.1 > 262.0 and  $m/z$  325.1 > 109.0). The calibration range was 5–500 nM for each analyte. The between-assay relative standard deviations were in the range of 3.4–4.5%. Recovery was 81–91% and matrix effects ranged from 96 to 101% (corrected with internal standard). After development and initial testing, the method has been successfully implemented in routine use in our laboratory for both separation and quantification of R/S-citalopram in more than 250 serum samples for therapeutic drug monitoring.

<https://doi.org/10.1016/j.jchromb.2017.07.009>

### 140. Coupling Supercritical Fluid Chromatography To Positive Ion Atmospheric Pressure Ionization Mass Spectrometry: Ionization Optimization Of Halogenated Environmental Contaminants

2017 - International Journal of Mass Spectrometry

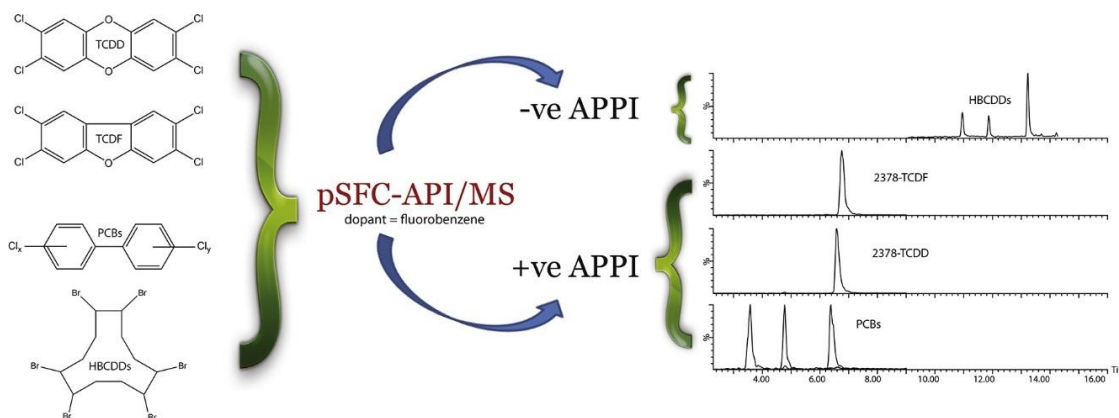
Keywords: SFC, Positive APPI-MS, Environmental contaminants, PCDD, PCDF, PCB

#### Abstract

Currently used analytical techniques for halogenated aromatic environmental contaminants such as polychlorinated dibenzo-*p*-dioxins (PCDDs), dibenzofurans (PCDFs), and biphenyls (PCBs), also known as legacy persistent organic pollutants, are based on gas chromatographic separation of target analytes and detection by mass spectrometry. The coupling of packed column supercritical fluid chromatography (SFC) to atmospheric pressure ionization mass spectrometry (API/MS) could allow for the concurrent analysis of thermally labile and legacy halogenated environmental contaminants if ionization can be sufficiently optimized. The evaluation of positive ion atmospheric pressure chemical ionization (APCI) and atmospheric pressure photoionization (APPI) as well as possible charge transfer dopants for the generation of molecular ion isotopomeric clusters of halogenated environmental contaminants with minimal fragmentation has been completed. Using the investigated parameters, positive ion APPI was found to be the more sensitive technique. Of the aromatic and cycloalkane dopants investigated, only fluorobenzene and trifluorotoluene were found to be effective dopants for the halogenated aromatic target analytes (PCDDs, PCDFs, and

PCBs). Experiments involving deuterated dopants confirmed that reactive species generated by cycloalkanes were quenched by the SFC eluent rendering them unusable in conjunction with the investigated separation technique. Alternatively, aromatic dopants were found to be less susceptible to quenching by the SFC eluent and fluorobenzene was determined to be the most effective charge transfer dopant for PCDDs, PCDFs, and PCBs. To demonstrate the applicability of the optimized ionization conditions, SFC-API/MS has been used for the concurrent analysis of legacy halogenated aromatic environmental contaminants (PCDDs, PCDFs, and PCBs) and thermally labile analytes ( $\alpha$ ,  $\beta$ , and  $\gamma$  isomers of hexabromocyclododecane).

<https://doi.org/10.1016/j.ijms.2017.07.005>



### 141. Analysis Of Oxylipins In Human Plasma: Comparison Of Ultrahigh-Performance Liquid Chromatography And Ultrahigh-Performance Supercritical Fluid Chromatography Coupled To Mass Spectrometry

2017 – Journal of Chromatography A

Keywords: Oxylipin, Eicosanoid, Prostaglandin, Plasma, UHPSFC/MS, UHPLC/MS, SPE, ESI

#### Abstract

The potential of ultrahigh-performance liquid chromatography–mass spectrometry (UHPLC/MS) and ultrahigh-performance supercritical fluid chromatography (UHPSFC) coupled to negative-ion electrospray ionization mass spectrometry (ESI–MS) for the analysis of 46 oxylipins and 2 fatty acid standards is compared in terms of their chromatographic resolution with the emphasis on distinguishing isobaric interferences and the method sensitivity. UHPLC provides the baseline separation of 24 isobaric oxylipins within 13 min, while UHPSFC enables the separation of only 20 isobaric oxylipins within 8 min. Moreover, the UHPLC/ESI–MS method provides an average improvement of sensitivity by 3.5-fold. A similar trend is observed in the analysis of human plasma samples, but lower ion suppression effects caused by lysophospholipids (LPL) are observed in case of UHPSFC/ESI–MS due to better separation of LPL. Both methods are fully applicable for the analysis of oxylipins, but UHPLC/ESI–MS method is preferred due to better separation and higher sensitivity, which results in the identification of 31 oxylipins in human plasma based on available standards and additional tentative 20 identifications based on accurate  $m/z$  values and the fragmentation behavior known from the literature.

<https://doi.org/10.1016/j.chroma.2017.06.070>

### 142. A Systematic Investigation Of Sample Diluents In Modern Supercritical Fluid Chromatography

2017 – Journal of Chromatography A

Keywords: Supercritical fluid chromatography, Sample diluent, Peak shape, UHPSFC, Injection

#### Abstract

This paper focuses on the possibility to inject large volumes (up to 10  $\mu$ L) in ultra-high performance supercritical fluid chromatography (UHPSFC) under generic gradient conditions.

Several injection and method parameters have been individually evaluated (i.e. analyte concentration, injection volume, initial percentage of co-solvent in the gradient, nature of the weak needle wash solvent, nature of the sample diluent, nature of the column and of the analyte). The most critical parameters were further investigated using in a multivariate approach. The overall results suggested that several aprotic solvents including methyl *tert*-butyl ether (MTBE), dichloromethane, acetonitrile or cyclopentyl methyl ether (CPME) were well adapted for the injection of large volume in UHPSFC, while MeOH was generally the worst alternative. However, the nature of the stationary phase also had a strong impact and some of these diluents did not perform equally on each column. This was due to the existence of a competition in the adsorption of the analyte and the diluent on the stationary phase. This observation introduced the idea that the sample diluent should not only be chosen according to the analyte but also to the column chemistry to limit the interactions between the diluent and the ligands. Other important characteristics of the "ideal" SFC sample diluent were finally highlighted. Aprotic solvents with low viscosity are preferable to avoid strong solvent effects and viscous fingering, respectively. In the end, the authors suggest that the choice of the sample diluent should be part of the method development, as a function of the analyte and the selected stationary phase.

<https://doi.org/10.1016/j.chroma.2017.06.075>

### 143. The Effect Of High Concentration Additive On Chiral Separations In Supercritical Fluid Chromatography

2017 - Journal of Chromatography A

Keywords: Supercritical fluid chromatography, Polysaccharide stationary phases, Enantiomer elution order reversal, High concentration of additive

#### Abstract

Supercritical Fluid Chromatography is frequently used to efficiently handle separations of enantiomers. The separation of basic analytes usually requires the addition of a basic additive in the mobile phase to improve the peak shape or even to elute the compounds. The effect of increasing the concentration of 2-propylamine as additive on the elution of a series of basic compounds on a Chiralpak-AD stationary phase was studied. In this study, unusual additive concentrations ranging from 0.3% to 10% of 2-propylamine *2-propylamine* in the modifier were explored and the effect on retention, peak shape, selectivity and resolution was evaluated. The addition of a large quantity of additive allowed to drastically improve the selectivity and the resolution, and even enantiomers elution order reversal was observed by changing the concentration of basic additive. The role of the ratio additive/modifier appeared a key to tune the enantioselectivity. Finally, the impact of these drastic conditions on the column material was evaluated.

<https://doi.org/10.1016/j.chroma.2017.06.049>

### 144. Separation Of Furostanol Saponins By Supercritical Fluid Chromatography

2017 - Journal of Pharmaceutical and Biomedical Analysis

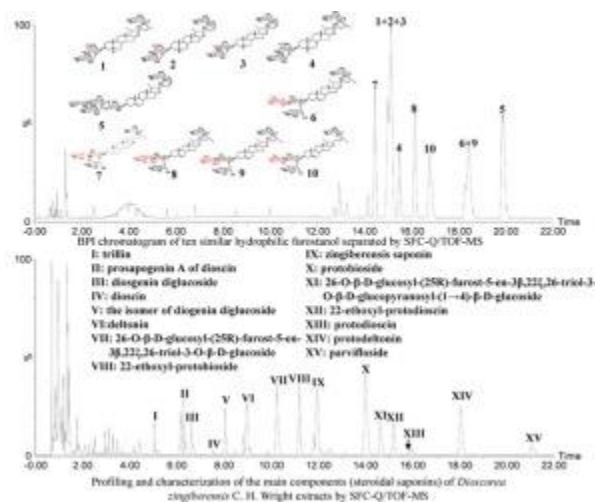
Keywords: Chromatographic behavior, Furostanol saponin, Methoxylation, Supercritical fluid chromatography

#### Abstract

Supercritical fluid chromatography (SFC) has good separation efficiency and is suitable for separating weakly polar compounds. Furostanol saponins, as an important kind of steroidal saponins, generally have two sugar chains, which are polar and hydrophilic. The hydroxyl group at the C-22 position of furostanol saponins is active and easily reacts with lower alcohols under appropriate conditions. The separation of hydrophilic furostanol saponins was tested by SFC in this study. The effects of chromatographic conditions on the separation of the mixed furostanol saponins and their hydroxyl derivatives at the C-22 position were studied. The conditions for SFC, which included different column polarity, modifier, additive, and column temperature, were tested. After optimization, the mixed 10 similar structures of furostanol saponins were separated in 22 min on the Diol column at a temperature of 40 °C. The mobile phase was CO<sub>2</sub> (mobile phase A) and methanol (containing 0.2% NH<sub>3</sub>·H<sub>2</sub>O and 3% H<sub>2</sub>O) (mobile phase B). The backpressure was maintained isobarically at 11.03 MPa. SFC was found to be effective in separating the furostanol

saponins that shared the same aglycone but varied in sugar chains. SFC was sensitive to the number and type of sugars. The resolution of furostanol saponin isomers was not ideal. The extract of *Dioscorea zingiberensis* C. H. Wright was profiled by SFC–quadrupole time-of-flight mass spectrometry. The main saponins of the extract were well separated. Therefore, SFC could be used for separating hydrophilic furostanol saponins and analyzing traditional Chinese medicines that mainly contained steroidal saponins.

<https://doi.org/10.1016/j.jpba.2017.05.023>



## 145. Purification Of Lignans From *Fructus Arctii* Using Off-Line Two-Dimensional Supercritical Fluid Chromatography/Reversed-Phase Liquid Chromatography

2017 - Journal of Separation Science

Keywords: lignans, reversed-phase liquid chromatography, supercritical fluid chromatography, traditional Chinese medicine, two-dimensional chromatography

### Abstract

As a common traditional Chinese medicine, *Fructus Arctii* has important clinical medical values. Its main components are lignans, which are difficult to separate and analyze because of the complex composition, similar chemical structures, and close properties. In this study, an off-line two-dimensional supercritical fluid chromatography/reversed-phase liquid chromatography method, as well as an effective sample pretreatment method based on hydrophilic interaction chromatography material, was developed to enrich the minor lignan fractions and obtain high-purity compounds. In total, 12 high-purity compounds were isolated from *Fructus Arctii*. Their structures were identified by using high-resolution mass spectrometry and nuclear magnetic resonance spectroscopy, which showed that all were lignans and that most of them were isomers. The results demonstrated the effective off-line two-dimensional supercritical fluid chromatography/reversed-phase liquid chromatography method for the purification of lignans from *Fructus Arctii*. The separation protocol established here will be beneficial for the separation of complex samples from other kinds of natural products.

<https://doi.org/10.1002/jssc.201700139>

## 146. Rapid Purification Of Diastereoisomers From *Piper Kadsura* Using Supercritical Fluid Chromatography With Chiral Stationary Phases

2017 - Journal of Chromatography A

Keywords: Chiral supercritical fluid chromatography, Achiral separation, Diastereoisomers, Purification, Piper kadsura

### Abstract

Supercritical fluid chromatography (SFC) with chiral stationary phases (CSPs) is an advanced solution for the separation of achiral compounds in *Piper kadsura*. Analogues and stereoisomers are abundant in natural products, but there are obstacles in separation using conventional method. In this paper, four lignan diastereoisomers, (-)-Galbelgin, (-)-Ganschisandrin, Galgravin and (-)-Veraguensin, from *Piper kadsura* were separated and purified by chiral SFC. Purification strategy was designed, considering of the compound enrichment, sample purity and purification throughput. Two-step achiral purification method on chiral preparative columns with stacked automated injections was developed. Unconventional mobile phase modifier dichloromethane (DCM) was applied to improve the sample solubility. Four diastereoisomers was prepared at the respective weight of 103.1 mg, 10.0 mg, 152.3 mg and 178.6 mg from 710 mg extract with the purity of greater than 98%.

<https://doi.org/10.1016/j.chroma.2017.06.020>

### 147. Rapid Determination Of 9 Aromatic Amines In Mainstream Cigarette Smoke By Modified Dispersive Liquid Liquid Microextraction And Ultraperformance Convergence Chromatography Tandem Mass Spectrometry

2017 – Journal of Chromatography A

Keywords: Aromatic amines, Dispersive liquid liquid microextraction, Ultraperformance convergence chromatography tandem mass spectrometry, Mainstream cigarette smoke

#### Abstract

Aromatic amines in mainstream cigarette smoke have long been monitored due to their carcinogenic toxicity. In this work, a reliable and rapid method was developed for the simultaneous determination of 9 aromatic amines in mainstream cigarette smoke by modified dispersive liquid liquid microextraction (DLLME) and ultraperformance convergence chromatography tandem mass spectrometry (UPC<sup>2</sup>-MS/MS). Briefly, the particulate phase of the cigarette smoke was captured by a Cambridge filter pad, and diluted hydrogen chloride aqueous solution is employed to extract the aromatic amines under mechanical shaking. After alkalization with sodium hydroxide solution, small amount of toluene was introduced to further extract and enrich aromatic amines by modified DLLME under vortexing. After centrifugation, toluene phase was purified by a universal QuEChERS cleanup kit and was finally analyzed by UPC<sup>2</sup>-MS/MS. Attributing to the superior performance of UPC<sup>2</sup>-MS/MS, this novel approach allowed the separation and determination of 9 aromatic amines within 5.0 min with satisfactory resolution and sensitivity. The proposed method was finally validated using Kentucky reference cigarette 3R4F, and emission levels of targeted aromatic amines determined were comparable to previously reported methods. At three different spiked levels, the recoveries of most analytes were ranged from 74.01% to 120.50% with relative standard deviation (RSD) less than 12%, except that the recovery of *p*-toluidine at low spiked level and 3-aminobiphenyl at medium spiked level was 62.77% and 69.37% respectively. Thus, this work provides a novel alternative method for the simultaneous analysis of 9 aromatic amines in mainstream cigarette smoke.

<https://doi.org/10.1016/j.chroma.2017.05.056>

### 148. Development Of A Supercritical Fluid Chromatography Method With Ultraviolet And Mass Spectrometry Detection For The Characterization Of Biomass Fast Pyrolysis Bio Oils

2017 – Journal of Chromatography A

Keywords: Supercritical fluid chromatography, Mass spectrometry, Bio-oil, Fast pyrolysis, Complex sample

#### Abstract

The characterization of complex mixtures is a challenging issue for the development of innovative processes dedicated to biofuels and bio-products production. The huge number of compounds present in biomass fast pyrolysis oils combined with the large diversity of chemical functions represent a bottleneck as regards analytical technique development. For the extensive characterization of complex samples, supercritical fluid chromatography (SFC) can be alternative to usual separation techniques such as gas (GC) or liquid chromatography (LC). In this study, an approach is proposed to define the best conditions for the SFC separation of a fast pyrolysis bio-



oil. This approach was based on SFC data obtained directly from the bio-oil itself instead of selecting model compounds as usually done. SFC conditions were optimized by using three specific, easy-to-use and quantitative criteria aiming at maximizing the separation power. Polar stationary phases (ethylpyridine bonded silica) associated to a mix of acetonitrile and water as polarity modifier provided the best results, with more than 120 peaks detected in SFC-UV.  
<https://doi.org/10.1016/j.chroma.2017.06.003>

### 149. Routine Supercritical Fluid Chromatography Tandem Mass Spectrometry Method For Determination Of Vitamin K1 Extracted From Serum With A 96-Well Solid-Phase Extraction Method

2017 - Article - American Association for Clinical Chemistry

Keywords: LC, liquid chromatography; SFC, supercritical fluid chromatography; SFC-MS/MS, supercritical fluid chromatography–tandem mass spectrometry; CRM, certified reference material; DWP, deep-well plate; SPE, solid-phase extraction; BS, bovine serum; KEQAS, external quality assurance scheme for phyloquinone; PPT, protein precipitation; RLH, robotic liquid handler; UPC2, Ultra Performance Convergence Chromatography; ESI, electrospray ionization

#### Abstract

With the developed method, measurement of vitamin K1 level in patient serum samples can be performed rapidly and reliably. The method includes a semi-automated solid-phase extraction sample preparation method without the need of an evaporation step before quantification by supercritical fluid chromatography–tandem mass spectrometry (SFC-MS/MS). The method provides a faster analysis than that of LC-MS/MS, and in a period of 3 months, the method has been applied to analysis of >5000 samples. The method is suitable for use in high-throughput medical laboratories. The method allows high-throughput reliable determination of vitamin K1 in serum in the range 0.1–50 ng/mL.

<http://jalm.aaccjnls.org/content/jalm/early/2017/03/22/jalm.2016.021717.full.pdf>

### 150. General Screening And Optimization Strategy For Fast Chiral Separations In Modern Supercritical Fluid Chromatography

2017 - Analytica Chimica Acta

Keywords: Supercritical fluid chromatography, SFC, Chiral stationary phases, Organic modifier, Combined additive, Enantioselectivity, Pharmaceuticals

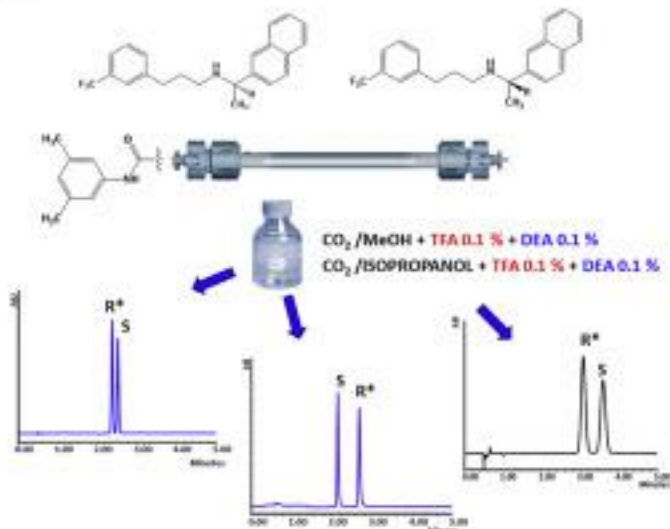
#### Abstract

High throughput general chiral screening method using supercritical fluid chromatography was developed. This method takes an advantage of very fast gradient screening (3 min + 1 min isocratic hold) and generic enantioselectivity of the combined additive formed by 0.1% trifluoroacetic (TFA) acid and 0.1% diethylamine (DEA). The TFA/DEA combined additive was systematically added to organic modifiers methanol and isopropanol. Among five tested polysaccharide-based chiral stationary phases, amylose tris(3,5-dimethylphenylcarbamate) and cellulose tris(3,5-dimethylphenylcarbamate) provided the best enantioseparation success rate. Therefore, the proposed initial first-line screening includes four experiments using these two stationary phases and the above mentioned two combinations: CO<sub>2</sub>/methanol and CO<sub>2</sub>/isopropanol + the combined additive. If these stationary phases fail in the screening step, cellulose tris(3-chloro-4-methylphenylcarbamate) and cellulose tris(3,5-dichlorophenylcarbamate) can be proposed for the screening in the second line.

For further optimization in case of insufficient resolution obtained in the screening phase fine tuning of temperature, BPR pressure and gradient slope was tested with unsuccessful results. An improvement of enantioselectivity was obtained only when gradient elution was replaced by isocratic elution with substantially lower amount of organic modifier, when changing the concentration of the additive or when using combined organic modifier, such as methanol/acetonitrile (1:1). Finally, to enable the MS compatibility, also volatile additives including ammonium formate and ammonium acetate were tested. The results were more encouraging than expected. Volatile buffers thus make an interesting option in chiral SFC screening methods, however, at the cost of somewhat lower enantioselectivity.

<http://dx.doi.org/10.1016/j.aca.2016.11.002>



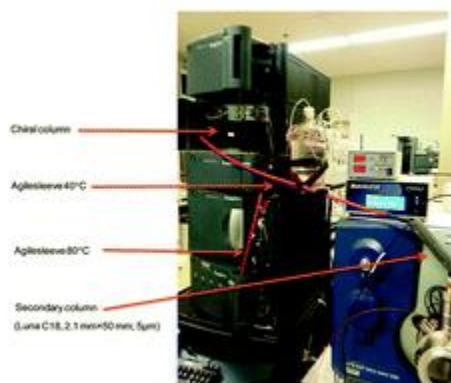


## 151. New Insights Into Supercritical Fluid Chromatography For Chiral Separations

2017 - Analytical Methods

### Abstract

Bioanalysis of stereoisomers represents a great challenge, as chromatographic separation is not feasible using conventional reversed or normal-phase chromatography. Supercritical fluid chromatography in combination with chiral stationary phases has proven to be a great tool for chiral resolution, alleviating some of the challenges associated with bioanalysis of stereoisomers. This technical note describes an alternative to the traditional SFC instrument configuration without the use of a back pressure regulator (BPR) and makeup pump; thereby simplifying its usage and improving the robustness and quality of measurements. This alternative configuration has been successfully employed in our laboratory for multiple chiral applications; in particular for the separation of *cis/trans* geometric stereoisomers. Four case studies are presented – one of which was validated demonstrating the robustness of the technology for bioanalytical applications. <http://dx.doi.org/10.1039/C7AY00452D>



## 152. The Application Of Green Solvents In Separation Processes - Chapter 16 – Supercritical Fluid Chromatography

2017 - Book Chapter

Keywords: Supercritical carbon dioxide; supercritical fluid chromatography; mass spectrometry; lipidomics; unified chromatography

### Abstract

Supercritical fluid chromatography (SFC) is a separation technique that characteristically a hybrid of both gas chromatography (GC) and liquid chromatography (LC). With the favorable properties of green solvent supercritical carbon dioxide (SCCO<sub>2</sub>) as the main mobile phase, SFC has gained much attraction for analyzing and separating a wide range of compounds. Having remarkable sensitivity and selectivity, mass spectrometer (MS) is widely hyphenated to SFC system. SFC coupled to MS (SFC/MS) approach offers comprehensive lipid analysis that has not been resolved due to the complexity of lipid constituents and the existing isomers. Therefore, SFC/MS has more potential for application in lipidomics field compared to other analytical platforms. The prowess of SFC/MS technology as integral part of green chemistry has also been demonstrated in various fields from food science to biomedical research.

<https://doi.org/10.1016/B978-0-12-805297-6.00016-4>

## 153. Plant Lipidomics At The Crossroads: From Technology To Biology Driven Science

2017 - Biochimica et Biophysica Acta (BBA) – Molecular and cell biology of Lipids

Keywords: Plant, lipidomics

### Abstract

The identification and quantification of lipids from plant tissues have become commonplace and many researchers now incorporate lipidomics approaches into their experimental studies. Plant lipidomics research continues to involve technological developments such as those in mass spectrometry imaging, but in large part, lipidomics approaches have matured to the point of being accessible to the novice. Here we review some important considerations for those planning to apply plant lipidomics to their biological questions, and offer suggestions for appropriate tools and practices. This article is part of a Special Issue entitled: BBALIP\_Lipidomics Opinion Articles edited by Sepp Kohlwein.

<https://doi.org/10.1016/j.bbaliip.2017.02.011>

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## 154. Examination Of Technical Mixtures Of Halogen-Free Phosphorus Based Flame Retardants Using Multiple Analytical Techniques

2017 - Chemosphere

Keywords: Organophosphate flame retardants (OPFRs); pSFC/MS method; NMR; RDBPP; BPA-BDPP; DOPO

### Abstract

Technical RDBPP, BPA-BDPP and DOPO mixtures were characterized using NMR.

pSFC/MS enabled fast separation and analysis of all OPFRs and impurities.

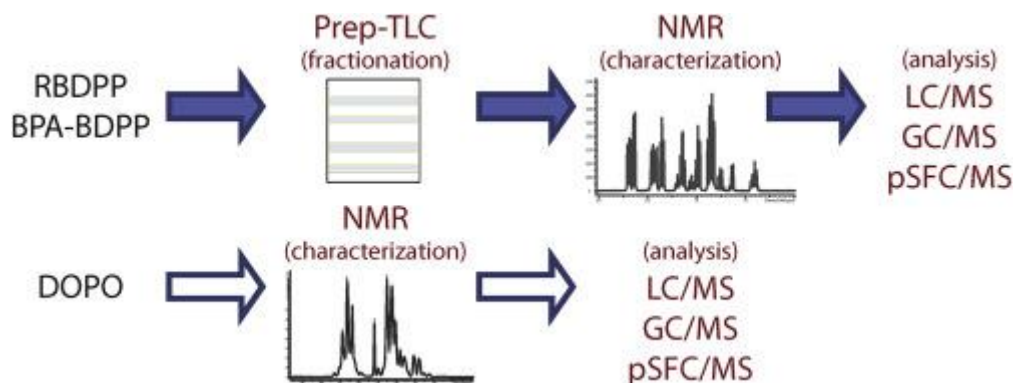
RDBPP, BPA-BDPP and DOPO mixtures were analyzed by multiple analytical techniques.

The application of phosphorus based flame retardants as replacements for commonly used halogenated flame retardants has been gaining interest due to the possibility that these compounds may have a less significant impact on human and environmental health.

Unfortunately, little is known about the chemical compositions of many of the technical products (which often are mixtures) and a single separation technique for concurrent analysis of these types of compounds has not been identified. This paper reports the results of an investigation into

the constituents of three halogen free organophosphate flame retardants (OPFRs), resorcinol bis(diphenyl phosphate) (RDBPP), bisphenol A bis(diphenyl phosphate) (BPA-BDPP), and 9,10-dihydro-9-oxa-10-phosphaphenanthrene-10-oxide (DOPO). The major components of commercial samples of RDBPP and BPA-BDPP were isolated by preparative TLC and characterized by NMR. A commercial sample of DOPO was found to be essentially pure, but its analysis is complicated by the fact that it can exist in ring-open and ring-closed forms. With the structures of the components confirmed by NMR, multiple analytical separation techniques (gas chromatography (GC), liquid chromatography (LC), and packed column supercritical fluid chromatography (pSFC)) were investigated for the analysis of these three technical products. Packed column supercritical fluid chromatography allows the separation of the components of all three OPFRs, including the two forms of DOPO, in a single run.

<https://doi.org/10.1016/j.chemosphere.2017.02.129>



### 155. Enantioseparation Of Chiral Sulfoxides On Amylose-Based Columns: Comparison Of Normal Phase Liquid Chromatography And Supercritical Fluid Chromatography

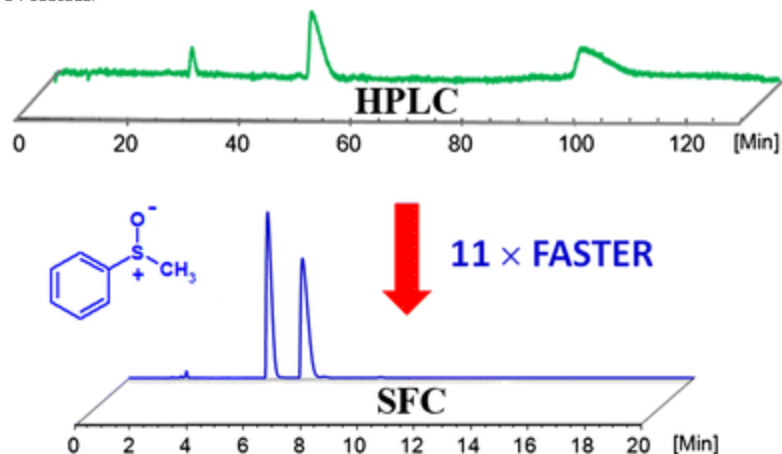
2017 - Chromatographia

Keywords: Enantioseparation; Sulfoxides; Polysaccharide chiral stationary phases; Amylose; Supercritical fluid chromatography; Liquid chromatography

#### Abstract

We present enantioseparation of a series of racemic sulfoxides on three different amylose-based polysaccharide columns. Two of them have the amylose units modified with dimethylphenyl carbamoyl groups (Chiralpak AD-H and Chiralpak IA), while the third one possesses a carbamoyl moiety with an additional chiral centre (Chiralpak AS-H). The enantioseparation of selected analytes was achieved in high-performance liquid chromatography (HPLC) and the full analyte set was enantiomerically resolved using supercritical fluid chromatography (SFC). Comparing the results obtained in both modes, we show that enantioseparation under SFC conditions is superior to HPLC mode in terms of speed, while retaining excellent enantioselectivity and resolution. Faster elution of analytes was observed on increasing the polarity of the co-solvent (modifier) in the mobile phase. This trend is apparent in both chromatographic modes. Documenting the important role of the additional chiral centre, Chiralpak AS-H provided the best chromatographic parameters resulting in the enantioseparation of all analytes.

<https://link.springer.com/article/10.1007/s10337-016-3234-6>



## 156. The Role Of Diode Array Ultraviolet Detection For The Identification Of Synthetic Cathinones

2017 - Drug Testing and Analysis

Keywords: diode array; UV detection; UHPSFC; synthetic cathinones

### Abstract

The utility of diode array UV detection for aiding in the identification of synthetic cathinones, including different sub classes and positional isomers is presented. For 35 synthetic cathinones' unique UV spectra are obtained for seven sub classes including mostly beta ketones, where position and type of substitution on benzene rings give rise to differences in UV maxima and relative intensity of the spectral bands. This aspect is key to distinguishing positional isomers which contain differences in R substitution (mono and di) around the benzene ring, which provides complementary information to electron ionization mass spectrometry, where the latter technique cannot distinguish between these types of positional isomers. In addition it is possible to ascertain the substitution position based on the UV spectra. For ten sets of positional isomers it was possible to distinguish most of the positional isomers within a set. For ultra high performance supercritical fluid chromatography (UHPSFC) vs reversed phase ultra-high performance liquid chromatography (UHPLC) there was at least a 10 nm blue shift in UV maximum (shift to shorter wavelengths). This highlights the importance of taking in account the effect of mobile phase on the UV maximum when performing method development in UHPSFC.

<http://onlinelibrary.wiley.com/doi/10.1002/dta.2163/abstract>

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## 157. Selection Of The HPLC Method In Chemical Analysis - Chapter 3 – Short Overviews Of The Main Analytical Techniques Containing A Separation Step

2017 – Elsevier Book

Keywords: Electrochromatography; Electrophoresis; Gas chromatography; HPLC classification; Separation; Supercritical fluid chromatography

### Abstract

This chapter presents the main analytical techniques containing a separation step with the goal of online delivering of the separated sample components to a detection device. These techniques can be used as core analytical operations applied for separation and measurement of the components of complex samples. They include chromatographic techniques, solid phase extraction, electroseparations, and membrane separations. Presentation of the main chromatographic

separations is also included here: gas chromatography (GC), supercritical fluid chromatography (SFC), high-performance liquid chromatography (HPLC), electrophoresis, and electrochromatography. Selections between various chromatographic techniques with the description of advantages and disadvantages in selecting HPLC as a method of analysis versus GC, SFC, or zone electrophoresis (CZE) are discussed.

<http://www.sciencedirect.com/science/article/pii/B9780128036846000032>

### 158. Triacylglycerol Compositions Of Sunflower, Corn And Soybean Oils Examined With Supercritical CO<sub>2</sub> Ultra-Performance Convergence Chromatography Combined With Quadrupole Time-Of-Flight Mass Spectrometry

2017 - Food Chemistry

Keywords: Triacylglycerol, Sunflower oil, Corn oil, Soybean oil, Ultra-performance convergence chromatography (UPC<sup>2</sup>), Quadrupole time-of-flight mass spectrometry (Q-TOF MS)

#### Abstract

A supercritical CO<sub>2</sub> ultra-performance convergence chromatography (UPC<sup>2</sup>) system was utilized with a quadrupole time-of-flight mass spectrometry (Q-TOF MS) to examine the triacylglycerol compositions of sunflower, corn and soybean oils. UPC<sup>2</sup> provided an excellent resolution and separation for the triacylglycerols, while the high performance Q-TOF MS system was able to provide the molecular weight and fragment ions information for triacylglycerol compound characterization. A total of 33 triacylglycerols were identified based on their elementary compositions and MS<sup>2</sup> fragment ion profiles, and their levels in the three oils were estimated. The combination of UPC<sup>2</sup> and Q-TOF MS may determine triacylglycerol compositions for oils and fats, and provide sn-position information for fatty acids, which may be important for food nutritional value and stability.

<http://dx.doi.org/10.1016/j.foodchem.2016.09.099>

### 159. Enantioseparation Of Methamphetamine By Supercritical Fluid Chromatography With Cellulose- Based Packed Column

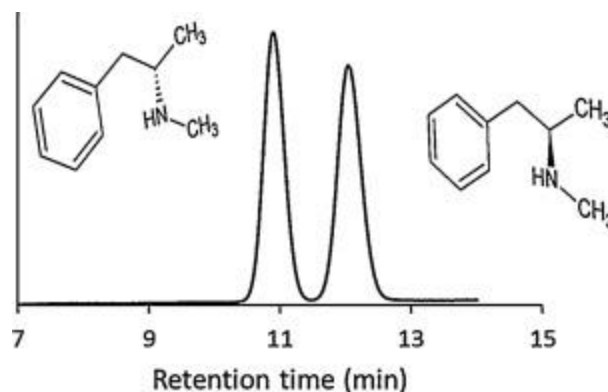
2017 - Forensic Science International

Keywords: Supercritical fluid chromatography; Enantiomer; Methamphetamine

#### Abstract

The enantiomers of methamphetamine were differentiated by supercritical fluid chromatography (SFC) with an enantioselective cellulose-based packed column. The optimization of the chromatographic conditions was achieved by changing column temperature, co-solvent proportion, additive concentration, flow rate and back pressure. In particular, the additive concentration crucially changed the resolution between the enantiomers. After determining the optimized conditions, the enantiomers of methamphetamine were successfully separated. The analytical precision, accuracy and limit of detection were checked by using the authentic standard and seized real samples. We believe that chiral SFC is a promising method for enantioseparation of forensic samples.

<http://dx.doi.org/10.1016/j.forsciint.2017.01.025>



## 160. Physicochemical Properties Of *Acer truncatum* Seed Oil Extracted Using Supercritical Carbon Dioxide

2017 - Journal of the American Oil Chemists Society

Keywords: *Acer truncatum* seed oil, Nervonic acid, UPC2-Q-TOF-MS analysis, sn-2, Nutraceutical constituents, Physicochemical properties

### Abstract

*Acer truncatum* seed oil rich in nervonic acid was extracted using supercritical carbon dioxide. GC (Gas Chromatography) analysis revealed that the oil contained approximately 6.22% nervonic acid. The sn-2 compositions were also determined using lipase hydrolysis. A total of 52 triacylglycerides (TAG) were tentatively identified in the oil using an ultra-performance convergence chromatography (UPC<sup>2</sup>) coupled with quadrupole time-of-flight mass spectrometry (Q-TOF-MS) for the first time. In addition, the contents of phytosterols (1961.9–2402.8  $\mu\text{mol/kg}$ ) and  $\beta$ -carotene (2.09–2.35  $\mu\text{mol/kg}$ ) were also quantified for the first time, along with tocopherols (2352.0–2654.3  $\mu\text{mol/kg}$ ). The  $\gamma$ -tocopherol (1296.9–1442.3  $\mu\text{mol/kg}$ ) was the primary tocopherol, while  $\beta$ -sitosterol (1355.2–1631.3  $\mu\text{mol/kg}$ ) was the dominant phytosterol. The physicochemical properties of the oil were also investigated. This study indicated that *A. truncatum* seed oil is rich in nervonic acid and other nutraceutical constituents. It has a high potential in functional foods for improving human health.

<http://dx.doi.org/10.1007/s11746-017-2983-1>

## 161. Preparative Supercritical Fluid Chromatography: A Powerful Tool For Chiral Separations

2016 - Journal of Chromatography A

Keywords: Research Department Janssen France, Univ. Lille, Pharmaceutical compounds, Chirality, Supercritical fluid chromatography, Preparative scale, Review

### Abstract:

In 2012, the 4 biggest pharmaceutical blockbusters were pure enantiomers and separating racemic mixtures is now frequently a key step in the development of a new drug. For a long time, preparative liquid chromatography was the technique of choice for the separation of chiral compounds either during the drug discovery process to get up to a hundred grams of a pure enantiomer or during the clinical trial phases needing kilograms of material. However the advent of supercritical Fluid Chromatography (SFC) in the 1990s has changed things. Indeed, the use of carbon dioxide as the mobile phase in SFC offers many advantages including high flow rate, short equilibration time as well as low solvent consumption. Despite some initial teething troubles, SFC is becoming the primary method for preparative chiral chromatography. This article will cover recent developments in preparative SFC for the separation of enantiomers, reviewing several aspects such as instrumentation, chiral stationary phases, mobile phases or purely preparative considerations including overloading, productivity or large scale chromatography.

<http://dx.doi.org/10.1016/j.chroma.2016.07.050>

## 162. Scaling Rule In SFC. II. A Practical Rule For Isocratic Systems

2017- Journal of Chromatography A

Keywords: Supercritical fluid chromatography; Method-transfer; Pressure-drop; Density variation; Density modulation; Preparative; Scaling; Scale-up

### Abstract:

Scaling methods, either from analytical to analytical systems or from analytical to preparative systems and vice versa, are commonly performed in chromatography. For liquid chromatography



there exist geometric rules for scaling, which provide guidelines to select column dimensions, particle sizes and flow rates. For SFC, on the other hand, there are no such rules or any well-understood principles behind scaling. In a recent report [1] this issue was addressed, proposing a rule of maintaining the same average density in the target system as it was in the original system. The problem with the criterion of maintaining average density, however, is the availability of density data. Not only one needs access and relevant experience of working with physical property data, in many cases density data may not be available at all. The current report demonstrates that a simpler approach, of matching average pressures, is equally applicable for acceptable scaling over most of the operating conditions used in SFC.

<http://dx.doi.org/10.1016/j.chroma.2016.12.044>

### 163. Optimization And Validation Of A Fast Supercritical Fluid Chromatography Method For The Quantitative Determination Of Vitamin D3 And Its Related Impurities

2017 - Journal of Chromatography A

Keywords: SFC; Green analytical chemistry; Vitamin D3; Method validation; Accuracy profile; Design space

#### Abstract

In the uprising context of green analytical chemistry, Supercritical Fluid Chromatography (SFC) is often suggested as an alternative to Normal Phase Liquid Chromatography. Indeed, SFC provides fast, efficient and green separations. In this report, the quantitative performances of SFC were challenged on a real-life case study: the Quality Control (QC) of vitamin D3. A rapid and green SFC method was optimized thanks to the Design of Experiments–Design Space (DoE–DS) methodology. It provided robust and high quality separation of the compounds within a 2 min timeframe, using a gradient of ethanol as co-solvent of the carbon dioxide. The analytical method was fully validated according to the total error approach, demonstrating the compliance of the method to the specifications of U.S. Pharmacopeia (USP: 97.0–103.0%) and European Pharmacopeia (EP: 97.0–102.0%) for an interval of [50–150%] of the target concentration. In order to allow quantification of impurities using vitamin D3 as an external standard in SFC–UV, correction factors were determined and verified during method validation. Thus, accurate quantification of impurities was demonstrated at the specified levels (0.1 and 1.0% of the main compound) for a 70.0–130.0% dosing range. This work demonstrates the validity of an SFC method for the QC of vitamin D3 raw material and its application to real samples. Therefore, it supports the switch to a greener and faster separative technique as an alternative to NPLC in the pharmaceutical industry.

<http://dx.doi.org/10.1016/j.chroma.2017.01.090>

### 164. Unravelling The Effects Of Mobile Phase Additives In Supercritical Fluid Chromatography. Part I: Polarity And Acidity Of The Mobile Phase

2017 - Journal of Chromatography A

Keywords: Additives, Colour indicators, Mobile phase acidity, Solvatochromic dye, Supercritical fluid chromatography

#### Abstract

Polarity effects of mobile phase additives are assessed with a solvatochromic probe.

Additives in usual concentration ranges cause no significant change in polarity.

Acidity of SFC mobile phases is assessed with pH colour indicators.

Apparent pH in carbon dioxide-methanol mixtures is around 5.

Basic additives do not yield basic conditions, acidic additives yield acidic conditions.

The mobile phases employed in current supercritical fluid chromatography (SFC) are usually composed of a mixture of pressurized carbon dioxide and a co-solvent. The co-solvent is most often an alcohol and may contain a third component in small proportions, called an additive (acid, base or salt). The polarity of such mobile phase compositions is here re-evaluated with a solvatochromic dye (Nile Red), particularly to assess the contribution of additives. It appears that additives, when employed in usual concentration range (0.1% or 20 mM) do not modify the polarity in the immediate environment of the probe.

In addition, the combination of carbon dioxide and an alcohol is known to form alkoxycarbonic acid, supposedly conferring some acidic character to SFC mobile phases. Direct measurements of the apparent pH are impossible, but colour indicators of pH can be used to define the range of apparent pH provided by carbon dioxide-alcohol mixtures, with or without additives. Five colour indicators (Thymol Blue, Bromocresol Green, Methyl Red, Bromocresol Purple, and Bromothymol Blue) were selected to provide a wide range of aqueous pKa values (from 1.7 to 8.9). UV-vis absorption spectra measured in liquid phases of controlled pH were compared to those measured with a diode-array detector employed in SFC, with the help of chemometric methods. Based on these observations, it is concluded that the apparent pH range in carbon dioxide-methanol mobile phases is close to 5. Increasing the proportion of methanol (in the course of a gradient elution for instance) causes decreasing apparent pH. Strong acids can further decrease the apparent pH below 1.7; strong bases have little influence on the apparent pH, probably because, in this range of concentrations, they are titrated by alkoxycarbonic acid or form ion pairs with alkoxycarbonate. However, bases and salts could stabilize the acidity in the course of gradient runs.

<https://doi.org/10.1016/j.chroma.2017.02.066>

### 165. Chemometric Evaluation Of The Combined Effect Of Temperature, Pressure, And Co-Solvent Fractions On The Chiral Separation Of Basic Pharmaceuticals Using Actual Vs Set Operational Conditions

2017 - Journal of Chromatography A

Keywords: Supercritical fluid chromatography; Basic pharmaceuticals; Chiral separations; Design of experiments; Actual conditions; Set conditions

#### Abstract

Six pharmaceutical compounds were used as chiral model compounds. Combined effects of pressure, temperature, and modifier fraction were investigated. The fraction of modifier in eluent had the strongest effect on the retention. The use of set vs. actual conditions as input data in the DoE was evaluated. Significant differences were found between models using set vs. actual conditions.

The need to determine the actual operational conditions, instead of merely using the set operational conditions, was investigated for in packed supercritical fluid chromatography (SFC) by design of experiments (DoE) using a most important type of compounds, pharmaceutical basics, as models. The actual values of temperature, pressure, and methanol levels were recorded and calculated from external sensors, while the responses in the DoE were the retention factors and selectivity. A Kromasil CelluCoat column was used as the stationary phase, carbon dioxide containing varying methanol contents as the mobile phase, and the six racemates of alprenolol, atenolol, metoprolol, propranolol, clenbuterol, and mianserin were selected as model solutes. For the retention modeling, the most important term was the methanol fraction followed by the temperature and pressure. Significant differences ( $p < 0.05$ ) between most of the coefficients in the retention models were observed when comparing models from set and actual conditions. The selectivity was much less affected by operational changes, and therefore was not severely affected by difference between set and actual conditions. The temperature differences were usually small, maximum  $\pm 1.4$  °C, whereas the pressure differences were larger, typically approximately +10.5 bar. The set and actual fractions of methanol also differed, usually by  $\pm 0.4$  percentage points. A cautious conclusion is that the primary reason for the discrepancy between the models is a mismatch between the set and actual methanol fractions. This mismatch is more serious in retention models at low methanol fractions. The study demonstrates that the actual conditions should almost always be preferred.

<https://doi.org/10.1016/j.chroma.2017.03.077>

### 166. Systematic Investigations Of Peak Deformations Due To Co-Solvent Adsorption In Preparative Supercritical Fluid Chromatography

2017 - Journal of Chromatography A

Keywords: Supercritical fluid chromatography; Co-solvent adsorption; Adsorption strength; Langmuir band shape; Anti-Langmuir band shape

### Abstract

An adsorbing co-solvent can cause deformed elution profiles. This effect is general for several co-solvents/stationary phase combinations. A simple test can evaluate the risk of these deformations. All solute peak deformations due to co-solvents result from competition.

Strangely shaped overloaded bands were recently reported using a standard supercritical fluid chromatographic system comprising a diol column as the stationary phase and carbon dioxide with methanol as the mobile phase. Some of these overloaded elution profiles appeared strongly deformed and even had "anti-Langmuirian" shapes although their solute compounds had "Langmuirian" adsorption. To obtain a more complete understanding of the generality of these effects, the investigation was expanded to cover also other common co-solvents, such as ethanol, 2-propanol, and acetonitrile, as well as various stationary phase materials, such as silica, and 2-ethylpyridine. From this expanded study it could be confirmed that the effects of deformed overloaded solute band shapes, due to co-solvent adsorption, is general phenomena in supercritical fluid chromatographic. It could also be concluded that these effects as well as previously observed "solvent effects" or "plug effects" are entirely due to competition between the solute and solvent molecules for the adsorption sites on the stationary phase surface. Finally, guidelines were given for how to evaluate the risk of deformations occurring for a given solvent-column combination, based simply on testing retention times of solutes and co-solvent.  
<https://doi.org/10.1016/j.chroma.2017.03.053>

## 167. Enantioseparation Of Novel Chiral Sulfoxides On Chlorinated Polysaccharide Stationary Phases In Supercritical Fluid Chromatography

2017 - Journal of Chromatography A

Keywords: Conformation; Enantiomer separation; Molecular modelling; Polysaccharide-based chiral stationary phase; Sulfoxides; Supercritical fluid chromatography

### Abstract

Chlorinated polysaccharide-based stationary phases yield high retention and enantioseparation of sulfoxides

Enantiorecognition is more favorable for folded analyte conformations than for linear conformations

Stationary phase conformation changes significantly when methanol percentage reaches about 60%

Asymmetric sulfoxides is a particular case of chirality that may be found in natural as well as synthetic products. Twenty-four original molecules containing a sulfur atom as a centre of chirality were analyzed in supercritical fluid chromatography on seven polysaccharide-based chiral stationary phases (CSP) with carbon dioxide – methanol mobile phases. While all the tested CSP provided enantioseparation for a large part of the racemates, chlorinated cellulosic phases proved to be both highly retentive and highly enantioselective towards these species.

Favourable structural features were determined by careful comparison of the enantioseparation of the probe molecules. Molecular modelling studies indicate that U-shaped (folded) conformations were most favorable to achieve high enantioresolution on these CSP, while linear (extended) conformations were not so clearly discriminated.

For a subset of these species adopting different conformations, a broad range of mobile phase compositions, ranging from 20 to 100% methanol in carbon dioxide, were investigated. While retention decreased continuously in this range, enantioseparation varied in a non-monotonous fashion. Abrupt changes in the tendency curves of retention and selectivity were observed when methanol proportion reaches about 60%, suggesting that a change in the conformation of the analytes and/or chiral selector is occurring at this point.

<https://doi.org/10.1016/j.chroma.2017.03.089>

## 168. Speed-Resolution Advantage Of Turbulent Supercritical Fluid Chromatography In Open Tubular Columns: II – Theoretical And Experimental Evidences

2017 - Journal of Chromatography A

Keywords: Supercritical fluid chromatography; Laminar-to-turbulent flow regime; Open tubular columns; Golay equation; Kinetic plots; Reynolds number

### Abstract

Golay's plate height equation extended from laminar to turbulent flow was used. Performance of open tubes in turbulent regime with carbon dioxide eluent is projected. Significant speed-resolution benefits are expected under turbulent flow regime. The theoretical predictions are in good agreement with experimental dispersion data.

The potential advantage of turbulent supercritical fluid chromatography (TSFC) in open tubular columns (OTC) was evaluated on both theoretical and practical viewpoints. First, the dispersion model derived by Golay in 1958 and recently extended from laminar to turbulent flow regime is used for the predictions of the speed-resolution performance in TSFC. The average dispersion coefficient of matter in the turbulent flow regime was taken from the available experimental data over a range of Reynolds number from 2000 to 6000. Kinetic plots are built at constant pressure drop ( $\Delta P = 4500$  psi) and Schmidt number ( $Sc = 15$ ) for four inner diameters (10, 30, 100, and 300  $\mu\text{m}$ ) of the OTC and for three retention factors (0, 1, and 10). Accordingly, in turbulent flow regime, for a Reynolds number of 4000 and a retention factor of 1 (the stationary film thickness is assumed to be negligible with respect to the OTC diameter), the theory projects that a 300  $\mu\text{m}$  i.d. OTC has the same speed-resolution power (200,000 theoretical plates; 2.4 min hold-up time) as that of a 10  $\mu\text{m}$  i.d. OTC operated in laminar flow regime.

Secondly, the experimental plate heights of *n*-butylbenzene are measured in laminar and turbulent flow regimes for a 180  $\mu\text{m} \times 4.8$  m fused silica capillary column using pure carbon dioxide as the mobile phase. The back pressure regulator was set at 1500 psi, the temperature was uniform at 297 K, and the flow rate was increased step-wise from 0.50 to 3.60 mL/min so that the experimental Reynolds number increases from 700 to 5400. The experiments are in good agreement with the plate heights projected in TSFC at high flow rates and with those expected at low flow rates in a laminar flow regime.

<https://doi.org/10.1016/j.chroma.2017.04.032>

## 169. Rapid Determination Of 9 Aromatic Amines In Mainstream Cigarette Smoke By Modified Dispersive Liquid Liquid Microextraction And Ultraperformance Convergence Chromatography Tandem Mass Spectrometry

2017 - Journal of Chromatography A

Keywords: aromatic amines; dispersive liquid liquid microextraction; ultraperformance convergence chromatography tandem mass spectrometry; mainstream cigarette smoke

### Abstract

A rapid and sensitive UPC<sup>2</sup>-MS/MS method was developed and validated. Nine aromatic amines were fully separated within 5.0 min. Simplified sample preparation by modified DLLME. Organic solvents were dramatically reduced attributing to DLLME and UPC<sup>2</sup>-MS/MS. The method was successfully applied to mainstream cigarette smoke.

Aromatic amines in mainstream cigarette smoke have long been monitored due to their carcinogenic toxicity. In this work, a reliable and rapid method was developed for the simultaneous determination of 9 aromatic amines in mainstream cigarette smoke by modified dispersive liquid liquid microextraction (DLLME) and ultraperformance convergence chromatography tandem mass spectrometry (UPC<sup>2</sup>-MS/MS). Briefly, the particulate phase of the cigarette smoke was captured by a Cambridge filter pad, and diluted hydrogen chloride aqueous solution is employed to extract the aromatic amines under mechanical shaking. After alkalization with sodium hydroxide solution, small amount of toluene was introduced to further extract and enrich aromatic amines by modified DLLME under vortexing. After centrifugation, toluene phase

was purified by a universal QuEChERS cleanup kit and was finally analyzed by UPC<sup>2</sup>-MS/MS. Attributing to the superior performance of UPC<sup>2</sup>-MS/MS, this novel approach allowed the separation and determination of 9 aromatic amines within 5.0 min with satisfactory resolution and sensitivity. The proposed method was finally validated using Kentucky reference cigarette 3R4F, and emission levels of targeted aromatic amines determined were comparable to previously reported methods. At three different spiked levels, the recoveries of most analytes were ranged from 74.01% to 120.50% with relative standard deviation (RSD) less than 12%, except that the recovery of p-toluidine at low spiked level and 3-aminobiphenyl at medium spiked level was 62.77% and 69.37% respectively. Thus, this work provides a novel alternative method for the simultaneous analysis of 9 aromatic amines in mainstream cigarette smoke.  
<https://doi.org/10.1016/j.chroma.2017.05.056>

### 170. Simultaneous Quantification Of 11 Active Constituents In Shexiang Baoxin Pill By Ultraperformance Convergence Chromatography Combined With Tandem Mass Spectrometry

2017 - Journal of Chromatography B

Keywords: Shexiang Baoxin Pill; UPC<sup>2</sup>-MS/MS; Quantification; Non-volatiles; Volatiles

#### Abstract

Apply UPC<sup>2</sup>-MS/MS method to quantification of constituents in traditional Chinese medicines (TCMs)

Simultaneous quantification of 11 components in SBP including volatiles and non-volatiles. Methods have advantages with its rapidity, sensitivity, short time and a wide range of analyzing. This work also detailed analyzed the effects of 11 components on 13 batches of SBP samples.

On account of the complexity of chemical constituents of Shexiang Baoxin Pill (SBP), a famous traditional Chinese medicine (TCM) formula, a novel and effective UPC<sup>2</sup>-MS/MS method was developed to simultaneously determine the content of 11 active compounds of SBP with outstanding separation ability. Eleven components in SBP, including 2 ginsenosides, 2 bile acids, 3 bufadienolides and 4 volatiles were detected by electrospray ionization tandem mass spectrometry in positive and negative ion modes with multiple reaction monitor (MRM). The analysis was performed at 30 °C using an Acquity UPC<sup>2</sup> Diol (3.0 × 50 mm, 1.7 μm) column with linear gradient elution (eluent A, CO<sub>2</sub>; eluent B, methanol containing 20 mM ammonium acetate), back pressure of 2000 psi, flow rate of 1.2 mL/min and the injection volume of 1.0 μL. The method was extensively validated regarding the linearity ( $r \geq 0.9974$ ), precision ( $\leq 3.11\%$ ), recovery (93.34–104.50%), repeatability ( $\leq 2.00\%$ ) and stability ( $\leq 4.20\%$ ). Using this method, 11 active compounds of SBP with different polarity were simultaneously quantified in one chromatography analysis within 8 min. Statistical analysis of the effects of 11 compounds on the quality of SBP revealed that the content of cinnamaldehyde varied widely in different batches. This work presents an exemplary study for quality control of complex samples, especially for TCMs.

<https://doi.org/10.1016/j.jchromb.2017.03.033>

### 171. Effect Of Fatty Acid Chain Length On The Crystallization Behavior Of Trans-Free Margarine Basestocks During Storage

2017 - Journal of Oleo Science

Keywords: fully hydrogenated Acer truncatum oil, fatty acids, trans-free, interesterification, crystallization

#### Abstract

In order to obtain margarine free of trans-fatty acids, four interesterified basestocks were prepared by chemical interesterification (CIE) of oil blends. Different ratios of palm stearin, palm olein and soybean oil were mixed without and with 1) fully hydrogenated Acer truncatum oil (FHATO), 2) fully hydrogenated rapeseed oil or 3) palm kernel oil containing a similar amount of



saturated, monounsaturated and polyunsaturated fatty acids, but different saturated fatty acid length for CIE. Compared to the physical blends, the CIE samples demonstrated lower slip melting points and decreased solid fat contents, especially at high temperatures, indicating that the CIE samples might have improved mouthfeel. In all CIE samples, the  $\beta$  crystal form disappeared and only the  $\beta'$  crystal form was observed, except for sample 2, which contained a mixed  $\beta$  and  $\beta'$  forms. Furthermore, in all CIE samples, except sample 1, the  $\beta'$  crystal forms began transforming to  $\beta$  form after only two cycles of higher temperature treatments indicating that the CIE sample with FHATO had the most resistance to temperature fluctuation during storage which may be attributed to its longer saturated chains. In conclusion, the CIE basestocks containing longer saturated fatty acids could be more suitable for margarine use.

<http://dx.doi.org/10.5650/jos.ess16210>

[https://www.jstage.jst.go.jp/article/jos/66/4/66\\_ess16210/\\_pdf](https://www.jstage.jst.go.jp/article/jos/66/4/66_ess16210/_pdf)

### 172. Investigation Of The Effect Of Mobile Phase Composition On Selectivity Using A Solvent-Triangle Based Approach In Achiral SFC

2017 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: Achiral SFC, Drug impurity profiling, Eluotropic strength, Separation optimization, Modifiers

**Abstract:**

Defining a method development methodology for achiral drug impurity profiling in SFC requires a number of steps. Initially, diverse stationary phases are characterized and a small number of orthogonal or dissimilar phases are selected for further method development. In this paper, we focus on a next step which is the investigation of the modifier composition on chromatographic selectivity. A solvent-triangle based approach is used in which blends of organic solvents, mainly ethanol (EtOH), propanol (PrOH), acetonitrile (ACN) and tetrahydrofuran (THF) mixed with methanol (MeOH) are tested as modifiers on six dissimilar stationary phases. The tested modifier blends were composed to have equal eluotropic strengths as calculated on bare silica. The modifier leads to minor changes in terms of elution order, retention and mixture resolution. However, varying only the modifier composition on a given stationary phase does not lead to the creation of dissimilar systems. Therefore the modifier composition is an optimization parameter, with the stationary phase being the factor determining most the selectivity of a given mixture in achiral SFC.

<http://dx.doi.org/10.1016/j.jpba.2016.10.016>

### 173. Quantitative Determination Of Salbutamol Sulfate Impurities Using Achiral Supercritical Fluid Chromatography

2017 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: Supercritical fluid chromatography (SFC), Quality by design (QbD), Impurity profiling, Method validation, Total error approach, Salbutamol sulfate

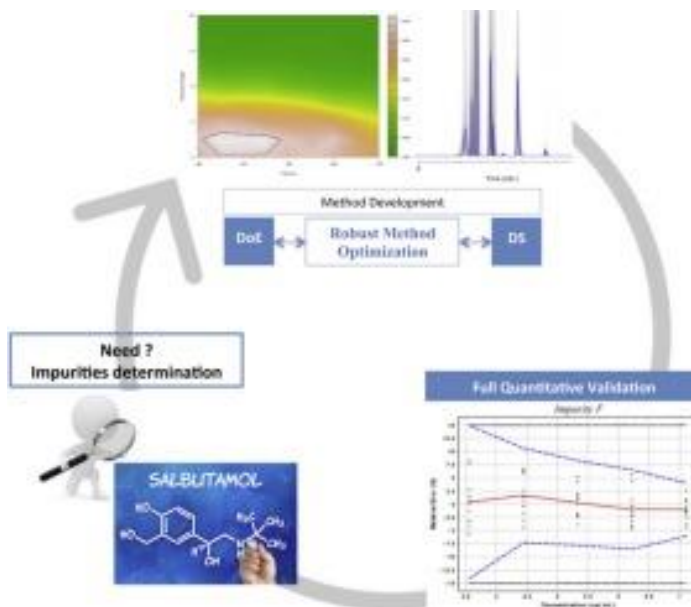
**Abstract:**

In the last years, supercritical fluid chromatography has largely been acknowledged as a singular and performing technique in the field of separation sciences. Recent studies highlighted the interest of SFC for the quality control of pharmaceuticals, especially in the case of the determination of the active pharmaceutical ingredient (API). Nevertheless, quality control requires also the determination of impurities. The objectives of the present work were to (i) demonstrate the interest of SFC as a reference technique for the determination of impurities in salbutamol sulfate API and (ii) to propose an alternative to a reference HPLC method from the European Pharmacopeia (EP) involving ion-pairing reagent. Firstly, a screening was carried out to select the most adequate and selective stationary phase. Secondly, in the context of robust optimization strategy, the method was developed using design space methodology. The separation of salbutamol sulfate and related impurities was achieved in 7 min, which is seven times faster than the LC-UV method proposed by European Pharmacopeia (total run time of 50 min). Finally, full validation using accuracy profile approach was successfully achieved for the determination of impurities B, D, F and G in salbutamol sulfate raw material. The validated dosing range covered 50



to 150% of the targeted concentration (corresponding to 0.3% concentration level), LODs close to 0.5 µg/mL were estimated. The SFC method proposed in this study could be presented as a suitable fast alternative to EP LC method for the quantitative determination of salbutamol impurities.

<http://dx.doi.org/10.1016/j.jpba.2016.11.039>



## 174. Fast Separation Of Flavonoids By Supercritical Fluid Chromatography Using A Column Packed With A Sub-2 Mm Particle Stationary Phase

2017 - Journal of Separation Science

Keywords: flavonoids; dietary supplements; Radix astragali; Chinese medicine;

### Abstract

The purpose of this study was to compare the effects of different chromatographic columns for the separation of seven flavonoids. Four different stationary phases are available, including bridged ethyl hybrid, BEH and the same hybrid phase modified with 2-ethylpyridine, CSH fluorophenyl, and HSS C<sub>18</sub> SB. The analytes included calycosin, genistein, medicarpin, calycosin-7-O-β-d-glucoside, formononetin, formononetin-7-O-β-d-glucoside, and liquiritigenin. The CSH fluorophenyl column was determined to be the most suitable and provided the fastest separation within 17 min using gradient elution with carbon dioxide as the mobile phase and methanol as the co-solvent. Good peak shapes were obtained, and the values of the peak asymmetry were close to 1.0 for all of the flavonoids. The resolution was more than 1.41 for all of the separated peaks. Baseline separation on the optimal columns was achieved by changing the co-solvent type and adjusting the temperature and pressure. Quantitative performance was evaluated under optimized conditions, and method validation was accomplished. The validation parameters, such as linearity, sensitivity, precision, and accuracy, were satisfactory. Good repeatability of both peak area (relative standard deviation <1.02%) and retention time (relative standard deviation <0.88%) was observed. The optimized chromatographic methods were successfully used for the determination of seven flavonoids in *Radix astragali*. The sensitivity was sufficient for the analysis of real samples.

<https://doi.org/10.1002/jssc.201601021>

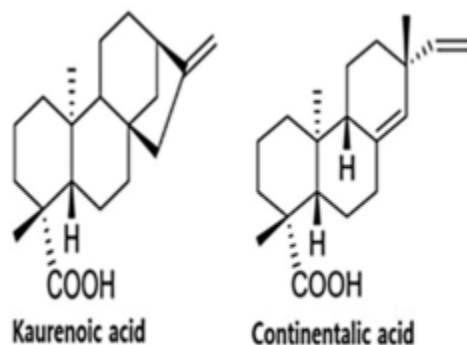
## 175. Ultra-Performance Convergence Chromatography For The Quantitative Determination Of Bioactive Compounds In *Aralia Continentalis* Kitagawa As Quality Control Markers

2017 - Journal of Separation Science

Keywords: Quality control, S.Korea, China

### Abstract

A rapid ultra-performance convergence chromatography method was developed for the quantitative determination of bioactive compounds in *Aralia continentalis* as quality control markers. Quantitative analysis indicated the presence of two major bioactive compounds: diterpenoid acids continentalic acid and kaurenoic acid. Using a Torus 1-aminoanthracene column, continentalic acid and kaurenoic acid were separated in less than 8 min. The method was validated with respect to precision, accuracy, and linearity according to the International Conference on Harmonization guidelines. The optimized method exhibited a good linear correlation ( $r^2 > 0.996$ ), excellent precision (RSD < 1.0%), and acceptable recoveries (99.97–100.26%). Limits of detection for continentalic acid and kaurenoic acid were 0.068 and 0.097  $\mu\text{g/mL}$ , respectively, while their corresponding limits of quantitation were 0.207 and 0.295  $\mu\text{g/mL}$ . The system performance of ultra-performance convergence chromatography was compared with that of conventional high-performance liquid chromatography with respect to analysis time and efficiency. The proposed method was found to be reliable and convenient for the quantitative analysis of continentalic acid and kaurenoic acid in *A. continentalis* from South Korea and *A. pubescens* from China. This study is expected to serve as a guideline for the quality control of *Aralia continentalis*. <https://doi.org/10.1002/jssc.201601261>



## 176. Simple, Rapid, And Environmentally Friendly Method For The Separation Of Isoflavones Using Ultra-High Performance Supercritical Fluid Chromatography

2017 - Journal of Separation Science

### Abstract

Isoflavones are natural substances that exhibit hormone-like pharmacological activities. The separation of isoflavones remains an analytical challenge because of their similar structures. We show that ultra-high performance supercritical fluid chromatography can be an appropriate tool to achieve the fast separation of 12 common dietary isoflavones. Among the five tested columns the Torus DEA column was found to be the most effective column for the separation of these isoflavones. The impact of individual parameters on the retention time and separation factor was evaluated. These parameters were optimized to develop a simple, rapid and green method for the separation of the 12 target analytes. It only took 12.91 min using gradient elution with methanol as an organic modifier and formic acid as an additive. These isoflavones were determined with limit of quantitation ranging from 0.10 to 0.50  $\mu\text{g/mL}$ , which was sufficient for reliable determination of various matrixes. <https://doi.org/10.1002/jssc.201601454>

## 177. Construction Of An Off-Line Two Dimensional Reversed-Phase Liquid Chromatography / Ultra-High Performance Supercritical Fluid Chromatography Method For Rapid And Comprehensive Analysis Of *Piper Kadsura*

2017 - The Journal of Supercritical Fluids

Keywords: Ultra-high performance supercritical fluid chromatography; Reversed-phase liquid chromatography; Two-dimensional chromatography; Rapid analysis; Piper kadsura

### Abstract

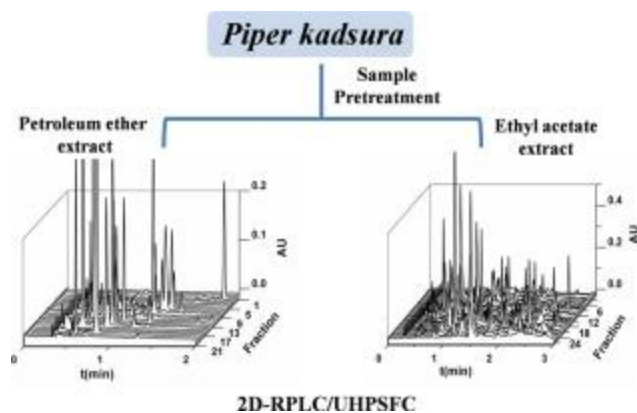
A 2D-RPLC/UHPSFC method for rapid and comprehensive analysis of Piper kadsura.

UHPSFC analysis of all fractions prepared from RPLC was within 3.0 min.

1033 peaks were identified using the 2D-RPLC × UHPSFC with excellent orthogonality.

In this study, ultra-high performance supercritical fluid chromatography (UHPSFC) was chosen to construct an off-line two dimensional chromatography with reversed-phase liquid chromatography (RPLC) for rapid and comprehensive analysis of *Piper kadsura*. The sample was firstly divided into a petroleum ether (PE) extract and an ethyl acetate (EA) extract, and then they were separated into 21 and 28 fractions in the first dimensional RPLC, respectively. In the second dimension, the effect of UHPSFC parameters on the analysis speed was investigated. Each PE fraction could be analyzed in 2.0 min, and every EA fraction could be analyzed in 3.0 min. In total, at least 1033 peaks were detected by this method, including 204 peaks from the PE fractions and 829 peaks from the EA fractions. The 2D-RPLC/UHPSFC system with the characteristics of fast separation and high orthogonality has a great potential for the rapid and comprehensive analysis of the complex samples.

<https://doi.org/10.1016/j.supflu.2017.03.004>



## 178. Fast And Green – CO<sub>2</sub> Based Extraction, Isolation, And Quantification Of Phenolic Styrox Constituents

2017 - Planta Med

Keywords: Liquidambar orientalis - Hamamelidaceae - supercritical fluid extraction - supercritical fluid chromatography - ultra-performance convergence chromatography – styrox

### Abstract

In this study the first supercritical fluid based protocol for the extraction, analysis, and isolation of six polar compounds, i.e., o-vanillin (**1**), styracin (**2**), vanillin (**3**), trans-cinnamic acid (**4**), vanillic

acid (**5**), and shikimic acid (**6**), was developed. First, eight styrax resin products (R1–R8) obtained from various *Liquidambar* tree species, which are known to contain compounds **2–6**, were extracted with a 1:1 mixture of supercritical CO<sub>2</sub> and EtOH. Within 4 minutes, the compounds were successfully baseline separated on an Acquity UPC<sup>2</sup> BEH 2-EP (3.0 × 100 mm, 1.7 μm) column using a mobile phase of supercritical CO<sub>2</sub> and MeOH with 0.1% phosphoric acid. The compounds were quantified and the method was validated according to current ICH guidelines. Scaling up to preparative supercritical fluid chromatography using a Viridis BEH 2-EP (10 × 250 mm, 5 μm) column allowed for a fast separation and isolation of the selected constituents **2** and **4** from R6 within 7 minutes. This supercritical fluid protocol is easily adaptable to compounds of similar polarity. The increase in speed and its environmental friendliness underline its superiority over conventional set-ups.

<http://dx.doi.org/10.1055/s-0043-105499>

### 179. Development And Application Of Sub-2-Mm Particle CO<sub>2</sub>-Based Chromatography Coupled To Mass Spectrometry For Comprehensive Analysis Of Lipids In Cottonseed Extracts

2017 - Rapid Communications in Mass Spectrometry

Keywords: Cotton Seed Oil, food and chemical industries; triacylglycerols; biological lipid extracts; lipid profiling

#### Abstract

Refined cottonseed oil has widespread applications in the food and chemical industries. Although the major lipids comprising cottonseed oil (triacylglycerols) are well known, there are many diverse lipid species in cotton seeds that occur at much lower levels and have important nutritional or anti-nutritional properties.

The lipid technical samples were prepared in chloroform. The biological samples were extracted using a mixture of isopropanol/chloroform/H<sub>2</sub>O (2:1:0.45). The data were collected using high and low collision energy with simultaneous data collection on a time-of-flight (TOF) mass spectrometer which allowed the characterization of lipids by precursor and product ion alignment. The supercritical fluid chromatography methodology is flexible and can be altered to provide greater retention and separation. The comprehensive method was used to screen seed lipid extracts from several cotton genotypes using multivariate statistical analysis.

Method variables influencing the peak integrity and chromatographic separation for a mixture of lipids with different degrees of polarity were explored. The experiments were designed to understand the chromatographic behavior of lipids in a controlled setting using a variety of lipid extracts. Influences of acyl chain length and numbers of double bonds were investigated using single moiety standards.

The methodology parameters were examined using single moiety lipid standards and standard mixtures. The method conditions were applied to biological lipid extracts, and adjustments were investigated to manipulate the chromatography. Insights from these method variable manipulations will help to frame the development of targeted lipid profiling and screening protocols.

<http://onlinelibrary.wiley.com/doi/10.1002/rcm.7825/full>

### 180. Enantioselective 4-Hydroxylation Of Phenols Under Chiral Organoiodine(I/III) Catalysis

2017 - Synthesis

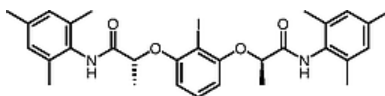
Keywords: catalysis, chiralit, dearomatization, hydroxylation, hypervalent iodine, oxidation

#### Abstract

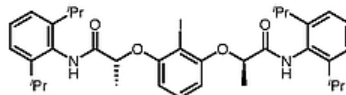
A procedure for the intermolecular enantioselective dearomatization of phenols under chiral (I/III) catalysis is reported. This protocol employs 3-chloroperoxybenzoic acid (*m*-CPBA) as the terminal oxidant together with a defined C<sub>2</sub>-symmetric aryl iodide as the effective organocatalyst. This enantioselective reaction proceeds with complete selectivity under mild conditions and enables the hydroxylative dearomatization of a number of phenols to give the corresponding *p*-quinol products with up to 50% ee.

HPLC measurements were carried out on a Acquity UPLC® system (Waters) UltraPerformance Convergence Chromatography™ (UPC2™) equipped with a detector Acquity UPLC PDA (Photodiode Array detector). The respective chiral stationary phase (Chiralpak IA, IC or IE) and exact conditions are specified for each individual compound within the compound characterization section.

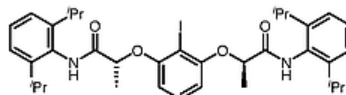
<http://dx.doi.org/10.1055/s-0036-1588808>



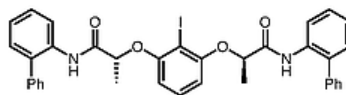
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## 181. Coupling Of Supercritical Fluid Chromatography To Mass Spectrometry For The Analysis Of Dechlorane Plus: Examination Of Relevant Negative Ion Atmospheric Pressure Chemical Ionization Mechanisms

2017 - Talanta

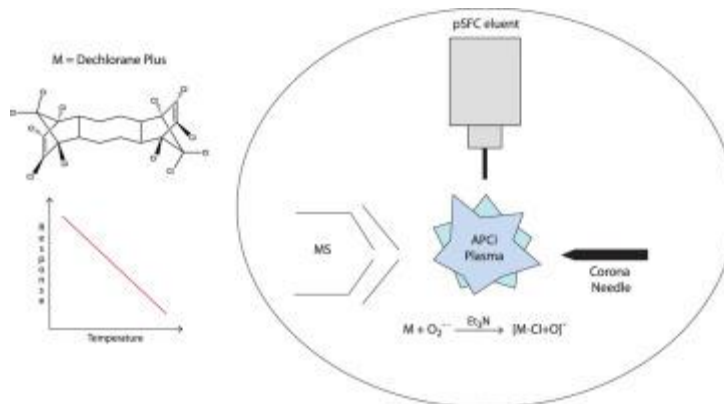
Keywords: Supercritical fluid chromatography; Negative APCI/MS; Dechlorane Plus; Ionization; Superoxide; Environmental analysis

### Abstract

The analysis of Dechlorane Plus (DP) by pSFC-APCI/MS is investigated. APCI pathways are discussed and triethylamine is optimized as an APCI reagent. Superoxide formation is correlated to APCI probe temperature and DP analyte response.

During an investigation of the potential associated with coupling packed column supercritical fluid chromatography (pSFC) to mass spectrometry for the analysis of Dechlorane Plus and related compounds, it was found that negative ion atmospheric pressure chemical ionization (APCI) was a promising ionization technique. In the course of maximizing the responses associated with the target analytes, it proved useful to examine some aspects of the complex nature and reactivity of the corona discharge plasma generated to explain the observed ionization products. Various dopants/reagents were screened for both APCI and atmospheric pressure photoionization (APPI) in negative ion mode and mechanisms of ionization involving superoxide were elucidated based on the results obtained. Superoxide formation was found to be temperature dependent and directly related to the intensity of the ion cluster  $[M-Cl+O]^-$  obtained for the target DP analytes. Furthermore, triethylamine was identified as a reagent capable of suppressing unwanted side reactions during the ionization process and maximizing response associated with the analytes of interest. The applicability of pSFC-APCI/MS for the separation and detection of Dechlorane Plus and related compounds was demonstrated by analyzing Lake Ontario sediment and comparing the results with values reported in the scientific literature.

<https://doi.org/10.1016/j.talanta.2017.04.066>



## 182. Advanced Analytical Techniques For Fat-Soluble Vitamin Analysis

2017 - TrAC Trends in Analytical Chemistry

Keywords: Fat soluble vitamins; HPLC; UHPLC; Supercritical fluid chromatography; Convergence chromatography; Miniaturized chromatographic techniques; Core-shell technology; Sample preparation; Miniaturized sample preparation techniques; Vitamin profiling

### Abstract

This review presents advancements in sample preparation and liquid chromatographic methods made during the last 10 years for the fat-soluble vitamin (FSV) analysis in foods. Since activity and bioavailability of organic micronutrients (MOs) depend on the form in which they are present in a food, special emphasis has been given to the most recent techniques, instruments and approaches which have allowed the extraction and separation of various vitamin homologues as



well as the comprehensive MO profiling in foods. Due to the numerous ancillary advantages, miniaturized techniques which have been applied in this analysis field are also discussed in this review. A number of selected applications are proposed to enable readers to access the most recent developments and trends aimed at gaining more in-depth knowledge of the vitamin composition of foods.

<http://dx.doi.org/10.1016/j.trac.2016.12.001>

### 183. Effects Of Free Fatty Acids On Insulin And Glucagon Secretion

2017 - PhD Thesis submission Uppsala University

#### Abstract

Free fatty acid analysis A sample of 100  $\mu$ l plasma was vortexed thoroughly with a 60  $\mu$ l mixture of internal standards (3.33  $\mu$ g/ml of nonanoic acid (C9:0) 3.33 mg/ml, 16.66  $\mu$ g/ml of heptanoic acid (C17:0), and 3.33  $\mu$ g/ml of tricosylic acid (C23:0)). Plasma lipids were extracted with 2 ml of organic solvent mixture (isopropanol: heptane: 1 M hydrochloric acid (40:10:1, v/v/v)) by vortexing for 30 min. During the extraction, lipids need to be protected against oxidation by adding 0.05 mg/ml butylated hydroxytoluene to the organic solvent mixture. The samples were incubated at room temperature for 10 min. One ml of water was added to the samples and the plasma lipids were extracted into 2 ml of heptane. Another lipid extraction step was performed by adding 1 ml of heptane. The heptane phase was dried under nitrogen gas and the dried lipids were redissolved in 100  $\mu$ l of heptane. The sample was stored at -20°C until Ultra-Performance Convergence Chromatography (UPC2) analysis. FFAs were analyzed with UPC2 (Waters ACQUITY® UPC2™, Milford, MA) coupled with tandem MS (XEVO® TQ-S, Milford, MA). The analysis was performed with an Acquity UPC2 HSS C18 column (100 mm 3.0 mm, 1.8  $\mu$ m at 40 °C, Waters, Milford, MA, USA). The mobile phase A is 99.99% pure compressed CO<sub>2</sub>. Methanol containing 0.1% formic acid was used as the co-solvent.

<http://www.diva-portal.org/smash/get/diva2:1084190/FULLTEXT01.pdf>

## 2016 Publications

### 184. Quantification Of The Neurotransmitters Melatonin And N-Acetyl-Serotonin In Human Serum By Supercritical Fluid Chromatography Coupled With Tandem Mass Spectrometry

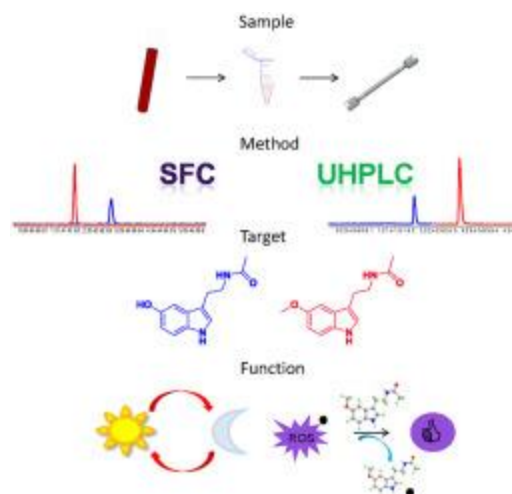
2016 - Analytica Chimica Acta

Keywords: Melatonin, N-acetyl-serotonin, UHPLC-MS/MS, SFC-MS/MS

#### Abstract

The aim of this study was developing a supercritical fluid chromatography tandem mass spectrometry (SFC-MS/MS) method and an ultra-high performance liquid chromatography tandem mass spectrometry (UHPLC-MS/MS) method, for the analysis of *N*-acetyl-serotonin (NAS) and melatonin (Mel) in human serum, and to compare the performance of these methods. Deuterated isotopologues of the neurotransmitters were synthesized and evaluated for suitability as internal standards in sample preparation. Liquid-liquid extraction was selected as sample preparation procedure. With chloroform, the best extraction solvent tested, an extraction yield of  $48 \pm 2\%$  for *N*-acetyl-serotonin and  $101 \pm 10\%$  for melatonin was achieved. SFC separation was accomplished within 3 min on a BEH stationary phase, employing isocratic elution with 90% carbon dioxide and 0.1% formic acid as well as 0.05% ammonium formate in methanol. For the 4 min UHPLC gradient separation with 0.1% formic acid in water and methanol, respectively, a Kinetex XB-C18 was used as stationary phase. Both chromatographic techniques were optimized regarding mobile phase composition, additives to the mobile phase and column temperature. Multiple reaction monitoring (MRM) analysis was used for quantification of the metabolites. Both methods were validated regarding retention time stability, LOD, LOQ, repeatability and reproducibility of quantification, process efficiency, extraction recovery and matrix effects. LOD and LOQ were  $0.017$  and  $0.05 \text{ pg } \mu\text{L}^{-1}$  for NAS and  $0.006$  and  $0.018 \text{ pg } \mu\text{L}^{-1}$  for Mel in SFC-MS/MS compared to  $0.028$  and  $0.1 \text{ pg } \mu\text{L}^{-1}$  for NAS and  $0.006$  and  $0.017 \text{ pg } \mu\text{L}^{-1}$  for Mel in UHPLC-MS/MS.

<http://dx.doi.org/10.1016/j.aca.2016.08.012>



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### 185. A Fast And Sensitive Method For The Separation Of Carotenoids Using Ultra-High Performance Supercritical Fluid Chromatography Mass Spectrometry

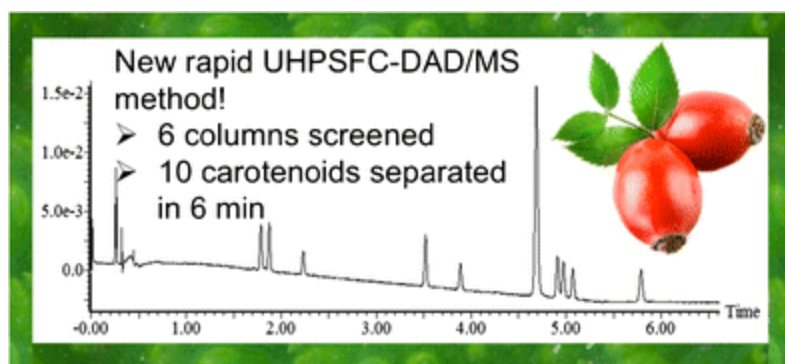
2016 - Analytical and Bioanalytical Chemistry

Keywords: Lund University, Carotene, Xanthophyll, Orthogonal column screening, Method development, Supercritical fluid, Mass spectrometry

### Abstract

In this study, a rapid and sensitive ultra-high performance supercritical fluid chromatography-mass spectrometry (UHPSFC-MS) method has been developed and partially validated for the separation of carotenoids within less than 6 min. Six columns of orthogonal selectivity were examined, and the best separation was obtained by using a 1-aminoanthracene (1-AA) column. The length of polyene chain as well as the number of hydroxyl groups in the structure of the studied carotenoids determines their differences in the physiochemical properties and thus the separation that is achieved on this column. All of the investigated carotenoids were baseline separated with resolution values greater than 1.5. The effects of gradient program, back pressure, and column temperature were studied with respect to chromatographic properties such as retention and selectivity. Electrospray ionization (ESI) and atmospheric pressure chemical ionization (APCI) were compared in both positive and negative mode, using both direct infusion and hyphenated with UHPSFC. The ESI in positive mode provided the highest response. The coefficient of determination ( $R^2$ ) for all calibration curves were greater than 0.998. Limit of detection (LOD) was in the range of 2.6 and 25.2 ng/mL for  $\alpha$ -carotene and astaxanthin, respectively, whereas limit of quantification (LOQ) was in the range of 7.8 and 58.0 ng/mL for  $\alpha$ -carotene and astaxanthin, respectively. Repeatability and intermediate precision of the developed UHPSFC-MS method were determined and found to be RSD < 3 % and RSD < 6 %, respectively. The method was applied in order to determine carotenoids in supercritical fluid extracts of microalgae and rosehip.

<http://dx.doi.org/10.1007/s00216-016-9707-5>



## 186. Regioisomeric And Enantiomeric Analysis Of Triacylglycerols

2016 - Analytical Biochemistry

Keywords: Institute of Microbiology, University of Chemistry and Technology, regioisomers, enantiomers, triacylglycerols, health science

### Abstract

A survey of useful methods for separation and identification of regioisomers and enantiomers of triacylglycerols. Gas chromatography, gas chromatography-mass spectrometry,  $^{13}\text{C}$  NMR determination of regioisomers by enzymatic methods, and supercritical fluid chromatography are briefly surveyed, whereas a detailed description is given of the analysis of triacylglycerols by liquid chromatography, especially with silver ion ( $\text{Ag}^+$ ; argentation), and nonaqueous reversed phase liquid chromatography. Special attention is paid to chiral chromatography. Details of mass spectrometry of triacylglycerols are also described, especially the identification of important triacylglycerol ions such as  $[\text{M} + \text{H}-\text{RCOOH}]^+$  in atmospheric pressure chemical ionization mass spectra.

<http://dx.doi.org/10.1016/j.ab.2016.05.028>

## 187. Enantioselective Separation Of Biologically Active Basic Compounds In Ultra-Performance Supercritical Fluid Chromatography

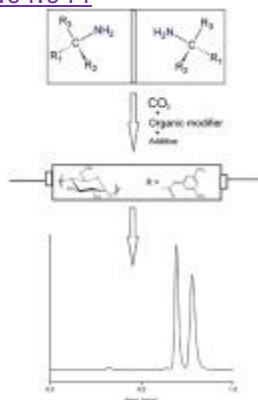
2016 - Analytica Chimica Acta

Keywords: Charles University, University of Graz, chiral compounds, enantioselectivity, Amylose-based chiral stationary phase, health science

### Abstract

The enantioseparation of basic compounds represent a challenging task in modern SFC. Therefore this work is focused on development and optimization of fast SFC methods suitable for enantioseparation of 27 biologically active basic compounds of various structures. The influences of the co-solvent type as well as different mobile phase additives on retention, enantioselectivity and enantioresolution were investigated. Obtained results confirmed that the mobile phase additives, especially bases (or the mixture of base and acid), improve peak shape and enhance enantioresolution. The best results were achieved with isopropylamine or the mixture of isopropylamine and trifluoroacetic acid as additives. In addition, the effect of temperature and back pressure were evaluated to optimize the enantioseparation process. The immobilized amylose-based chiral stationary phase, *i.e.* tris(3,5-dimethylphenylcarbamate) derivative of amylose proved to be useful tool for the enantioseparation of a broad spectrum of chiral bases. The chromatographic conditions that yielded baseline enantioseparations of all tested compounds were discovered. The presented work can serve as a guide for simplifying the method development for enantioseparation of basic racemates in SFC.

<http://dx.doi.org/10.1016/j.aca.2016.04.044>



## 188. Is The Solvation Parameter Model Or Its Adaptations Adequate To Account For Ionic Interactions When Characterizing Stationary Phases For Drug Impurity Profiling With Supercritical Fluid Chromatography?

2016 - Analytica Chimica Acta

Keywords: Vrije Universiteit, Université d'Orléans, solvation parameters, pharmaceuticals

### Abstract

Nine commercially available polar and aromatic stationary phases were characterized under supercritical fluid chromatographic (SFC) conditions. Retention data of 64 pharmaceutical compounds was acquired to generate models based on the linear solvation energy relationship (LSER) approach. Previously, adaptation of the LSER model was done in liquid chromatography by the addition of two solute descriptors to describe the influence of positive ( $D^+$ ) and negative ( $D^-$ ) charges on the retention of ionized compounds. In this study, the LSER models, with and without the ionization terms for acidic and basic solutes, were compared. The improved fits obtained for the modified models support inclusion of the  $D^+$  and  $D^-$  terms for pharmaceutical compounds. Moreover, the statistical significance of the new terms in the models indicates the importance of ionic interactions in the retention of pharmaceutical compounds in SFC. However, unlike characterization through the retention profiles, characterization of the stationary phases by modelling never explains the retention variance completely and thus seems less appropriate.

<http://dx.doi.org/10.1016/j.aca.2016.04.014>

### 189. Simultaneous Determination Of Topiramate, Carbamazepine, Oxcarbazepine And Its Major Metabolite In Human Plasma By SFC-ESI-MS/MS With Polarity Switching: Application To Therapeutic Drug Monitoring

2016 - Arabian Journal of Chemistry

Keywords: Antiepileptic drugs, SFC-ESI-MS/MS, Human plasma, Therapeutic drug monitoring

#### Abstract

Antiepileptic drugs are the first choice for epilepsy treatment. Monitoring antiepileptic drugs is important to minimize their adverse side effects by choosing the optimum drug dosage. An accurate and high throughput supercritical fluid chromatography-tandem mass spectrometry method has been developed for the simultaneous quantification of several antiepileptic drugs in human plasma. Plasma samples were extracted with ethyl acetate and the upper organic layer was directly injected into the supercritical fluid chromatography/mass spectrometry (SFC-MS/MS) system without further nitrogen evaporation and subsequent reconstitution. The analytes were eluted on a UPC<sup>2</sup>™ BEH, 2-EP column (100 × 3 mm, 1.7 μm) at a flow rate of 1.0 mL/min and multi-reaction monitoring (MRM) was performed for determination of the analytes and internal standard (IS) in polarity switching mode. Calibration curves were linear over the concentration ranges of 0.08–40, 0.01–15, 0.01–8 and 0.5–50 μg/mL with lower limit of quantifications of 0.08, 0.01, 0.01 and 0.50 μg/mL for topiramate, carbamazepine, oxcarbazepine and monohydroxycarbamazepine, respectively. This sensitive, accurate, novel method will be very useful for monitoring the above antiepileptic drugs and for pharmacokinetic studies.

<http://dx.doi.org/10.1016/j.arabjc.2016.09.016>

### 190. Ultraperformance Convergence Chromatography-High Resolution Tandem Mass Spectrometry For Lipid Biomarker Profiling And Identification

2016 - Biomedical Chromatography

Keywords: Lipids, biological samples, mouse lung tissue, intra class species, tandem mass spec, ceramides; convergence chromatography, lipidomics, lung irradiation, supercritical fluid chromatography

#### Abstract

Lipids represent biologically ubiquitous and highly dynamic molecules in terms of abundance and structural diversity. Whereas the potential for lipids to inform on disease/injury is promising, their unique characteristics make detection and identification of lipids from biological samples analytically demanding. We report the use of ultraperformance convergence chromatography (UPC<sup>2</sup>), a variant of supercritical fluid chromatography, coupled to high-resolution, data-independent tandem mass spectrometry for characterization of total lipid extracts from mouse lung tissue. The UPC<sup>2</sup> platform resulted in lipid class separation and when combined with orthogonal column chemistries yielded chromatographic separation of intra-class species based on acyl chain hydrophobicity. Moreover, the combined approach of using UPC<sup>2</sup> with orthogonal column chemistries, accurate mass measurements, time-aligned low- and high-collision energy total ion chromatograms, and positive and negative ion mode product ion spectra correlation allowed for confident lipid identification. Of great interest was the identification of differentially expressed ceramides that were elevated 24 h post whole thorax lung irradiation. The identification of lipids that were elevated 24 h post-irradiation signifies a unique opportunity to investigate early mechanisms of action prior to the onset of clinical symptoms in the whole thorax lung irradiation mouse model.

<http://dx.doi.org/10.1002/bmc.3822>

### 191. Synthesis Of Novel Amphiphilic Hyaluronan Containing-Aromatic Fatty Acids For Fabrication Of Polymeric Micelles

2016 - Carbohydrate Polymers

Keywords: Contipro a.s., Tomáš Bat'a University in Zlín, University Pardubice, hyaluronic acid,  $\omega$ -Phenylalkanoic acids, amphiphilic polysaccharides, resveratrol, retinyl palmitate, hyaluronan, benzoyl chloride, 4-Phenylbutanoic acid, separation science

**Abstract**

Novel hydrophobized hyaluronan (HA) derivatives, containing  $\omega$ -phenylalkanoic acids ( $\omega$ -PAA, 4-phenylbutyric acid, 6-phenylhexanoic, 8-phenyloctanoic or 11-tolylundecanoic acids) were prepared by esterification. Mixed anhydrides obtained after reaction of the carboxyl acid moiety and benzoyl chloride were found to be active acylating agents, affording hydrophobized HA in good yield and under mild conditions. The reactivity of the aromatic fatty acids towards esterification has decreased with the increasing length of the aliphatic spacer between the aromatic substituent and carboxylic acid moiety. The novel HA derivatives self-assembled from very low concentrations and were found to be non-cytotoxic. The potential use of  $\omega$ -phenylalkanoic acids grafted-HA towards drug delivery applications was demonstrated by hydrophobic drugs (resveratrol and retinyl palmitate) encapsulation. The drug loading capacity of the novel HA derivatives was significantly improved most likely because of  $\pi$ - $\pi$  interactions between the micelle core and loaded hydrophobic aromatic compound.

[doi:10.1016/j.carbpol.2016.06.085](https://doi.org/10.1016/j.carbpol.2016.06.085)

## 192. Determination Of Stereoisomers In Landiolol Hydrochloride By Ultra Performance Convergence Chromatography

2016 - Chinese Journal of Analytical Chemistry

Keywords: Ultra performance convergence chromatography; Landiolol hydrochloride; Stereoisomers; Chiral separation

**Abstract**

A new method for chiral separation and purity inspection of landiolol hydrochloride and its stereoisomers was developed by ultra-performance convergence chromatography (UPC<sup>2</sup>). The mobile phase was the mixture of supercritical CO<sub>2</sub> and methanol/*n*-butyl alcohol/acetonitrile (1:1:1, V/V) plus 0.5% NH<sub>3</sub>·H<sub>2</sub>O. The separation was carried out on the Daicel CHIRALPAK®IF column (150 mm×4.6 mm, 3  $\mu$ m) with a flow rate of 2.8 mL/min at 50°C using 223 nm as detection wavelength. Under the optimized experimental conditions, for *R,R*-stereoisomer, *R,S*-stereoisomer and *S,R*-stereoisomer, the detection limits (LOD, *S/N*=3) were 0.3, 0.4 and 0.3 mg/L, the linear ranges were 2-300 mg/L, 5-300 mg/L and 2-300 mg/L, the recoveries of spike samples were 103.4%±2.5%, 91.8%±2.5% and 101.7%±1.5%, and the injection repeatabilities were 0.06%, 0.09% and 0.08% (*n*=6), respectively. The experimental results demonstrate that the UPC<sup>2</sup>-based method can be used for the analysis and determination of landiolol hydrochloride and its stereoisomers.

<http://pesquisa.bvsalud.org/oncologiauy/resource/en/wprim-955918>

## 193. Residue Determination Of *Cis*-Epoiconazole Enantiomers In Fruit And Tea By Ultra Performance Convergence Chromatography Combined With Quadrupole Time-Of-Flight Mass Spectrometry

2016 - Chinese Journal of Analytical Chemistry

Keywords: Chiral enantiomers; Residue analysis; *cis*-Epoiconazole; Apple; Grape; Tea; Ultra performance convergence chromatography; QTOF mass spectrometry

**Abstract**

A chiral separation and residue determination method for *cis*-epoiconazole enantiomers in apple, grape and tea samples was developed and validated by ultra performance convergence chromatography combined with quadrupole time-of-flight mass spectrometry (UPC<sup>2</sup>-QTOF/MS). The Chiral CCA column was used to separate *cis*-epoiconazole enantiomers and the chromatography conditions (mobile phase modifier and proportion, column temperature, automated backpressure regulator, and auxiliary solvent) were optimized. Samples were extracted by acetonitrile, and respectively purified by Cleanert TPT or Pesti-Carb solid phase extraction (SPE) columns, then analyzed by UPC<sup>2</sup>-QTOF/MS. The optimum conditions were as follows: mobile phase was CO<sub>2</sub>/isopropanol(95:5, V/V), flow-rate was 2.0 mL/min, automated backpressure regulator (ABPR) was 13.79 MPa, column temperature was 30°C, with a post-column auxiliary solvent of methanol/water (1:1, V/V) containing 2 mmol/L ammonium formate. The analyte was



quantified by matrix external standard method. The results showed that linear range of this method was 0.01-1.00 mg/L, and the correlation coefficients were above 0.99. The recoveries of *cis*-epoxiconazole enantiomers at three spiked levels (0.005, 0.025 and 0.25 mg/kg) in fruit matrix were 67.9%-92.8% with relative standard deviations (RSDs,  $n=6$ ) less than 10%, and the limit of quantification (LOQ) of enantiomers was 0.005 mg/kg. The recoveries of *cis*-epoxiconazole enantiomers at three spiked levels (0.01, 0.05 and 0.5 mg/kg) in black tea were 74.1%-84.0% with RSDs ( $n=6$ ) less than 8%, and the LOQ for these two enantiomers was 0.01 mg/kg. This method is rapid, convenient and reliable, and could meet the requirement of residue analysis. <http://pesquisa.bvsalud.org/oncologiauy/resource/en/wprim-944171>

## 194. Separation Of Pharmaceuticals By SFC Using Mono And Di-Hydroxy Substituted Phenyl Stationary Phases

2016 - Chromatography Today

Keywords: Cannabinoids, chiral, synthetic

### Abstract

Ultra high performance supercritical fluid chromatography (UHPSFC) technology presents an alternative and orthogonal solution to GC and HPLC for the separation of synthetic cannabinoids. In particular, it offers excellent selectivity for structural analogs and stereoisomers. Here, a simple method development strategy is demonstrated for the chiral analysis of selected synthetic cannabinoids including: HU-210, HU-211, ( $\pm$ )-CP 47,497, ( $\pm$ )-epi CP 47,497, ( $\pm$ )-CP 55,940 and ( $\pm$ )-5-epi CP 55,940. Fast stereoisomeric separations, including related enantiomers and diastereomers, are achieved on the Waters ACQUITY UPC2 System using the Waters Trefoil chiral columns. The efficiency of UHPSFC is demonstrated for rapid enantiomeric separation of chiral synthetic cannabinoids. - See more at: [http://www.chromatographytoday.com/articles/supercritical-fluid-sfcgreen-chromatography/45/by\\_jacquelyn\\_runco\\_andrew\\_aubin\\_jo-ann\\_jablonski/simple\\_method\\_development\\_for\\_the\\_separation\\_of\\_chiral\\_synthetic\\_cannabinoids\\_using\\_ultra\\_high\\_performance\\_supercritical\\_fluid\\_chromatography/2090/#sthash.Zg7dEbKS.dpuf](http://www.chromatographytoday.com/articles/supercritical-fluid-sfcgreen-chromatography/45/by_jacquelyn_runco_andrew_aubin_jo-ann_jablonski/simple_method_development_for_the_separation_of_chiral_synthetic_cannabinoids_using_ultra_high_performance_supercritical_fluid_chromatography/2090/#sthash.Zg7dEbKS.dpuf)

## 195. Chiral Bioaccumulation Behavior Of Tebuconazole In The Zebrafish (*Danio Rerio*)

2016 - Ecotoxicology and Environmental Safety

Keywords: Shenyang Agricultural University, Chinese Academy of Agricultural Sciences, State Key Laboratory for Biology of Plant Diseases and Insect Pests, tebuconazole, zebrafish, bioaccumulation, health science

### Abstract

Tebuconazole is an effective chiral fungicide, and previous studies have demonstrated that tebuconazole enantiomers exhibit enantioselective toxicity to non-target aquatic organisms. Thus, the aim of the present study was to investigate the chiral bioaccumulation behavior of tebuconazole in zebrafish (*Danio rerio*). Two exposure concentrations (0.107 and 1.07 mg/L) of tebuconazole were used. The uptake experiments lasted for 8 days, and subsequently, the zebrafish were transferred to another clean tank containing water without tebuconazole for depuration experiments (up to 14 days). A significant trend in enantioselective bioaccumulation was observed in these zebrafish with the preferential accumulation of ( $-$ )-*R*-tebuconazole at two dose levels. The results of the depuration experiments indicated that the degradation of ( $-$ )-*R*-tebuconazole in zebrafish was slower than that of ( $+$ )-*S*-tebuconazole. The  $BCF_k$  values for ( $+$ )-*S*-tebuconazole and ( $-$ )-*R*-tebuconazole in a low dose of this chemical were 11.22 and 16.25, respectively, while at a high dose, these values were 9.79 and 10.31, respectively. The enantiomer fraction of tebuconazole in zebrafish and water ranged from 0.31-0.49. Hence, future research should focus on the fate of tebuconazole in the aquatic environment at the enantiomer levels. <http://dx.doi.org/10.1016/j.ecoenv.2015.12.007>

## 196. Fat-Soluble Vitamin And Carotenoid Analysis In Cooking Oils By Ultra-Performance Convergence Chromatography

2016 - Food Analytical Methods

Keywords: Fat soluble vitamins (FSV), Carotenoids, Ultra performance convergence chromatography (UPC<sup>2</sup>), Cooking oils

### Abstract

In the current study, a rapid ultra-performance convergence chromatography (UPC<sup>2</sup>) method for the determination of seven fat soluble vitamins (vitamin A: retinol, retinyl acetate; vitamin D: ergocalciferol, cholecalciferol; vitamin E:  $\alpha$ -tocopherol; vitamin K: phyloquinone, menaquinone) and three carotenoids (lutein, lycopene,  $\beta$ -carotene) in various cooking oils was developed. Fat soluble vitamins could be separated within 8 min on a UPC<sup>2</sup> system with a BEH column (3.0  $\times$  100 mm, 1.7  $\mu$ m) at 50  $^{\circ}$ C, using a gradient elution with a mobile phase of carbon dioxide and 2-propanol (99.9:0.1/99.2:0.8/99.9:0.1), at a flow rate of 2 mL/min and the automatic back pressure regulator (ABPR) set to 1800 psi. Carotenoids were separated within 3 min on a similar UPC<sup>2</sup> system with an HSS C<sub>18</sub> SB column (3.0  $\times$  100 mm, 1.8  $\mu$ m) at 40  $^{\circ}$ C, under isocratic conditions with a mobile phase of carbon dioxide and ethanol (75:25; v/v). The flow rate was set to 1.5 mL/min and the ABPR to 1800 psi. The limits of detection (LODs) and quantification (LOQs) were ranging between 0.01 and 1.17  $\mu$ g/mL and from 0.05 and 3.59  $\mu$ g/mL for fat soluble vitamins while carotenoid detection limits fell in the range of 0.03–0.11  $\mu$ g/mL and of 0.10–0.38  $\mu$ g/mL, respectively. The results showed excellent linearity for both methods ( $R^2$  0.9993–0.9999). A recovery study with standard addition technique into a selected coconut oil sample resulted in more than 90 % recovery for retinyl acetate, retinol, and vitamin K<sub>1</sub> and K<sub>2</sub>, whereas the recovery for vitamin D<sub>2</sub> and D<sub>3</sub> ranged between 70 and 80 %. The lowest recovery of 68–70 % was found for  $\alpha$ -tocopherol while almost comparable recovery rates above 80 % were observed for all three carotenoids.

<http://dx.doi.org/10.1007/s12161-016-0661-9>

## 197. Simultaneous Analysis Of Eight Vitamin E Isomers In *Moringa Oleifera* Lam. Leaves By Ultra Performance Convergence Chromatography

2016 - Food Chemistry

Keywords: Chinese Academy of Tropical Agricultural Sciences Center for Food Quality Supervision and Testing Ministry of Agriculture (Zhanjiang), Agricultural Product Processing Research Institute, Chinese Academy of Tropical Agricultural Sciences,  $\alpha$ -,  $\beta$ -,  $\gamma$ -, and  $\delta$ -tocopherol and  $\alpha$ -,  $\beta$ -,  $\gamma$ -, and  $\delta$ -tocotrienol, food

### Abstract

A new method for simultaneous determination of eight vitamin E isomers including  $\alpha$ -,  $\beta$ -,  $\gamma$ -, and  $\delta$ -tocopherol and  $\alpha$ -,  $\beta$ -,  $\gamma$ -, and  $\delta$ -tocotrienol by ultra-performance convergence chromatography (UPC<sup>2</sup>) equipped with a diode array detector was reported. They were separated on a BEH 2-EP column (3.0 mm  $\times$  100 mm, 1.7  $\mu$ m) using gradient elution (95:5–80:20) with a mobile phase consisted of CO<sub>2</sub> and methanol:isopropanol (1:1, v/v), back pressure of 1800 psi, flow rate of 1.5 ml/min and detection at 294 nm. The results showed good linearity ( $R^2$  = 0.9990–0.9998) and high resolution (1.48–7.67). Limits of detection (LOD) and quantification (LOQ) ranged from 23–49 ng/L and 70–150 ng/L, respectively. Relative standard deviations (RSD) for repeatability and reproducibility were 0.62–3.16% and 0.82–3.34%, respectively. Moreover, this method was successfully applied to analysis the vitamin E isomers in *Moringa oleifera* leaf samples.

<http://dx.doi.org/10.1016/j.foodchem.2016.03.089>

## 198. Vitamin E analysis by ultra-performance convergence chromatography and structural elucidation of novel $\alpha$ -tocodienol by high-resolution mass spectrometry

2016 - Food Chemistry

Keywords: Palm Nutraceuticals, Research Instruments SDN, Matrix Analytical Technologies, tocodienol, palm oil,  $\alpha$ -Tocodienol, tocopherol, tocotrienol, vitamins, food

### Abstract

We have developed a method for analysing vitamin E using ultra-performance convergence chromatography with a chromatographic runtime of 5.5 min. A well-resolved chromatogram with excellent precision in retention time revealed seven vitamin E components in the palm oil derived tocotrienol-rich fraction. The major vitamin E components were  $\alpha$ -tocopherol,  $\alpha$ -tocotrienol,  $\gamma$ -tocotrienol and  $\delta$ -tocotrienol whereas the minor vitamin E components were  $\alpha$ -tocotrienol,  $\beta$ -tocotrienol and an unreported trace component. The new component was positively identified by high-resolution mass spectrometry as 2-methyl-2(4',8',12'-trimethyltrideca-7',11'-dienyl)5,7,8-trimethylchroman-6-ol or  $\alpha$ -tocodienol

Highlights:

- A novel vitamin E component  $\alpha$ -tocodienol was elucidated.
- Vitamin E analysis by ultra-performance convergence chromatography.
- Excellent chromatographic resolution and precision in retention time.
- A rapid, simple, environmental friendly and economical analytical method.
- Can be developed into a mainstream analytical technique.
- 

<http://dx.doi.org/10.1016/j.foodchem.2015.09.073>

### 199. A Comparative Study Of Triacylglycerol Composition In Chinese Human Milk Within Different Lactation Stages And Imported Infant Formula By SFC Coupled With Q-TOF-MS

2016 - Food Chemistry

Keywords: Human milk, Infant formula, Triacylglycerol, Supercritical fluid chromatography

**Abstract**

Triacylglycerols (TAGs) as the major component of milk fat are significant factors to ensure the healthy growth of infants. An efficient method for identifying TAGs in human milk (HM) and infant formula (IF) was established using supercritical fluid chromatograph (SFC) coupled with quadruple time-of-flight mass spectrometry (Q-TOF-MS). The results indicated the feasibility of this method with satisfactory recoveries (>80%) and correlation coefficients ( $r^2 \geq 0.993$ ). More than 60 TAGs in HM and 50 TAGs in IF were identified. The profiling results demonstrated that TAGs in HM were greatly affected by lactation stage. Significant differences were found between HM and IF, such as much higher medium chain TAGs and saturated TAGs in IF, indicating that the formulas developed by foreign manufacturers were not suitable for Chinese babies. This high-throughput method exhibits a huge potential for analysis of milk samples and the result may serve as an important guide for Chinese infants diet.

<http://dx.doi.org/10.1016/j.foodchem.2016.09.099>

### 200. Tocopherols And Tocotrienols In Plants And Their Products: A Review On Methods Of Extraction, Chromatographic Separation, And Detection

2016 - Food Research International

Keywords: Konkuk University, tocopherols, antioxidants, food, tocopherols, vitamin E, fruits, vegetables, grains, food

**Abstract**

Vitamin E consists of four tocopherols ( $\alpha$ -,  $\beta$ -,  $\gamma$ -, and  $\delta$ -tocopherol) and four tocotrienols ( $\alpha$ -,  $\beta$ -,  $\gamma$ -, and  $\delta$ -tocotrienols), collectively referred to as tocopherols or tocopherols. Tocopherols are well-known for potent antioxidant, anticancer, anti-inflammatory, immuno-stimulatory and nephroprotective properties. For human nutrition, diet is the major source of tocopherols (vitamin E) in the body. Thus, there is a need to analyze the different forms of tocopherols in the diet for the recommendations and to monitor the intake in the body accurately. Several methods have been developed for effective extraction, selective chromatographic separation and sensitive detection of tocopherols in food. Major advancements also have been made in the field of mass spectrometry for high throughput analysis of primary and secondary metabolites in fruits, vegetables, and grains. This review discusses the theoretical aspects and modern developments in methods of extraction, chromatographic separation, and detection of tocopherols in plants and their products. Additionally, future research challenges in this perspective are also identified.

## 201. Direct Enantiomer Determination Of Methorphan By HPLC-MS And SFC-MS

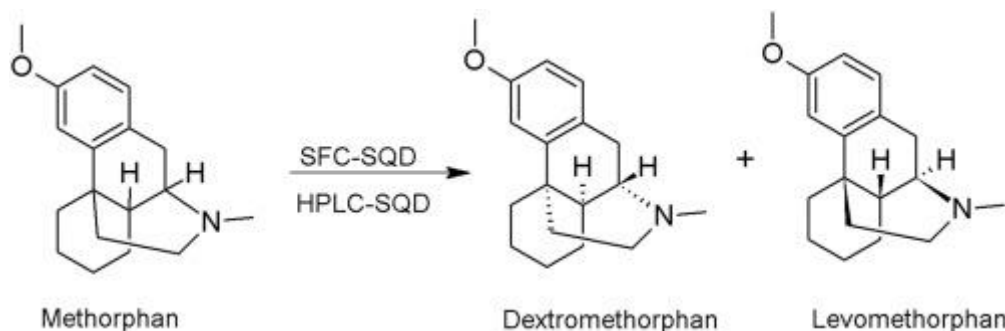
2016 - Forensic Chemistry

Keywords: Dextromethorphan, Levomethorphan, High performance liquid chromatograph, Supercritical fluid chromatography, Mass spectrometry, Enantiomer determination

### Abstract

The direct and rapid chiral analysis of methorphan was achieved with excellent sensitivity and selectivity using ultra high-performance liquid chromatography-single quadrupole mass spectrometry (HPLC-SQD) and supercritical fluid chromatography-single quadrupole mass spectrometry (SFC-SQD). The optimized separation of dextromethorphan and levomethorphan by HPLC-SQD was accomplished in under 9 min using a Chirobiotic V2 (2.1 × 250 mm, 5 μm) column with a mobile phase consisting of MeOH/NH<sub>4</sub>OH/HOAc (100/0.02/0.1, v/v/v). The optimal separation by SFC-SQD was achieved in less than 3 min using a Trefoil AMY1 (2.1 × 150 mm, 2.5 μm) column with a mobile phase comprised of CO<sub>2</sub>, 9% MeOH as a co-solvent, and 0.3% cyclohexylamine as a modifier. The limit of detection was 10 ng/mL in the selected ion recording mode for both systems.

<http://dx.doi.org/10.1016/j.forc.2016.10.004>



## 202. Exploring The Scope Of New Arylamino Alcohol Derivatives: Synthesis, Antimalarial Evaluation, Toxicological Studies, And Target Exploration

2016 - International Journal for Parasitology: Drugs and Drug Resistance

Keywords: Antimalarial, Antiplasmodial, Arylamino alcohol, Plasmepsin II enzyme, Hemozoin inhibition, Mannich reaction, UPC2

### Abstract

Synthesis of new 1-aryl-3-substituted propanol derivatives followed by structure-activity relationship, *in silico* drug-likeness, cytotoxicity, genotoxicity, *in silico* metabolism, *in silico* pharmacophore modeling, and *in vivo* studies led to the identification of compounds **22** and **23** with significant *in vitro* antiplasmodial activity against drug sensitive (D6 IC<sub>50</sub> ≤ 0.19 μM) and multidrug resistant (FCR-3 IC<sub>50</sub> ≤ 0.40 μM and C235 IC<sub>50</sub> ≤ 0.28 μM) strains of *Plasmodium falciparum*. Adequate selectivity index and absence of genotoxicity was also observed. Notably, compound **22** displays excellent parasitemia reduction (98 ± 1%), and complete cure with all treated mice surviving through the entire period with no signs of toxicity. One important factor is the agreement between *in vitro* potency and *in vivo* studies. Target exploration was performed; this chemotype series exhibits an alternative antimalarial mechanism.

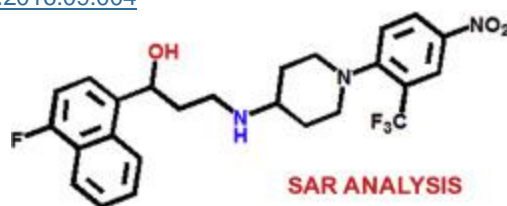
<http://dx.doi.org/10.1016/j.ijpddr.2016.09.004>

## 203. Exploring The Scope Of New Arylamino Alcohol Derivatives: Synthesis, Antimalarial Evaluation, Toxicological Studies, And Target Exploration

Keywords: Antimalarial, Antiplasmodia, Arylamino alcohol, Plasmeprin II enzyme, Hemozoin inhibition, Mannich reaction, Genotoxicity

**Abstract**

Synthesis of new 1-aryl-3-substituted propanol derivatives followed by structure-activity relationship, *in silico* drug-likeness, cytotoxicity, genotoxicity, *in silico* metabolism, *in silico* pharmacophore modeling, and *in vivo* studies led to the identification of compounds **22** and **23** with significant *in vitro* antiplasmodial activity against drug sensitive (D6  $IC_{50} \leq 0.19 \mu M$ ) and multidrug resistant (FCR-3  $IC_{50} \leq 0.40 \mu M$  and C235  $IC_{50} \leq 0.28 \mu M$ ) strains of *Plasmodium falciparum*. Adequate selectivity index and absence of genotoxicity was also observed. Notably, compound **22** displays excellent parasitemia reduction ( $98 \pm 1\%$ ), and complete cure with all treated mice surviving through the entire period with no signs of toxicity. One important factor is the agreement between *in vitro* potency and *in vivo* studies. Target exploration was performed; this chemotype series exhibits an alternative antimalarial mechanism. <http://dx.doi.org/10.1016/j.ijpddr.2016.09.004>



**Arylamino alcohol**

**Antiplasmodial activity**

D6, FCR-3, and C235  $IC_{50} \leq 0.15 \mu M$

Excellent parasitemia reduction *in vivo*

Target exploration (unknown primary mechanism of action)

**204. Screening Of Indian Lingzhi Or Reishi Medicinal Mushroom, *Ganoderma Lucidum* (Agaricomycetes): A UPC<sup>2</sup>-SQD-MS Approach**

Keywords: Defence Institute of Physiology and Allied Sciences, Waters, medicinal mushrooms, *Ganoderma lucidum*, principal component analysis, antioxidant activity, metabolite profiling, natural products, pharmaceuticals

**Abstract**

Oriental medicinal mushroom *Ganoderma lucidum* has been widely used for the promotion of health and longevity owing to its various bioactive constituents. Therefore, comprehending metabolomics of different *G. lucidum* parts could be of paramount importance for investigating their pharmacological properties. Ultra-performance convergence chromatography (UPC2) along with mass spectrometry (MS) is an emerging technique that has not yet been applied for metabolite profiling of *G. lucidum*. This study has been undertaken to establish metabolomics of the aqueous extracts of mycelium (GLM), fruiting body (GLF), and their mixture (GLMF) using ultra-performance convergence chromatography single quadrupole mass spectrometry (UPC2-SQD-MS). Aqueous extracts of *G. lucidum* prepared using an accelerated solvent extraction technique have been characterized for their mycochemical activities in terms of total flavonoid content, 1,1-diphenyl-2-picryl-hydrazyl scavenging activity, and ferric ion reducing antioxidant power. The UPC2-SQD-MS technique has been used for the first time for metabolite profiling of *G. lucidum* on a Princeton Diol column (4.6 × 250 mm; 5 μm) using supercritical CO<sub>2</sub> (solvent) and 20 mM ammonium acetate in methanol (co-solvent). In the present study, UPC2-SQD-MS was found to be a rapid, efficient, and high-throughput analytical technique, whose coupling to



principal component analysis (PCA) and phytochemical evaluation could be used as a powerful tool for elucidating metabolite diversity between mycelium and fruiting body of *G. lucidum*. PCA showed a clear distinction in the metabolite compositions of the samples. Mycochemical studies revealed that overall GLF possessed better antioxidant properties among the aqueous extracts of *G. lucidum*.

<http://dx.doi.org/10.1615/IntJMedMushrooms.v18.i2.80>

## 205. Influence Of Uptake Pathways On The Stereoselective Dissipation Of Chiral Neonicotinoid Sulfoxaflor In Greenhouse Vegetables

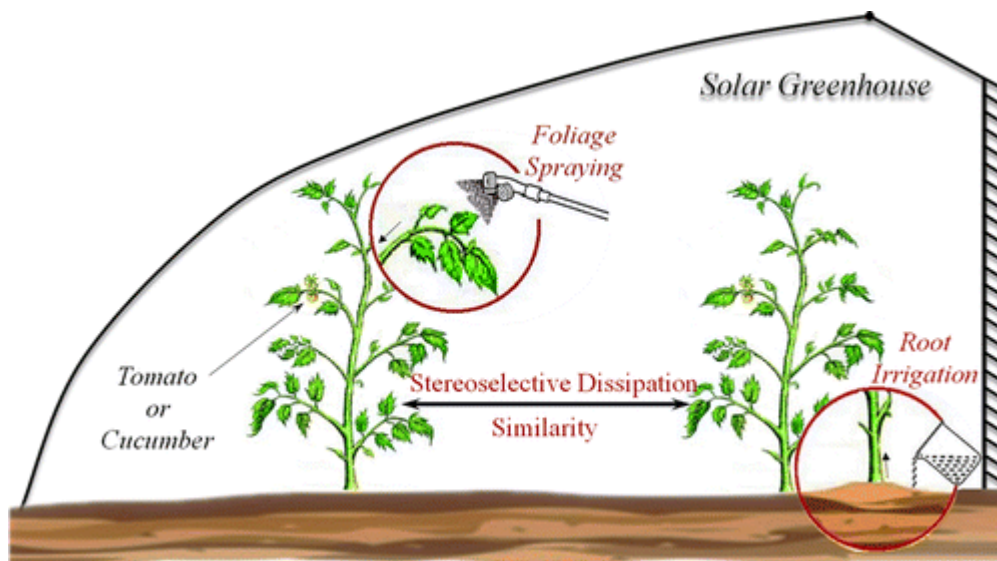
2016 - Journal of Agricultural and Food Chemistry

Keywords: solar greenhouse, stereoselectivity, sulfoxaflor, ultrahigh performance supercritical fluid chromatography–tandem mass spectrometry, uptake pathways

### Abstract

Stereoselectivity is of vital importance in our environment and needs to be taken into account for comprehensive risk assessment and regulatory decisions of chiral neonicotinoid sulfoxaflor. However, little is known about the dissipation of sulfoxaflor stereoisomers with respect to stereoselectivity in plants under greenhouse cultivation. To bridge the knowledge gap, the current study was initiated to investigate the stereoselective degradation of sulfoxaflor in solar greenhouse cucumber and tomato from foliage and root uptake pathways. The stereoselective dissipation of sulfoxaflor was not statistically different between enantiomer pairs from foliage and root pathways of vegetables ( $P < 0.05$ ). The persistence of sulfoxaflor stereoisomers was consistently prolonged under the foliage uptake pathway ( $t_{1/2}$ , 3.38–14.09 days) compared to the root uptake pathway ( $t_{1/2}$ , 2.65–5.07 days) in both vegetable fruits. Nevertheless, the concentrations of (+)-sulfoxaflor A and (–)-sulfoxaflor B were both slightly higher than that of their antipode. The tiny difference should be emphasized because it might be magnified to a significant difference by the high-potential bioaccumulation of sulfoxaflor in the food chain.

<http://dx.doi.org/10.1021/acs.jafc.5b05940>



## 206. Comparison Of Liquid And Supercritical Fluid Chromatography Mobile Phases For Enantioselective Separations On Polysaccharide Stationary Phases

2016 - Journal of Chromatography A



Keywords: Université d'Orléans, Novartis Institutes for BioMedical Research, active pharmaceutical ingredients, achiral probes, enantiomers, enantiomer separation, racemates pharmaceutical

**Abstract**

Analysis and production of enantiomerically pure compounds is a major topic of interest when active pharmaceutical ingredients are concerned. Enantioselective chromatography has become a favourite both at the analytical and preparative scales. High-performance liquid chromatography (HPLC) and supercritical fluid chromatography (SFC) are dominating the scene and are often seen as complementary techniques. Nowadays, for economic and ecologic reasons, SFC may be preferred over normal-phase HPLC (NPLC) as it allows significant reductions in solvent consumption. However, the transfer of NPLC methods to SFC is not always straightforward. In this study, we compare the retention of achiral molecules and separation of enantiomers under supercritical fluid (carbon dioxide with ethanol or isopropanol) and liquid normal-phase (heptane with ethanol or isopropanol) elution modes with polysaccharide stationary phases in order to explore the differences between the retention and enantioselectivity properties between the two modes. Chemometric methods (namely quantitative structure-retention relationships and discriminant analysis) are employed to compare the results obtained on a large set of analytes (171 achiral probes and 97 racemates) and gain some understanding on the retention and separation mechanisms. The results indicate that, contrary to popular belief, carbon dioxide - solvent SFC mobile phases are often weaker eluents than liquid mobile phases. It appears that SFC and NPLC elution modes provide different retention mechanisms. While some enantioselectivities are unaffected, facilitating the transfer between the two elution modes, other enantioselectivities may be drastically different due to different types and strength of interactions contributing to enantioselectivity.

[doi:10.1016/j.chroma.2016.06.060](https://doi.org/10.1016/j.chroma.2016.06.060)

## 207. Liquid Chromatography And Supercritical Fluid Chromatography As Alternative Techniques To Gas Chromatography For The Rapid Screening Of Anabolic Agents In Urine

2016 - Journal of Chromatography A

Keywords: University of Geneva, Charles University, Universitaire Vaudois and University of Lausanne, anabolic steroids, doping control, health science

**Abstract**

This work describes the development of two methods involving supported liquid extraction (SLE) sample treatment followed by ultra-high performance liquid chromatography or ultra-high performance supercritical fluid chromatography coupled to tandem mass spectrometry (UHPLC-MS/MS and UHPSFC-MS/MS) for the screening of 43 anabolic agents in human urine. After evaluating different stationary phases, a polar-embedded C18 and a diol columns were selected for UHPLC-MS/MS and UHPSFC-MS/MS, respectively. Sample preparation, mobile phases and MS conditions were also finely tuned to achieve highest selectivity, chromatographic resolution and sensitivity. Then, the performance of these two methods was compared to the reference routine procedure for steroid analyses in anti-doping laboratories, which combines liquid-liquid extraction (LLE) followed by gas chromatography coupled to tandem mass spectrometry (GC-MS/MS). For this purpose, urine samples spiked with the compounds of interest at five different concentrations were analyzed using the three analytical platforms. The retention and selectivity of the three techniques were very different, ensuring a good complementarity. However, the two new methods displayed numerous advantages. The overall procedure was much faster thanks to high throughput SLE sample treatment using 48-well plates and faster chromatographic analysis. Moreover, the highest sensitivity was attained using UHPLC-MS/MS with 98% of the doping agents detected at the lowest concentration level (0.1ng/mL), against 76% for UHPSFC-MS/MS and only 14% for GC-MS/MS. Finally, the weakest matrix effects were obtained with UHPSFC-MS/MS with 76% of the analytes displaying relative matrix effect between -20 and 20%, while the GC-MS/MS reference method displayed very strong matrix effects (over 100%) for all of the anabolic agents.

[doi:10.1016/j.chroma.2016.05.004](https://doi.org/10.1016/j.chroma.2016.05.004)

## 208. Ultra-High Performance Supercritical Fluid Chromatography Coupled With Quadrupole-Time-Of-Flight Mass Spectrometry As A Performing Tool For Bioactive Analysis

2016 - Journal of Chromatography A

Keywords: University of Geneva, Nestle Institute of Health Sciences, natural products, plant metabolites, health science

### Abstract

Secondary metabolites are an almost unlimited reservoir of potential bioactive compounds. In view of the wide chemical space covered by natural compounds, their comprehensive analysis requires multiple cutting-edge approaches. This study evaluates the applicability of ultra-high performance supercritical fluid chromatography coupled to quadrupole-time-of-flight mass spectrometry (UHPSFC-QqToF-MS) as an analytical strategy for plant metabolites profiling. Versatility of this analytical platform was first assessed using 120 highly diverse natural compounds (according to lipophilicity, hydrogen bond capability, acid-base properties, molecular mass and chemical structure) that were screened on a set of 15 rationally chosen stationary phase chemistries. UHPSFC-QqToF-MS provides a suitable analytical solution for 88% of the tested compounds. Three stationary phases (Diol, not endcapped C18 and 2-EP) were highlighted as particularly polyvalent, since they allow suitable elution of 101 out of 120 natural compounds. The systematic evaluation of retention and selectivity of natural compounds further underlined the suitability of these three columns for the separation of natural compounds. This reduced set of key stationary phases constitutes a basis for untargeted scouting analysis and method development. Even if they were less versatile, stationary phases such as endcapped T3C18, polar P-PFP, were nevertheless found to provide extended selectivity for specific natural molecules sub-classes. Finally, the identified polyvalent conditions were successfully applied for the analysis of complex polar and non-polar plant extracts. These first experimental hits demonstrate the full applicability and potential of UHPSFC-QqToF-MS for plant metabolite profiling.

[doi:10.1016/j.chroma.2016.04.053](https://doi.org/10.1016/j.chroma.2016.04.053)

## 209. Analysis Of Polar Urinary Metabolites For Metabolic Phenotyping Using Supercritical Fluid Chromatography And Mass Spectrometry

2016 - Journal of Chromatography A

Keywords: King's College, Imperial College, Waters Corporation, method development, health science

### Abstract

Supercritical fluid chromatography (SFC) is frequently used for the analysis and separation of non-polar metabolites, but remains relatively underutilised for the study of polar molecules, even those which pose difficulties with established reversed-phase (RP) or hydrophilic interaction liquid chromatographic (HILIC) methodologies. Here, we present a fast SFC-MS method for the analysis of medium and high-polarity ( $-7 \leq \text{cLogP} \leq 2$ ) compounds, designed for implementation in a high-throughput metabolomics setting. Sixty polar analytes were first screened to identify those most suitable for inclusion in chromatographic test mixtures; then, a multi-dimensional method development study was conducted to determine the optimal choice of stationary phase, modifier additive and temperature for the separation of such analytes using SFC. The test mixtures were separated on a total of twelve different column chemistries at three different temperatures, using CO<sub>2</sub>-methanol-based mobile phases containing a variety of polar additives. Chromatographic performance was evaluated with a particular emphasis on peak capacity, overall resolution, peak distribution and repeatability. The results suggest that a new generation of stationary phases, specifically designed for improved robustness in mixed CO<sub>2</sub>-methanol mobile phases, can improve peak shape, peak capacity and resolution for all classes of polar analytes. A significant enhancement in chromatographic performance was observed for these urinary metabolites on the majority of the stationary phases when polar additives such as ammonium salts (formate, acetate and hydroxide) were included in the organic modifier, and the use of water or alkylamine additives was found to be beneficial for specific subsets of polar analytes. The utility of these findings was confirmed by the separation of a mixture of polar metabolites in human urine using an optimised 7min gradient SFC method, where the use of the recommended column and co-solvent combination resulted in a significant improvement in chromatographic performance.

[doi:10.1016/j.chroma.2016.04.040](https://doi.org/10.1016/j.chroma.2016.04.040)

## 210. Selective Enrichment In Bioactive Compound From *Kniphofia Uvaria* By Super/Subcritical Fluid Extraction And Centrifugal Partition Chromatography

2016 - Journal of Chromatography A

Keywords: Orleans University, LVMH Recherche, anthraquinones, natural products, antioxidants, bioactives, seeds, pharmaceutical

### Abstract

Nowadays, a large portion of synthetic products (active cosmetic and therapeutic ingredients) have their origin in natural products. *Kniphofia uvaria* is a plant from Africa which has proved in the past by in-vivo tests an antioxidant activity due to compounds present in roots. Recently, we have observed anthraquinones in *K. uvaria* seeds extracts. These derivatives are natural colorants which could have interesting bioactive potential. The aim of this study was to obtain an extract enriched in anthraquinones from *K. uvaria* seeds which mainly contains glycerides. First, the separation of the seed compounds was studied by using supercritical fluid chromatography (SFC) in the goal to provide a rapid quantification method of these bioactive compounds. A screening of numerous polar stationary phases was achieved for selecting the most suited phase to the separation of the four anthraquinones founded in the seeds. A gradient elution was optimized for improving the separation of the bioactive compounds from the numerous other families of major compounds of the extracts (fatty acids, di- and triglycerides). Besides, a non-selective and green Supercritical Fluid Extraction (SFE) with pure CO<sub>2</sub> was applied to seeds followed by a Centrifugal Partition Chromatography (CPC). The CPC system was optimized by using the Arizona phase system, to enrich the extract in anthraquinones. Two systems were selected to isolate the bioactive compounds from the oily extract with varied purity target. The effect of the injection mode for these very viscous samples was also studied. Finally, in order to directly apply a selective process of extraction to the seeds, the super/subcritical fluid extraction was optimized to increase the anthraquinone yield in the final extract, by studying varied modifier compositions and nature, as well as different temperatures and backpressures. Conditions suited to favour an enrichment factor bases on the ratio of anthraquinone and trilycerides extracted are described.

[doi:10.1016/j.chroma.2016.04.029](https://doi.org/10.1016/j.chroma.2016.04.029)

## 211. Evaluation Of Innovative Stationary Phase Ligand Chemistries And Analytical Conditions For The Analysis Of Basic Drugs By Supercritical Fluid Chromatography

2016 - Journal of Chromatography A

Keywords: Geneva, 2-Picolylamine ligand chemistry, 1-Aminoanthracene ligand chemistry, Diethylamine ligand chemistry, pharmaceutical

### Abstract

Similar to reversed phase liquid chromatography, basic compounds can be highly challenging to analyze by supercritical fluid chromatography (SFC), as they tend to exhibit poor peak shape, especially those with high pK<sub>a</sub> values. In this study, three new stationary phase ligand chemistries available in sub -2 μm particle sizes, namely 2-picolylamine (2-PIC), 1-aminoanthracene (1-AA) and diethylamine (DEA), were tested in SFC conditions for the analysis of basic drugs. Due to the basic properties of these ligands, it is expected that the repulsive forces may improve peak shape of basic substances, similarly to the widely used 2-ethylpyridine (2-EP) phase. However, among the 38 tested basic drugs, less of 10% displayed Gaussian peaks (asymmetry between 0.8 and 1.4) using pure CO<sub>2</sub>/methanol on these phases. The addition of 10mM ammonium formate as mobile phase additive, drastically improved peak shapes and increased this proportion to 67% on 2-PIC. Introducing the additive in the injection solvent rather than in the organic modifier, gave acceptable results for 2-PIC only, with 31% of Gaussian peaks with an average asymmetry of 1.89 for the 38 selected basic drugs. These columns were also compared to hybrid silica (BEH), DIOL and 2-EP stationary phases, commonly employed in SFC. These phases commonly exhibit alternative retention and selectivity. In the end, the two most interesting ligands used as complementary columns were 2-PIC and BEH, as they provided suitable peak shapes for the basic drugs and almost orthogonal selectivities.

## 212. A Closer Study Of Methanol Adsorption And Its Impact On Solute Retentions In Supercritical Fluid Chromatography

2016 - Journal of Chromatography A

Keywords: Karlstadt University, AstraZeneca, tracer pulse, solute retention factors, separation science

### Abstract

Surface excess adsorption isotherms of methanol on a diol silica adsorbent were measured in supercritical fluid chromatography (SFC) using a mixture of methanol and carbon dioxide as mobile phase. The tracer pulse method was used with deuterium labeled methanol as solute and the tracer peaks were detected using APCI-MS over the whole composition range from neat carbon dioxide to neat methanol. The results indicate that a monolayer (4Å) of methanol is formed on the stationary phase. Moreover, the importance of using the set or the actual methanol fractions and volumetric flows in SFC was investigated by measuring the mass flow respective pressure and by calculations of the actual volume fraction of methanol. The result revealed a significant difference between the value set and the actually delivered volumetric methanol flow rate, especially at low modifier fractions. If relying only on the set methanol fraction in the calculations, the methanol layer thickness should in this system be highly overestimated. Finally, retention times for a set of solutes were measured and related to the findings summarized above concerning methanol adsorption. A strongly non-linear relationship between the logarithms of the retention factors and the modifier fraction in the mobile phase was revealed, prior to the established monolayer. At modifier fractions above that required for establishment of the methanol monolayer, this relationship turns linear which explains why the solute retention factors are less sensitive to changes in modifier content in this region.

[doi:10.1016/j.chroma.2016.03.006](https://doi.org/10.1016/j.chroma.2016.03.006)

## 213. An Improved Classification Of Stationary Phases For Ultra-High Performance Supercritical Fluid Chromatography

2016 - Journal of Chromatography A

Keywords: University of Orleans, superficially porous particles, ionic interactions, selectivity, solvation parameter model, separation science

### Abstract

Supercritical fluid chromatography (SFC) has recently benefited of new instrumentation, together with the availability of many ultra-high performance columns (sub -2µm fully porous particles or sub -3µm superficially porous particles), rendering it more attractive than ever. Most of these columns commonly used in SFC were initially developed for HPLC use, with an increasing number of stationary phases specifically designed for SFC. While the availability of different stationary phase chemistries is an advantage to achieve successful SFC separations, selecting a column for method development remains difficult. For this reason, we have previously developed a classification of stationary phases dedicated to SFC use. It is based on linear solvation energy relationships (LSER) with Abraham descriptors (for neutral species). While current interest in SFC is strong in the pharmaceutical industry, the need to take account of interactions occurring with ionisable species is pressing. We have previously shown how a modified version of the solvation parameter model, adapted to take account of ionic and ionizable species, could be applied to the characterization of SFC systems. In the present paper, based on this modified LSER model, and on the analysis of 109 neutral and ionisable species, we propose an improved classification of 31 ultra-high performance stationary phases to facilitate method development with SFC.

[doi:10.1016/j.chroma.2016.02.052](https://doi.org/10.1016/j.chroma.2016.02.052)

## 214. Assessment Of Ultra High Performance Supercritical Fluid Chromatography As A Separation Technique For The Analysis Of Seized Drugs: Applicability To Synthetic Cannabinoids

2016 - Journal of Chromatography A

Keywords: George Washington University, Florida International University, positional isomers, health science

**Abstract**

The recent development of modern methods for ultra high performance supercritical fluid chromatography (UHPSFC) has great potential for impacting the analysis of seized drugs. In the separation of synthetic cannabinoids the technique has the potential to produce superior resolution of positional isomers and diastereomers. To demonstrate this potential we have examined the capability of UHPSFC for the analysis of two different groups of synthetic cannabinoids. The first group was a mixture of 22 controlled synthetic cannabinoids, and the second group included JWH018 and nine of its non-controlled positional isomers. The clear superiority of UHPSFC over other separation techniques was demonstrated, in that it was capable of near baseline separation of all 10 positional isomers using a chiral column. In total we examined four achiral columns, including Acquity UPC<sup>2</sup> Torus 2-PIC, Acquity UPC<sup>2</sup> Torus Diol, Acquity UPC<sup>2</sup> Torus DEA and Acquity UPC<sup>2</sup> Torus 1-AA (1.7 $\mu$ m 3.0 $\times$ 100mm), and three chiral columns, including Acquity UPC<sup>2</sup> Trefoil AMY1, Acquity UPC<sup>2</sup> Trefoil CEL1 and Acquity UPC<sup>2</sup> Trefoil CEL2 (2.5 $\mu$ m 3.0 $\times$ 150mm), using mobile phase compositions that combined carbon dioxide with methanol, acetonitrile, ethanol or isopropanol modifier gradients. Detection was performed using simultaneous PDA UV detection and quadrupole mass spectrometry. The orthogonality of UHPSFC, GC and UHPLC for the analysis of these compounds was demonstrated using principal component analysis. Overall we feel that this new technique should prove useful in the analysis and detection of seized drug samples, and will be a useful addition to the compendium of methods for drug analysis.

[doi:10.1016/j.chroma.2016.02.047](https://doi.org/10.1016/j.chroma.2016.02.047)

## 215. Separation Of Substrates And Closely Related Glucuronide Metabolites Using Various Chromatographic Modes

2016 - Journal of Chromatography A

Keywords: University of Geneva, University of Lausanne, pharmaceutical

**Abstract**

A method for the determination of 200 pesticides and pesticide metabolites in honeybee samples has been developed and validated. Almost 98% of compounds included in this method are approved to use within European Union, as active substances of plant protection products or veterinary medicinal products used by beekeepers to control mites *Varroa destructor* in hives. Many significant metabolites, like metabolites of imidacloprid, thiacloprid, fipronil, methiocarb and amitraz, are also possible to detect. The sample preparation was based on the buffered QuEChERS method. Samples of bees were extracted with acetonitrile containing 1% acetic acid and then subjected to clean-up by dispersive solid phase extraction (dSPE) using a new Z-Sep+ sorbent and PSA. The majority of pesticides, including neonicotinoids and their metabolites, were analyzed by liquid chromatography tandem mass spectrometry (LC-MS/MS) but some of pesticides, especially pyrethroid insecticides, were analyzed by gas chromatography tandem mass spectrometry (GC-MS/MS). The procedure was validated according to the Guidance document SANCO/12571/2013 at four concentration levels: 1, 5, 10 and 100 ng/g bees and verified in the international proficiency test. The analysis of bee samples spiked at the limit of quantification (LOQ) showed about 98% mean recovery value (trueness) and 97% of analytes showed recovery in the required range of 70-120% and RSDr (precision) below 20%. Linearity and matrix effects were also established. The LOQs of pesticides were in the range of 1-100 ng/g. The developed method allows determination of insecticides at concentrations of 10 ng/g or less, except abamectin and tebufenozide. LOQ values are lower than the median lethal doses LD50 for bees. The method was used to investigate more than 70 honeybee poisoning incidents. Data about detected pesticides and their metabolites are included.

[doi:10.1016/j.chroma.2016.01.033](https://doi.org/10.1016/j.chroma.2016.01.033)

## 216. A Simple, Accurate, Time-Saving And Green Method For The Determination Of 15 Sulfonamides And Metabolites In Serum Samples By Ultra-High Performance Supercritical Fluid Chromatography

2016 - Journal of Chromatography A



Keywords: Chinese Academy of Inspection and Quarantine, Chinese Medical University, pharmaceuticals

**Abstract**

An analytical method based on ultra-high performance supercritical fluid chromatography (UHPSFC) with photo-diode array detection (PDA) has been developed to quantify 15 sulfonamides and their N4-acetylation metabolites in serum. Under the optimized gradient elution conditions, it took only 7min to separate all 15 sulfonamides and the critical pairs of each parent drug and metabolite were completely separated. Variables affecting the UHPSFC were optimized to get a better separation. The performance of the developed method was evaluated. The UHPSFC method allowed the baseline separation and determination of 15 sulfonamides and metabolites with limit of detection ranging from 0.15 to 0.35µg/mL. Recoveries between 90.1 and 102.2% were obtained with satisfactory precision since relative standard deviations were always below 3%. The proposed method is simple, accurate, time-saving and green, it is applicable to a variety of sulfonamides detection in serum samples.

[doi:10.1016/j.chroma.2015.12.075](https://doi.org/10.1016/j.chroma.2015.12.075)

## 217. Ultra-Fast High-Efficiency Enantioseparations By Means Of A Teicoplanin-Based Chiral Stationary Phase Made On Sub-2 Totally Porous Silica Particles Of Narrow Size Distribution

2016 - Journal of Chromatography A

Keywords: Sapienza, Ferrara, Sigma Aldrich, chiral carboxylic acids, separation science

**Abstract**

A new ultra-high performance teicoplanin-based stationary phase was prepared starting from sub-2 µm totally porous silica particles of narrow size distribution. Columns of different lengths were packed at high pressure and a deep and systematic evaluation of kinetic performance, in terms of van Deemter analysis, was performed under different elution conditions (HILIC, POM, RP and NP) by using both achiral and chiral probes. For the achiral probes, the efficiency of the columns at the minimum of the van Deemter curves were very high leading to some 278,000, 270,000, 262,000 and 232,000 plates/m in hydrophilic interaction liquid chromatography (HILIC), polar organic mode (POM), normal phase (NP) and reversed phase (RP) respectively. The lowest plate height,  $H_{min}=3.59 \mu\text{m}$  ( $h(\lambda)=1.89$ ), was obtained under HILIC conditions at a flow rate of 1.4 mL/min. Efficiency as high as 200,000-250,000 plates/m (at the optimum flow rate) was obtained in the separation of the enantiomers of chiral probes under HILIC/POM conditions. N-protected amino acids,  $\alpha$ -aryloxy acids, herbicides, anti-inflammatory agents were baseline separated on short (2-cm) and ultra-short (1-cm) columns, with analysis time in the order of 1 min. The enantiomers of N-BOC-d,l-methionine were successfully baseline separated in only 11s in HILIC mode. Several examples of fast and efficient resolutions in sub/supercritical fluid chromatography were also obtained for a range of chiral carboxylic acids.

[doi:10.1016/j.chroma.2015.11.071](https://doi.org/10.1016/j.chroma.2015.11.071)

## 218. Supercritical Fluid Chromatography Coupled With In-Source Atmospheric Pressure Ionization Hydrogen/Deuterium Exchange Mass Spectrometry For Compound Speciation

2016 - Journal of Chromatography A

Keywords: Kyungpook National University, hydrogen/deuterium exchange, hdx, separation science

**Abstract**

An experimental setup for the speciation of compounds by hydrogen/deuterium exchange (HDX) with atmospheric pressure ionization while performing chromatographic separation is presented. The proposed experimental setup combines the high performance supercritical fluid chromatography (SFC) system that can be readily used as an inlet for mass spectrometry (MS) and atmospheric pressure photo ionization (APPI) or atmospheric pressure chemical ionization (APCI) HDX. This combination overcomes the limitation of an approach using conventional liquid chromatography (LC) by minimizing the amount of deuterium solvents used for separation. In the SFC separation, supercritical CO<sub>2</sub> was used as a major component of the mobile phase, and methanol was used as a minor co-solvent. By using deuterated methanol (CH<sub>3</sub>OD), AP HDX was achieved during SFC separation. To prove the concept, thirty one nitrogen- and/or oxygen-



containing standard compounds were analyzed by SFC-AP HDX MS. The compounds were successfully speciated from the obtained SFC-MS spectra. The exchange ions were observed with as low as 1% of CH<sub>3</sub>OD in the mobile phase, and separation could be performed within approximately 20min using approximately 0.24mL of CH<sub>3</sub>OD. The results showed that SFC separation and APPI/APCI HDX could be successfully performed using the suggested method.  
[doi:10.1016/j.chroma.2016.03.011](https://doi.org/10.1016/j.chroma.2016.03.011)

## 219. Advances In High-Throughput And High-Efficiency Chiral Liquid Chromatographic Separations

2016 - Journal of Chromatography A

Keywords: The University of Texas at Arlington, High-efficiency chiral separations, High-throughput chromatography, Superficially porous particles, HPLC and SFC enantiomeric separations, Ultrafast separations, Instrument optimizations

### Abstract:

The need for improved liquid chromatographic chiral separations has led to the advancement of chiral screening techniques as well as the development of new, high efficiency chiral separation methods and stationary phases. This review covers these advancements, which primarily occurred over the last 15 years. High throughput techniques include multi-column screening units, multiple injection sequences, and fast gradient SFC screening. New separation methods and column technologies that aim at high efficiency chiral separations include the use of achiral UHPLC (i.e. sub-2 μm) columns for separating derivatized chiral analytes or using chiral additives in the run buffer, UHPLC chiral stationary phases, and superficially porous particle based chiral stationary phases. Finally, the enhancement of chiral separations through these new technologies requires that certain instrumental considerations be made. Future directions in continuing to improve chiral separations are also discussed.

<http://dx.doi.org/10.1016/j.chroma.2016.07.040>

## 220. Rapid Characterization Of Commercial Polysorbate 80 By Ultra-High Performance Supercritical Fluid Chromatography Combined With Quadrupole Time-Of-Flight Mass Spectrometry

2016 - Journal of Chromatography A

Keywords: UHPSFC-QTOF-MS, Polysorbate 80, Retention model

### Abstract:

Polysorbate 80, as a nonionic surfactant, is widely used in the food, personal care, and pharmaceutical industries due to the advantages of high surface activity, low toxicity, etc. In fact, the products of polysorbate 80 are complex mixtures of oligomers. In this work, a novel and fast method was developed to characterize the commercial polysorbate 80 by ultra-high performance supercritical fluid chromatography (UHPSFC) combined with quadrupole time-of-flight mass spectrometry (QTOF-MS). Some crucial parameters, such as temperature, back pressure and flow rate were optimized. UHPSFC could distinguish n-mer from (n - 1)-mer and (n + 1)-mer in the same series, which provided the high separation resolution needed for quantitative determination of each oligomer in same series. It was not achieved in previous studies. Furthermore, the characteristic ion fragments were found in MS/MS experiment and used to identify different series. The results revealed that main components of this nonionic surfactant comprise polyethylene oxide (PEO), PEO-monooleate, PEO-isosorbide, PEO-isosorbide monooleate, PEO-isosorbide dioleate, PEO-sorbitan, PEO-sorbitan monooleate, PEO-sorbitan dioleate and PEO-sorbitan trioleate, etc. The separation was performed using BEH stationary phase, so the relationship between molecular structure of these oligomers and chromatographic retention behavior in supercritical fluid chromatography were also investigated for first time. The whole analytical process only takes 8 min for one sample. Therefore, UHPSFC-QTOF-MS is a simple, novel and efficient tool to analyze polysorbate 80.

<http://dx.doi.org/10.1016/j.chroma.2016.08.051>

## 221. Maximizing Performance In Supercritical Fluid Chromatography Using Low-Density Mobile Phases

2016 - Journal of Chromatography A

Keywords: Supercritical fluid chromatography, Low-density carbon dioxide, Column efficiency, Vacuum technology, Decoupling between inlet eluent temperature and oven temperature, Insulating material

### Abstract

The performance of a 3.0 mm × 150 mm column packed with 1.8 μm fully porous HSS-SB-C<sub>18</sub> particles was investigated in supercritical fluid chromatography (SFC) with low-density, highly expandable carbon dioxide. These conditions are selected for the analysis of semi-volatile compounds. Elevated temperatures (>100 °C) were then combined with low column back pressures (<100 bar). In this work, the inlet temperature of pure carbon dioxide was set at 107 °C, the active back pressure regulator (ABPR) pressure was fixed at 100 bar, and the flow rate was set at 2.1 mL/min at 12 °C (liquefied carbon dioxide) and at an inlet column pressure close to 300 bar. Nine *n*-alkylbenzenes (from benzene to octadecylbenzene) were injected under linear (no sample overload) conditions. The severe steepness of the temperature gradients across the column diameter were predicted from a simplified heat transfer model. Such conditions dramatically lower the column performance by affecting the symmetry of the peak shape. In order to cope with this problem, three different approaches were experimentally tested. They include (1) the decoupling and the proper selection of the inlet eluent temperature with respect to the oven temperature, (2) the partial thermal insulation of the column using polyethylene aerogel, and (3) the application of a high vacuum (10<sup>-5</sup> Torr provided by a turbo-molecular pump) in a housing chamber surrounding the whole column body.

The results reveal that (1) the column efficiency can be maximized by properly selecting the difference between the eluent and the oven temperatures, (2) the mere wrapping of the column with an excellent insulating material is insufficient to fully eliminate heat exchanges by conduction and the undesirable radial density gradients across the column i.d., and (3) the complete thermal insulation of the SFC column under high vacuum allows to maximize the column efficiency by maintaining the integrity of the peak shape.

<http://dx.doi.org/10.1016/j.chroma.2016.09.024>

## 222. Unexpected Retention And Efficiency Behaviors In Supercritical Fluid Chromatography: A Thermodynamic Interpretation

2016 - Journal of Chromatography A

Keywords: Supercritical fluid chromatography, Sample solvent effects, Retention shift, Band compression, Band enlargement

### Abstract

Experimental conditions leading to unexpected shift in retention, band compression, and to band enlargement of small molecules in supercritical fluid chromatography are reported. The stationary phase is a 3.0 mm × 150 mm column packed with 1.8 μm fully porous high strength silica (HSS) StableBond (SB) C<sub>18</sub> particles. The mobile phase is pure carbon dioxide preheated at 107 °C and the column back pressure is set at 100 bar. The column was thermally insulated in a vacuum chamber at a pressure of 10<sup>-5</sup> Torr in order to maintain the integrity of the peak symmetry. The sample solution was prepared by dissolving seven *n*-alkylbenzenes (from benzene to dodecylbenzene) in pure acetonitrile. The injected sample volume (1 μL) was three orders of magnitude smaller than the column volume. Remarkably, the retention time of octylbenzene is found 15% smaller than that expected for this series of homologous compounds. Most strikingly, the plate counts change from about 20 000 for the three least retained analytes (benzene, ethylbenzene, and butylbenzene) to 60 000 for hexylbenzene and to only 5000 for the three most retained compounds (octylbenzene, decylbenzene, and dodecylbenzene). These unexpectedly high (reduced plate height of 1.3) and low (reduced plate height of 15) column efficiencies observed for closely related compounds are consistent with the overlap between the spatial concentration zone of the sample solvent (acetonitrile, Langmuir isotherm,  $k \approx 2$ ) and those of the analytes (competitive linear isotherms,  $0 < k < 10$ ). The present observations are fully supported by

chromatogram simulations which assume that the Henry's constants of the infinitely diluted analytes are strongly dependent on the concentration of the sample solvent in the mobile phase.

<http://dx.doi.org/10.1016/j.chroma.2016.09.020>

## 223. Peak Deformations In Preparative Supercritical Fluid Chromatography Due To Co-Solvent Adsorption

2016 - Journal of Chromatography A

Keywords: Supercritical fluid chromatography, SFC, Solvent adsorption, Adsorption strength, Langmuir band shape, Anti-Langmuir band shape

### Abstract:

In supercritical fluid chromatography (SFC) the mobile phase comprises of carbon dioxide (CO<sub>2</sub>) as main solvent and smaller amounts of an organic polar solvent (often an alcohol) as co-solvent. The co-solvent is considered to function by changing the overall polarity of the eluent, *i.e.* by acting as a "modifier". However, recent studies indicate that the co-solvent methanol can also adsorb to some common SFC stationary phases. Hence, the co-solvent should also be able to function as an "adsorbing additive", *i.e.* an eluent component that competes with the injected solutes about the stationary phase surface. In this study it was found by fitting different mechanistic models to systematic experimental data, that the co-solvent methanol can have both functions: at low co-solvent fractions, methanol acts as an additive whereas at larger fractions it acts as a modifier. Moreover, it was found that when the co-solvent adsorbs more strongly to the stationary phase than the solute, "bizarre" deformations of the preparative band shapes can occur. This is illustrated by a solute that converts from a normal "Langmuirian" band shape to an "anti-Langmuirian" shape when changing from neat carbon dioxide (CO<sub>2</sub>) to an eluent containing co-solvent. This peak shape transition is dependent on both (i) the relative retention of the solute and co-solvent to the stationary phase in eluent containing neat CO<sub>2</sub> and on (ii) the relative retention of the additive perturbation peak and the solute peak in eluent containing also co-solvent.

<http://dx.doi.org/10.1016/j.chroma.2016.09.019>

## 224. Comparison Of Ultra-High Performance Methods In Liquid And Supercritical Fluid Chromatography Coupled To Electrospray Ionization – Mass Spectrometry For Impurity Profiling Of Drug Candidates

2016 - Journal of Chromatography A

Keywords: High-resolution separations, Impurity profiling, Orthogonal methods, Performance comparison, Pharmaceutical ingredients

### Abstract:

Impurity profiling of organic products synthesized as possible drug candidates represents a major analytical challenge. Complementary analytical methods are required to ensure that all impurities are detected. Both high-performance liquid chromatography (HPLC) and supercritical fluid chromatography (SFC) can be used for this purpose. In this study, we compared ultra-high performance HPLC (UHPLC) and ultra-high performance SFC (UHPSFC) using a large dataset of 140 pharmaceutical compounds. Four previously optimized methods (two on each technique) were selected to ensure fast high-resolution separations. The four methods were evaluated based on response rate, peak capacity, peak shape and capability to detect impurities (UV). The orthogonality between all methods was also assessed. The best UHPLC method and UHPSFC methods provided comparable quality for the 140 compounds included in this study. Moreover, they were found to be highly orthogonal. At last, the potential of the combined use of UHPLC and UHPSFC for impurity profiling is illustrated with practical examples.

<http://dx.doi.org/10.1016/j.chroma.2016.10.045>

## 225. Bridging The Gap Between Gas And Liquid Chromatography

2016 - Journal of Chromatography A

Keywords: Low-density fluid chromatography, Supercritical fluid chromatography, Vacuum technology, Carbon dioxide, Volatile and non-volatile compounds, Fast and high-resolution separation

### Abstract:

The rapid and complete baseline separation of both volatile ( $C_5$  to  $C_{16}$  alkanes in gasoline or terpenes in plant extracts) and non-volatile ( $>C_{20}$  alkanes) organic compounds was achieved by combining (1) low-density fluid chromatography (LDFC) using carbon dioxide at elevated temperature ( $>90$  °C) and low pressure (1500 psi) designed to increase the retention of the most volatile compounds and (2) high-vacuum technology ( $<10^{-4}$  Torr) in order to preserve the maximum efficiency of short analytical columns (3.0 mm  $\times$  150 mm packed with 1.8  $\mu$ m fully porous HSS-SB- $C_{18}$  particles) when used in LDFC. The volatile compounds are eluted first under isobaric conditions (1500 psi) in less than a minute followed by a linear gradient of the column back pressure (from 1500 to 3500 psi in 5 min) for the elution of the non-volatile compounds up to  $C_{40}$ . The experimental results demonstrate that LDFC performed with short 3.0 mm i.d. columns packed with sub-2  $\mu$ m particles and placed under adiabatic conditions enables the analysts to deliver a single, fast, and high-resolution separation of both volatile and non-volatile compounds. <http://dx.doi.org/10.1016/j.chroma.2016.10.038>

## 226. Development Of Separation Methods For The Chiral Resolution Of Hexahelicenes

2016 - Journal of Chromatography A

Keywords: Helicene, P/M enantiomer, Chirality, High-performance liquid chromatography, Supercritical fluid chromatography, Capillary electrophoresis

### Abstract:

In this short communication we report optimized procedures for the chiral separation of non-charged [6]helicene (**1**) and cationic derivative 1-butyl-3-(2-methyl[6]helicenyl)-imidazolium bromide (**2**) using high-performance liquid chromatography (HPLC) and supercritical fluid chromatography (SFC) methods. The possibility of using capillary electrophoresis (CE) was also tested. The satisfactory results were obtained with SFC, where the highly selective resolution of four enantiopure **1** and **2** helicenes was achieved in a single run within 5 min. The semi-preparative procedure for the isolation of P and M enantiomers of compound **2**, including circular dichroism data, is reported here for the first time. The results could be used in further separations and analytical applications targeting carbohelicenes vs. positively charged helicene derivatives. <http://dx.doi.org/10.1016/j.chroma.2016.10.083>

## 227. A Case Of Z/E-Isomers Elution Order Inversion Caused By Cosolvent Percentage Change In Supercritical Fluid Chromatography

2016 - Journal of Chromatography A

Keywords: Supercritical fluid chromatography, Retention mechanisms, Z/E-isomers, Elution order inversion, Modifier adsorption

### Abstract:

A case of elution order inversion caused by cosolvent percentage change in supercritical fluid chromatography was observed and investigated in some detail. Z- and E-isomers of phenylisobutylketone oxime experience an elution order reversal on most columns if the mobile phase consists of  $CO_2$  and alcohol. At lower percentages of alcohol Z-oxime is retained less, somewhere at 2–5% coelution occurs and at larger cosolvent volume elution order reverses – Z-oxime is eluted later than E-oxime. We suppose inversion with  $CO_2$ -ROH phases happens due to a shift in balance between two main interactions governing retention. At low ROH percentages stationary phase surface is only slightly covered by ROH molecules so oximes primarily interact with adsorption sites via hydrogen bond formation. Due to intramolecular sterical hindrance Z-oxime is less able to form hydrogen bonds and consequently is eluted first. At higher percentages alcohols occupy most of strong hydrogen bonding sites on silica surface thus leaving non-specific electrostatic interactions predominantly responsible for Z/E selectivity. Z-oxime has a much larger dipole moment than E-oxime and at these conditions it is eluted later. Additional experimental data with  $CO_2$ - $CH_3CN$ , hexane-*i*PrOH and  $CHF_3$ -ROH mobile phases supporting this explanation are presented. <http://dx.doi.org/10.1016/j.chroma.2016.11.037>

## 228. Enantioseparation And Determination Of Isofenphos-Methyl Enantiomers In Wheat, Corn, Peanut And Soil With Supercritical Fluid Chromatography/Tandem Mass Spectrometric Method

2016 - Journal of Chromatography B

Keywords: State Key Laboratory for Biology of Plant Diseases and Insect Pests, Institute of Plant Protection, QuEChERS, food

### Abstract

Supercritical fluid chromatography/tandem mass spectrometry (SFC-MS/MS) is an effective tool in separation science which uses the nontoxic CO<sub>2</sub> fluid for better control of analyte retention. Also the technology of a postcolumn additive to complement MS/MS ensure the high-selectivity determination. In this paper, a green and sensitive analytical method was developed for the enantioselective separation and determination of isofenphos-methyl enantiomers in foodstuff and soil by SFC-MS/MS. The enantioseparation was performed within 3.50 min using Chiralpak IA-3 column with CO<sub>2</sub>/isopropanol (90:10, v/v) as the mobile phase at 2.2 mL/min flow rate. The postcolumn compensation technology provided with 0.1% formic acid/methanol greatly improved the ionization efficiency of mass spectrometry. Column temperature, auto back pressure regulator pressure, and flow rate of compensation solvent were optimized to 30 °C, 2200 psi, and 0.1 mL/min, respectively. The QuEChERS method was adopted in this study, which mean recoveries of isofenphos-methyl enantiomers ranged from 75.7% to 111.4%, with relative standard deviations less than 11.3% at three concentration levels in all matrices. The limits of detection for both enantiomers varied from 0.02 µg/kg to 0.15 µg/kg, while the limit of quantification did not exceed 0.50 µg/kg. The proposed method was then successfully applied to analyze authentic samples, confirming that it was a versatile strategy for the analysis of isofenphos-methyl enantiomers in food and environmental matrices.

[doi:10.1016/j.jchromb.2016.02.003](https://doi.org/10.1016/j.jchromb.2016.02.003)

## 229. Development And Validation Of An Enantioselective SFC-MS/MS Method For Simultaneous Separation And Quantification Of Oxcarbazepine And Its Chiral Metabolites In Beagle Dog Plasma

2016 - Journal of Chromatography B

Keywords: Jilin University, University of Otago, Oxcarbazepine, *S*-Licarbazepine; *R*-Licarbazepine, chiral analysis, health science

### Abstract

A rapid and sensitive assay based on supercritical fluid chromatography-tandem mass spectrometry (SFC-MS/MS) has been developed and validated for the determination of oxcarbazepine (OXC) and its chiral metabolite licarbazepine (Lic) in beagle dog plasma using carbamazepine as internal standard. Chiral analysis in a run time of only 3min was performed on an ACQUITY UPC(2)™ Trefoil™ CEL2 column (3.0×150mm, 2.5µm) at 50°C by isocratic elution with a mobile phase of supercritical carbon dioxide (purity≥99.99%) and methanol (60:40, v/v) at a flow rate of 2.3mL/min. The assay was linear over the concentration ranges 5-1000ng/mL for OXC and 0.5-100ng/mL for the enantiomers of Lic with corresponding lower limits of quantitation of 5ng/mL and 0.5ng/mL. Intra- and inter-day precisions were in the range 0.78-14.14% with accuracies in the range -10.80% to 0.42%. The method was successfully applied to a pharmacokinetic study involving a single oral administration of 16mg/kg OXC as Trileptal(®) tablets to beagle dogs.

[doi:10.1016/j.jchromb.2016.03.013](https://doi.org/10.1016/j.jchromb.2016.03.013)

## 230. Overcoming Bioanalytical Challenges Associated With The Separation And Quantitation Of GSK1278863, A HIF-Prolyl Hydroxylase Inhibitor And Its 14 Stereoisomeric Metabolites

2016 - Journal of Chromatography B

Keywords: GSK, GlaxoSmithKline, anemia, kidney disease, health science

### Abstract

GSK1278863 is an investigative drug under investigation for treatment of anemia associated with chronic kidney disease. Its metabolism is primarily metabolized by P450 enzymes where 19



unique metabolic species have been identified. These include multiple products of mono-, di-, and tri-oxygenation. Initially, two separate and complex ultra high performance liquid chromatography (UHPLC) reverse phase methodologies were developed, validated and applied to measure parent and various predominant and circulating metabolites in numerous clinical studies. However, 5 of the 6 oxidative metabolites may exist in different stereoisomeric forms, resulting in 14 separate species; therefore a chiral methodology was required to determine which stereoisomeric forms circulated in human. A variety of conventional approaches were explored, where in the end a supercritical fluid chromatography (SFC) method was required to separate this complex mixture of 14 stereoisomeric metabolites; data from these experiments provided important information on which species circulate in human. The details of these methodologies will be discussed herein. <http://dx.doi.org/10.1016/j.jchromb.2015.11.057>

### 231. An Improvement Of Separation And Response Applying Post-Column Compensation And One-Step Acetone Protein Precipitation For The Determination Of Coenzyme Q10 In Rat Plasma By SFC-MS/MS

2016 - Journal of Chromatography B

Keywords: Shenyang Pharmaceutical University, Coenzyme Q10, Post-column compensation, SFC-ESI-MS/MS, Pharmacokinetic study, Rat plasma

#### Abstract

Coenzyme Q10 (CoQ10) solid dispersion was prepared to improve its oral bioavailability due to the poor solubility of CoQ10. To evaluate the pharmacokinetic behaviors of CoQ10 solid dispersion, a simple, rapid, sensitive and environment friendly method for the determination of CoQ10 in rat plasma was developed. In this study, samples were prepared by one-step protein precipitation with acetone and then the supercritical fluid chromatography-electrospray ionization tandem mass spectrometry (SFC-ESI-MS/MS) method was used. The separation was achieved by an ACQUITY UPC<sup>2</sup>™ BEH 2-EP column (100 mm × 3 mm, 1.7 μm) maintained at 35 °C, using carbon dioxide (≥99.99%) and methanol (85:15, v/v) as the mobile phase at a flow rate of 1.0 ml/min. To improve the response and sensitivity, the compensation solvent of methanol with 2 mM ammonium acetate at a flow rate of 0.2 ml/min was used and the total analysis time was only 1.5 min for each sample. The detection was carried out on a tandem mass spectrometer with electrospray ionization (ESI) source and the mass transition ion pair was  $m/z$ 881.0 → 197.0 and 285.1 → 193.0 for CoQ10 and diazepam, internal standard (IS), respectively. Calibration curve was linear over the concentration range of 2.00–500.00 ng/ml ( $r^2 \geq 0.998$ ) with a lower limit of quantification of 2.00 ng/ml. The intra- and inter-day accuracy and precision were below 15% for all quality control samples. The proposed method was rapid, accurate and reproducible, which was suitable to compare the pharmacokinetic behaviors in rats after a single oral dose of 100 mg/kg CoQ10 solid dispersion or tablets.

<http://dx.doi.org/10.1016/j.jchromb.2016.07.050>

### 232. High-Throughput Analysis Of 19 Endogenous Androgenic Steroids By Ultra-Performance Convergence Chromatography Tandem Mass Spectrometry

2016 - Journal of Chromatography B

Keywords: Stellenbosch University, University of Birmingham, Adrenal androgens, Gas chromatography, Steroids, Supercritical fluid chromatography, Ultra performance convergence chromatography, Ultra performance liquid chromatography

#### Abstract:

11-Oxygenated steroids such as 11-ketotestosterone and 11-ketodihydrotestosterone have recently been shown to play a putative role in the development and progression of castration resistant prostate cancer. In this study we report on the development of a high throughput ultra-performance convergence chromatography tandem mass spectrometry (UPC<sup>2</sup>-MS/MS) method for the analysis of thirteen 11-oxygenated and six canonical C19 steroids isolated from a cell culture matrix. Using an Acquity UPC<sup>2</sup> BEH 2-EP column we found that UPC<sup>2</sup> resulted in superior selectivity, increased chromatographic efficiency and a scattered elution order when compared to conventional reverse phase ultra-performance liquid chromatography (UPLC). Furthermore, there was a significant improvement in sensitivity (5–50 times). The lower limits of quantification ranged



between 0.01–10 ng mL<sup>-1</sup>, while the upper limit of quantification was 100 ng mL<sup>-1</sup> for all steroids. Accuracy, precision, intra-day variation, recovery, matrix effects and process efficiency were all evaluated and found to be within acceptable limits. Taken together we show that the increased power of UPC<sup>2</sup>-MS/MS allows the analyst to complete *in vitro* assays at biologically relevant concentrations for the first time and in so doing determine the routes of steroid metabolism which is vital for studies of androgen responsive cancers, such as prostate cancer, and could highlight new mechanisms of disease progression and new targets for cancer therapy.

<http://dx.doi.org/10.1016/j.jchromb.2016.07.024>

### 233. Hydroxypyridyl Imines: Enhancing Chromatographic Separation And Stereochemical Analysis Of Chiral Amines Via Circular Dichroism

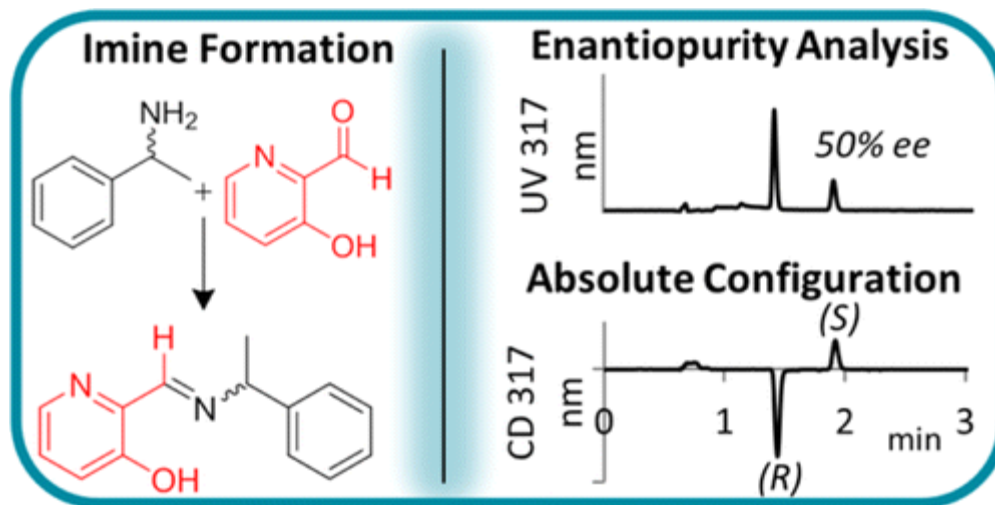
2016 - Journal of Organic Chemistry

Keywords: Chiral Amines, imine-bond formation, amino alcohols, stereocenters

#### Abstract

Imine-bond formation between chiral amines and commercially available 3-hydroxypyridine-2-carboxaldehyde (HCA) was exploited for rapid determination of stereochemical composition. Chiral supercritical fluid chromatography (SFC) screening of the derivatized imine compounds led to the elucidation of multiple combinations of mobile and stationary phases that gave resolution of all members of a series of chiral amines. The first eluting enantiomer was generally the derivative of the (*R*)-amine enantiomer across the series that was studied, indicating that the imine formed from the (*S*)-amine has more favorable interaction with the chiral stationary phase of the column. These conditions were then applied to more challenging compounds, namely amino alcohols and diastereomers possessing more than one stereocenter. The approach was utilized to monitor stereoselective biocatalytic transamination and assign the absolute configuration of the enantiomeric products. Finally, hydrolysis of the imine bond of the derivative was shown to generate enantiopure amine starting materials without racemization. This further highlights the value of this approach for creating readily reversed derivatives that enhance chromatographic separation and aid in the determination of absolute configuration.

<http://dx.doi.org/10.1021/acs.joc.6b01162>



### 234. Development, Validation And Comparison Of UHPSFC And UHPLC Methods For The Determination Of Agomelatine And Its Impurities

2016 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: Charles University, Zentiva, k.s. Praha (a Sanofi company), antidepressants, pharmaceuticals

#### Abstract

Agomelatine is one of the newest antidepressants. Due to a different mechanism of action it offers a completely new approach in the treatment of depressive disorders. Two chromatographic methods for determination of agomelatine and its impurities were developed. The separations on UHPSFC system were accomplished using stationary phase based on BEH 2-EP and gradient elution with CO<sub>2</sub> and methanol containing 20mM ammonium formate and 5% of water. The UHPLC separations were performed on stationary phase BEH Shield RP18. The mixture of acetonitrile and methanol in ratio 1:1 and ammonium acetate buffer pH 9.5 were used as mobile phase. Both developed methods were properly validated in terms of linearity, sensitivity (LOD, LOQ), accuracy and precision according to ICH guidelines. The UHPSFC method was linear in the range 0.25-70µg/ml for all analytes with method accuracy  $\geq 97.4\%$  and  $\geq 100.2\%$  and method intra-day precision RSD  $\leq 2.4$  and  $\leq 0.8$  for impurities and API (active pharmaceutical ingredient), respectively. The UHPLC method was linear in the range 0.1-10µg/ml for all analytes except three impurities for which the linear range was larger 0.1-25µg/ml. Method accuracy  $\geq 95.7\%$  and  $\geq 95.2\%$  and method intra-day precision RSD  $\leq 2.6$  and  $\leq 1.5$  were found for impurities and API, respectively. The measurement of tablet samples was performed and the selected parameters of the methods were compared. In conclusion, both methods were appropriate for the determination of agomelatine and its impurities in pharmaceutical quality control (QC), although the UHPSFC method was found as more convenient especially in the method development phase. The advantages of newly developed UHPSFC-PDA (photo diode array detector) method were its environmental friendliness due to the mobile phase used, a very good resolution, selectivity and high speed of analysis (total time of separation was 4.1min).

**doi:10.1016/j.jpba.2016.04.020**



### 235. Screening Study Of SFC Critical Method Parameters For The Determination Of Pharmaceutical Compounds

2016 - Journal of Pharmaceutical and Biomedical Analysis

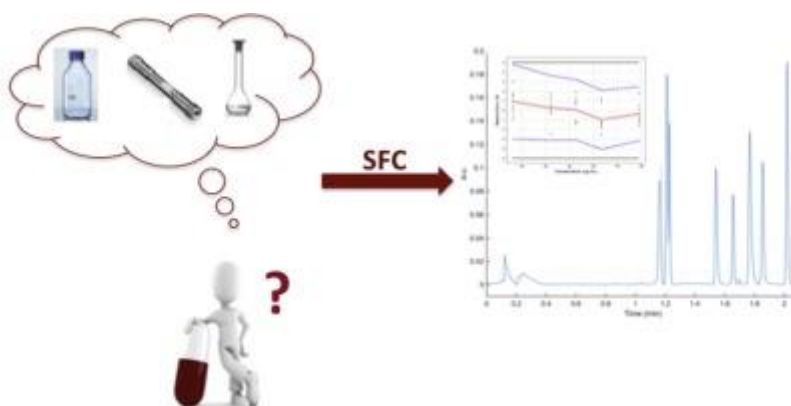
Keywords: University of Liege, Arlenda s.a., antimalarial molecules, pharmaceuticals, separation science, method development

#### **Abstract**

Nowadays, supercritical fluid chromatography is commonly presented as a promising alternative technique in the field of separation sciences. Nevertheless the selection of chromatographic conditions and sample preparation of pharmaceutical compounds remain a challenge and peak distortion was previously highlighted. The main objective of the present work was to evaluate the impact of different critical method parameters (CMPs), i.e. stationary phase, mobile phase composition and injection solvent nature. The experiments were performed considering two groups of antimalarial molecules: one group with neutral/apolar compounds and the other one with salt form of polar compounds. In this context, another objective was to propose a suitable sample solvent for quantitative analysis. The interest of new generation stationary phase to obtain good peak shape and the interest to tune the mobile phase composition were demonstrated.

During this study, design of experiments and desirability function approach enabled to highlight optimal chromatographic conditions in order to maximise peak capacity and to get acceptable value of symmetry factor. Regarding sample injection solvent composition, some counterintuitive results were observed: solvents closer to the mobile phase polarity (i.e. heptane or 2-propanol/heptane mixture) did not provide best results in terms of peak symmetry. In addition, acetonitrile and short aliphatic alcohols offered an interesting alternative as injection solvent: toxicity of solvents used is clearly reduced and better quantitative performances could be expected while keeping high peak capacity and symmetric sharp peaks. Finally, the quantitative performances were evaluated by the method validation for the quantitative determination of quinine sulfate in a pharmaceutical formulation. These better understandings on critical method parameters led SFC to be an even more promising technique in the field of the analysis of pharmaceutical compounds.

[doi:10.1016/j.jpba.2016.04.005](https://doi.org/10.1016/j.jpba.2016.04.005)



### 236. Chiral Separations Of Cathinone And Amphetamine-Derivatives: Comparative Study Between Capillary Electrochromatography, Supercritical Fluid Chromatography And Three Liquid Chromatographic Modes

2016 - Journal of Pharmaceutical and Biomedical Analysis

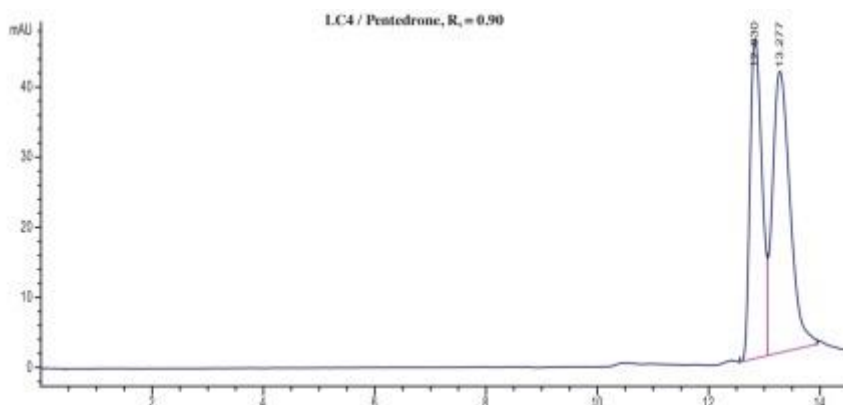
Keywords: Vrije Universiteit Brussel-VUB, Karl-Franzens-Universitat Graz, Tbilisi State University, pharmaceutical

#### Abstract

The screening part of an earlier defined chiral separation strategy in capillary electrochromatography (CEC) was used for the separation of ten cathinone- and amphetamine derivatives. They were analyzed using 4 polysaccharide-based chiral stationary phases (CSPs), containing cellulose tris(3,5-dimethylphenylcarbamate) (ODRH), amylose tris(3,5-dimethylphenylcarbamate) (ADH), amylose tris(5-chloro-2-methylphenylcarbamate) (LA2), and cellulose tris(4-chloro-3-methylphenylcarbamate) (LC4) as chiral selectors. After applying the screening to each compound, ADH and LC4 showed the highest success rate. In a second part of the study, a comparison between CEC and other analytical techniques used for chiral separations i.e., supercritical fluid chromatography (SFC), polar organic solvent chromatography (POSC), reversed-phase (RPLC) and normal-phase liquid chromatography (NPLC), was made. For this purpose, earlier defined screening approaches for each technique were applied to separate the 10 test substances. This allowed an overall comparison of the success rates of the screening steps of the 5 techniques for these compounds. The results showed that CEC had a similar enantioselectivity rate as NPLC and RPLC, producing the highest number of separations (9 out of 10 racemates). SFC resolved 7 compounds, while POSC gave only 2 separations. On the other hand, the baseline separation success rates for NPLC and RPLC was better than for CEC. For a

second comparison, the same chiral stationary phases as in the CEC screening were also tested with all techniques at their specific screening conditions, which allowed a direct comparison of the performance of CEC versus the same CSPs in the other techniques. This comparison revealed that RPLC was able to separate all tested compounds, and also produced the highest number of baseline separations on the CSP that were used in the CEC screening step. CEC and NPLC showed the same success rate: nine out of ten substances were separated. When CEC and NPLC are combined, separation of the ten compounds can be achieved. SFC and POSC resolved eight and three compounds, respectively. POSC was the least attractive option as it expressed only limited enantioselectivity toward these compounds.

[doi:10.1016/j.jpba.2015.12.007](https://doi.org/10.1016/j.jpba.2015.12.007)



### 237. Comparison Of Ultra-High-Performance Supercritical Fluid Chromatography And Ultra-High-Performance Liquid Chromatography For The Separation Of Spirostanol Saponins

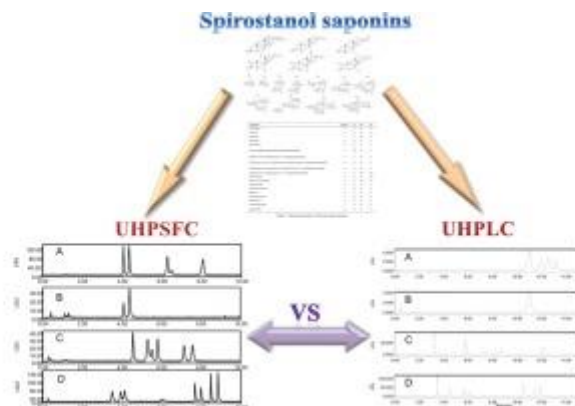
2016 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: Beijing Institute of Radiation Medicine, Waters, Ovation Health Science and Technology Co. Ltd., herbal medicines, isolation, purification, tcm, natural products, health science

#### Abstract

Spirostanol saponins are important active components of some herb medicines, and their isolation and purification are crucial for the research and development of traditional Chinese medicines. We aimed to compare the separation of spirostanol saponins by ultra-high performance supercritical fluid chromatography (UHPSFC) and ultra-high performance liquid chromatography (UHPLC). Four groups of spirostanol saponins were separated respectively by UHPSFC and UHPLC. After optimization, UHPSFC was performed with a HSS C18 SB column or a Diol column and with methanol as the co-solvent. A BEH C18 column and mobile phase containing water (with 0.1% formic acid) and acetonitrile were used in UHPLC. We found that UHPSFC could be performed automatically and quickly. It is effective in separating the spirostanol saponins which share the same aglycone and vary in sugar chains, and is very sensitive to the number and the position of hydroxyl groups in aglycones. However, the resolution of spirostanol saponins with different aglycones and the same sugar moiety by UHPSFC was not ideal and could be resolved by UHPLC instead. UHPLC is good at differentiating the variation in aglycones, and is influenced by double bonds in aglycones. Therefore, UHPLC and UHPSFC are complementary in separating spirostanol saponins. Considering the naturally produced spirostanol saponins in herb medicines are different both in aglycones and in sugar chains, a better separation can be achieved by combination of UHPLC and UHPSFC. UHPSFC is a powerful technique for improving the resolution when UHPLC cannot resolve a mixture of spirostanol saponins and vice versa.

[doi:10.1016/j.jpba.2015.12.002](https://doi.org/10.1016/j.jpba.2015.12.002)



### 238. Supercritical Fluid Chromatography For GMP Analysis In Support Of Pharmaceutical Development And Manufacturing Activities

2016 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: Merck, enantiomers, gmp, impurities, chiral stationary phases, method validation, pharmaceutical

#### Abstract

Supercritical fluid chromatography (SFC) has long been a preferred method for enantiopurity analysis in support of pharmaceutical discovery and development, but implementation of the technique in regulated GMP laboratories has been somewhat slow, owing to limitations in instrument sensitivity, reproducibility, accuracy and robustness. In recent years, commercialization of next generation analytical SFC instrumentation has addressed previous shortcomings, making the technique better suited for GMP analysis. In this study we investigate the use of modern SFC for enantiopurity analysis of several pharmaceutical intermediates and compare the results with the conventional HPLC approaches historically used for analysis in a GMP setting. The findings clearly illustrate that modern SFC now exhibits improved precision, reproducibility, accuracy and robustness; also providing superior resolution and peak capacity compared to HPLC. Based on these findings, the use of modern chiral SFC is recommended for GMP studies of stereochemistry in pharmaceutical development and manufacturing.

[doi:10.1016/j.jpba.2015.09.014](https://doi.org/10.1016/j.jpba.2015.09.014)

### 239. Supercritical Fluid Chromatography For Separation And Preparation Of Tautomeric 7-Epimeric Spiro Oxindole Alkaloids From Uncaria Macrophylla

2016 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: Spiro oxindole alkaloid, Uncaria macrophylla, Isomerization, Ultra-performance convergence chromatography, Preparative scale supercritical fluid chromatography

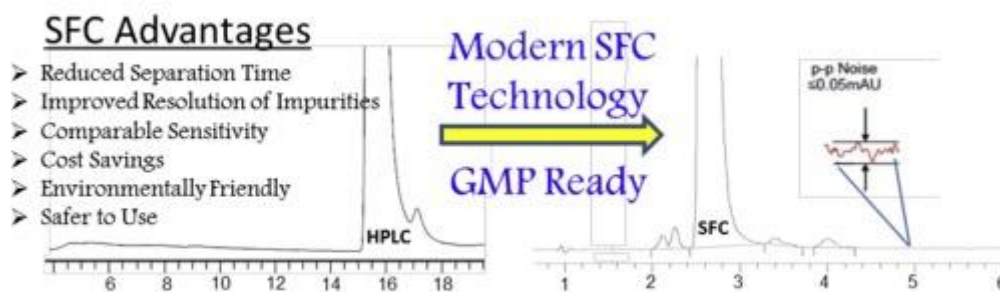
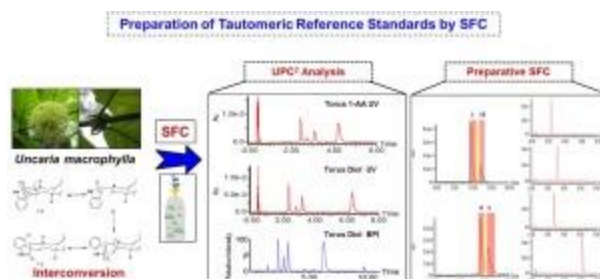
#### Abstract:

Increasing challenge arising from configurational interconversion in aqueous solvent renders it rather difficult to isolate high-purity tautomeric reference standards and thus largely hinders the holistic quality control of traditional Chinese medicine (TCM). Spiro oxindole alkaloids (SOAs), as the markers for the medicinal *Uncaria* herbs, can easily isomerize in polar or aqueous solvent via a retro-Mannich reaction. In the present study, supercritical fluid chromatography (SFC) is utilized to separate and isolate two pairs of 7-epimeric SOAs, including rhynchophylline (**R**) and isorhynchophylline (**IR**), corynoxine (**C**) and corynoxine B (**CB**), from *Uncaria macrophylla*. Initially, the solvent that can stabilize SOA epimers was systematically screened, and acetonitrile was used to dissolve and as the modifier in SFC. Then, key parameters of ultra-high performance SFC (ultra-performance convergence chromatography, UPC<sup>2</sup>), comprising stationary phase, additive in modifier, column temperature, ABPR pressure, and flow rate, were optimized in sequence. Two isocratic UPC<sup>2</sup> methods were developed on the achiral Torus 1-AA and Torus Diol columns, suitable for UV and MS detection, respectively. MCI gel column chromatography fractionated the *U. macrophylla* extract into two mixtures (**R/IR** and **C/CB**). Preparative SFC,



using a Viridis Prep Silica 2-EP OBD column and acetonitrile-0.2% diethylamine in CO<sub>2</sub> as the mobile phase, was finally employed for compound purification. As a result, the purity of four SOA compounds was all higher than 95%. Different from reversed-phase HPLC, SFC, by use of water-free mobile phase (inert CO<sub>2</sub> and aprotic modifier), provides a solution to rapid analysis and isolation of tautomeric reference standards for quality control of TCM.

<http://dx.doi.org/10.1016/j.jpba.2016.10.021>



## 240. Evaluation Of Supercritical Fluid Chromatography For Testing Of PEG Adducts In Pharmaceuticals

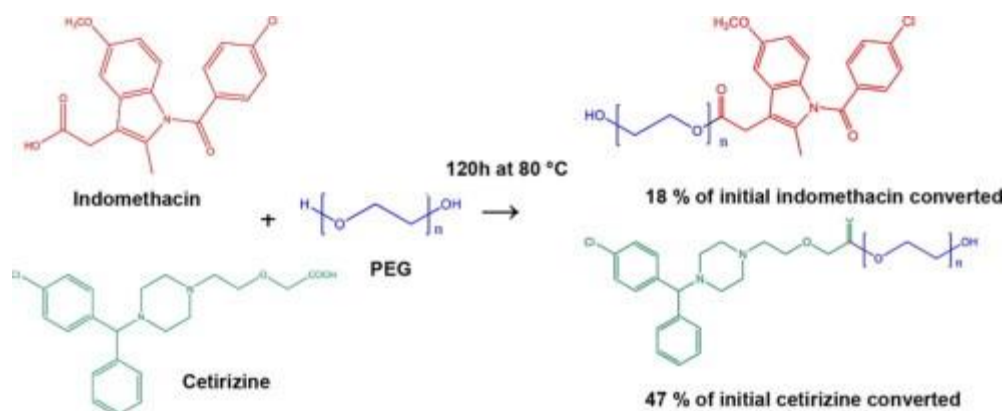
2016 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: University of Copenhagen, Waters, cetirizine, indomethacin, polyethylene glycol, drug-excipient, pharmaceutical

### Abstract

Drug formulations containing polyethylene glycol may give rise to formation of reaction products between the aforementioned and the active pharmaceutical ingredient. Supercritical fluid chromatography has recently achieved new interest and improved instrumentation is now available. Here, supercritical fluid chromatography has been evaluated for its possible use for determination of reactions products formed between polyethylene glycol and active pharmaceutical ingredients. A mixture of polyethylene glycols with average molecular weights of 400-6000Da was separated with supercritical fluid chromatography using silica columns and carbon dioxide modified with methanol as mobile phase. Satisfactory resolution ( $R_s=1.2$ ) of the individual oligomers up to a molecular weight of 1000Da was obtained using evaporative light scattering as detection technique. The active pharmaceutical ingredients, cetirizine or indomethacin were investigated in a reaction mixture containing polyethylene glycol 400 after incubation at 80°C for 120h. Polyethylene glycol esters formed upon reaction with both active pharmaceutical ingredients were observed as polymeric patterns with ultraviolet detection and identified with mass spectrometry. Cetirizine was observed to be more reactive than indomethacin. The observed difference in reactivity is due to differences in polar and steric effects between cetirizine and indomethacin. Evaporative light scattering, ultraviolet absorbance and mass spectrometric detection were investigated and each detection technique has its own advantages and disadvantages, but in order to be able to detect selected impurities in the complex mixture of impurities formed, mass spectrometry is superior.





## 241. Simultaneous Quantitation Of The Diastereoisomers Of Scholarisine And 19-Epischolarisine, Vallesamine And Picrinine In Rat Plasma By Supercritical Fluid Chromatography With Tandem Mass Spectrometry And Its Application To A Pharmacokinetic Study

2016 - Journal of Separation Science

Keywords: Jilin University, Waters, pharmaceutical

### Abstract

Dengtaiye tablet has been used to treat chronic bronchitis cough. Scholarisine, 19-epischolarisine, vallesamine, and picrinine are the representative constituents of Dengtaiye. A rapid and sensitive assay based on supercritical fluid chromatography with tandem mass spectrometry has been developed and validated for the determination of the diastereoisomers of scholarisine and 19-epischolarisine, vallesamine, and picrinine in rat plasma using lamotrigine as internal standard. The analysis in a run time of only 6 min was performed on an ACQUITY UPC<sup>2</sup> Trefoil™ BEH 2-EP column (3.0 × 150 mm, 2.5 μm) at 50°C. The mobile phase consisting of carbon dioxide and methanol (2 mM ammonium formate) was performed as follows: 15% methanol (2 mM ammonium formate) maintained at 0–2 min, 15–19% methanol (2 mM ammonium formate) at 2–4 min, 19–15% methanol (2 mM ammonium formate) at 4–6 min. The flow rate was 1.50 mL/min. The assay was linear over the concentration ranges 50–10000 pg/mL for scholarisine, 19-epischolarisine, vallesamine, and picrinine with corresponding lower limits of quantitation of 50 pg/mL. Intra- and interday precisions were in the range 1.42–12.85% with accuracies in the range –11.71–2.48%. The method was successfully applied to a pharmacokinetic study involving a single oral administration of 108 mg/kg Dengtaiye tablet to rats.

<http://dx.doi.org/10.1002/jssc.201600243>

## 242. Simultaneous Determination Of 16 Polycyclic Aromatic Hydrocarbons In Reclaimed Water Using Solid-Phase Extraction Followed By Ultra-Performance Convergence Chromatography With Photodiode Array Detection

2016 - Journal of Separation Science

Keywords: Beijing University of Chemical Technology, Beijing Agro-Monitoring Station, environmental

### Abstract

A new fast and effective analysis method has been developed to simultaneously determine 16 polycyclic aromatic hydrocarbons in reclaimed water samples by ultra-performance convergence chromatography with photodiode array detection and solid-phase extraction. The parameters of ultra-performance convergence chromatography on the separation behaviors and the crucial condition of solid-phase extraction were investigated systematically. Under optimal conditions, the

16 polycyclic aromatic hydrocarbons could be separated within 4 min. The limits of detection and quantification were in the range of 0.4–4 and 1–10 µg/L in water, respectively. This approach has been applied to a real industrial wastewater treatment plant successfully. The results showed that polycyclic aromatic hydrocarbons were dramatically decreased after chemical treatment procedure, and the oxidation procedure was effective to remove trace polycyclic aromatic hydrocarbons.

<http://dx.doi.org/10.1002/jssc.201500823>

### 243. Characterization Of The Pigment Fraction In Sweet Bell Peppers (*Capsicum Annuum* L.) Harvested At Green And Overripe Yellow And Red Stages By Off-Line Multidimensional Convergence Chromatography/Liquid Chromatography-Mass Spectrometry

2016 - Journal of Separation Science

Keywords: University of Messina, Convergence chromatography, Liquid chromatography, Mass spectrometry, overripe fruits, Pigments, Sweet bell peppers

#### Abstract:

Off-line multidimensional supercritical fluid chromatography combined with reversed-phase liquid chromatography was employed for the carotenoid and chlorophyll characterization in different sweet bell peppers (*Capsicum annuum* L.) for the first time. The first dimension consisted of an Acquity HSS C<sub>18</sub> SB (100 mm × 3 mm I.D., 1.8 µm particles) column operated with a supercritical mobile phase in a ultra performance convergence chromatography system, whereas the second dimension was performed in reversed phase mode with a C<sub>30</sub> (250 mm × 4.6 mm I.D., 3.0 µm particles) stationary phase combined with photodiode array and mass spectrometry detection. This approach allowed the determination of 115 different compounds belonging to chlorophylls, free xanthophylls, free carotenes, xanthophyll monoesters and xanthophyll diesters, and proved to be a significant improvement in the pigments determination compared to the conventional one-dimensional liquid chromatography approach so far applied to the carotenoid analysis in the studied species. Moreover, the present study also aimed to investigate and to compare the carotenoid stability and composition in overripe yellow and red bell peppers collected directly from the plant, thus also evaluating whether biochemical changes are linked to carotenoid degradation in the non climacteric investigated fruits, for the first time.

<http://dx.doi.org/10.1002/jssc.201600220>

### 244. Development And Validation Of An Ultra-Performance Convergence Chromatography Method For The Quality Control Of *Angelica Gigas* Nakai

2016 - Journal of Separation Science

Keywords: Korea Institute of Oriental Medicine, *Angelica gigas* Nakai, Green chemistry, Supercritical fluid chromatography, Ultra-performance convergence chromatography

#### Abstract

Ultra-performance convergence chromatography, which integrates the advantages of supercritical fluid chromatography and ultra high performance liquid chromatography technologies, is an environmentally friendly analytical method that uses dramatically reduced amounts of organic solvents. An ultra-performance convergence chromatography method was developed and validated for the quantification of decursinol angelate and decursin in *Angelica gigas* using a CSH Fluoro-Phenyl column (2.1 mm × 150 mm, 1.7 µm) with a run time of 4 min. The method was developed in improved resolution and a shorter analysis time in comparison to the conventional high-performance liquid chromatography method. This method was validated in terms of linearity, precision, and accuracy. The limits of detection were 0.005 and 0.004 µg/mL for decursinol angelate and decursin, respectively, while the limits of quantitation were 0.014 and 0.012 µg/mL, respectively. The two components showed good regression (correlation coefficient ( $r^2$ ) > 0.999), excellent precision (relative standard deviation < 2.28%), and acceptable recoveries (99.75–102.62%). The proposed method can be used to efficiently separate, characterize, and quantify decursinol angelate and decursin in *Angelica gigas* and its related medicinal materials or

preparations, with the advantages of a shorter analysis time, greater sensitivity, and better environmental compatibility.

<http://dx.doi.org/10.1002/jssc.201600275>

## 245. Profiling Adrenal 11 $\beta$ -Hydroxyandrostenedione Metabolites In Prostate Cancer Cells, Tissue And Plasma: UPC<sup>2</sup>-MS/MS Quantification Of 11 $\beta$ -Hydroxytestosterone, 11keto-Testosterone And 11keto-Dihydrotestosterone

2016 - Journal of Steroid Biochemistry and Molecular Biology

Keywords: Stellenbosch University, prostate cells, prostate cancer, Adrenal C<sub>19</sub> steroids, active androgens, health science

### Abstract

Adrenal C<sub>19</sub> steroids serve as precursors to active androgens in the prostate. Androstenedione (A4), 11 $\beta$ -hydroxyandrostenedione (11OHA4) and 11 $\beta$ -hydroxytestosterone (11OHT) are metabolised to potent androgen receptor (AR) agonists, dihydrotestosterone (DHT), 11-ketotestosterone (11KT) and 11-ketodihydrotestosterone (11KDHT). The identification of 11OHA4 metabolites, 11KT and 11KDHT, as active androgens has placed a new perspective on adrenal C<sub>11</sub>-oxy C<sub>19</sub> steroids and their contribution to prostate cancer (PCa).

We investigated adrenal androgen metabolism in normal epithelial prostate (PNT2) cells and in androgen-dependent prostate cancer (LNCaP) cells. We also analysed steroid profiles in PCa tissue and plasma, determining the presence of the C<sub>19</sub> steroids and their derivatives using ultra-performance liquid chromatography (UHPLC)- and ultra-performance convergence chromatography tandem mass spectrometry (UPC<sup>2</sup>-MS/MS).

In PNT2 cells, sixty percent A4 (60%) was primarily metabolised to 5 $\alpha$ -androstenedione (5 $\alpha$ DIONE) (40%), testosterone (T) (10%), and androsterone (AST) (10%). T (30%) was primarily metabolised to DHT (10%) while low levels of A4, 5 $\alpha$ DIONE and 3 $\alpha$ ADIOL ( $\approx$ 20%) were detected. Conjugated steroids were not detected and downstream products were present at  $<0.05$   $\mu$ M. Only 20% of 11OHA4 and 11OHT were metabolised with the former yielding 11keto-androstenedione (11KA4), 11KDHT and 11 $\beta$ -hydroxy-5 $\alpha$ -androstenedione (11OH-5 $\alpha$ DIONE) and the latter yielding 11OHA4, 11KT and 11KDHT with downstream products  $<0.03$   $\mu$ M. In LNCaP cells, A4 (90%) was metabolised to AST-glucuronide via the alternative pathway while T was detected as T-glucuronide with negligible conversion to downstream products. 11OHA4 (80%) and 11OHT (60%) were predominantly metabolised to 11KA4 and 11KT and in both assays more than 50% of 11KT was detected in the unconjugated form. In tissue, we detected C<sub>11</sub>-oxy C<sub>19</sub> metabolites at significantly higher levels than the C<sub>19</sub> steroids, with unconjugated 11KDHT, 11KT and 11OHA4 levels ranging between 13 and 37.5 ng/g. Analyses of total steroid levels in plasma showed significant levels of 11OHA4 ( $\approx$ 230–440 nM), 11KT ( $\approx$ 250–390 nM) and 11KDHT ( $\approx$ 19 nM). DHT levels ( $<0.14$  nM) were significantly lower.

In summary, 11 $\beta$ -hydroxysteroid dehydrogenase type 2 activity in PNT2 cells was substantially lower than in LNCaP cells, reflected in the conversion of 11OHA4 and 11OHT. Enzyme substrate preferences suggest that the alternate pathway is dominant in normal prostate cells.

Glucuronidation activity was not detected in PNT2 cells and while all T derivatives were efficiently conjugated in LNCaP cells, 11KT was not. Substantial 11KT levels were also detected in both PCa tissue and plasma. 11OHA4 therefore presents a significant androgen precursor and its downstream metabolism to 11KT and 11KDHT as well as its presence in PCa tissue and plasma substantiate the importance of this adrenal androgen.

<http://dx.doi.org/10.1016/j.jsbmb.2016.06.009>

## 246. Chiral Analysis Of Poor UV Absorbing Pharmaceuticals By Supercritical Fluid Chromatography-Charged Aerosol Detection

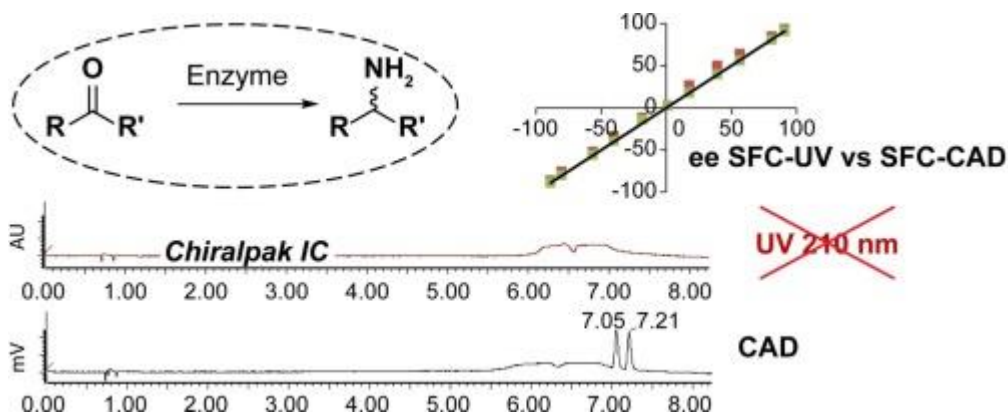
2016 - The journal of Supercritical Fluids

Keywords: Merck, enantiopurity, high-throughput analysis, SFC-CAD, pharmaceuticals

### Abstract

Fast and efficient chiral analysis of drugs and synthetic intermediates with weak UV absorption is one of the most challenging analytical tasks in modern pharmaceutical research and development. In this study, the use of supercritical fluid chromatography-charged aerosol detection (SFC-CAD)

for chiral analysis of poor UV absorbing analytes commonly encountered during pharmaceutical process research was investigated. Investigation of makeup flow rate showed that CAD responses remained largely steady from 1 to 1.5 mL/min for different mobile phase compositions. The effect of the additives in the mobile phase and the makeup flow on the background noise of CAD detection was also studied. Accurate measurement of the enantiopurity of pharmaceuticals from -100% to 100% enantiomeric excess (ee) was achieved under isocratic conditions. The SFC-CAD system was used as a chromatographic screening system for method development and successfully applied to high-throughput chiral analysis of reaction mixtures in microtiter plates. <http://dx.doi.org/doi:10.1016/j.supflu.2016.04.014>



## 247. Evaluation Of The Migration Of UV-Ink Photoinitiators From Polyethylene Food Packaging By Supercritical Fluid Chromatography Combined With Photodiode Array Detector And Tandem Mass Spectrometry

2016 - Polymer Testing

Keywords: Beijing University of Chemical Technology, Beijing Center for Disease Control and Prevention, Chinese Academy of Inspection and Quarantine, UV-ink photoinitiators, polyethylene food packaging migration, leachables, chemical materials

### Abstract

UV-ink photoinitiators (PIs), which are used to initiate polymerization reaction for the curing of inks and lacquers, have become a kind of contaminant residues in printing plastic food packaging. The residual PIs in packaging may pose a potential threat to customers. In this work, migration behaviors of 13 PIs from a polyethylene (PE) packaging to food simulants according to regulation EU No 10/2011 were studied by supercritical fluid chromatography combined with photodiode array detector and tandem mass spectrometry (SFC-PDA-MS/MS). The method simultaneously analyzed 13 PIs within 4.5 min and was sensitively with low limits of detection of 0.02–2.16 µg/L, which could meet high throughput analysis for control the quality of food packaging. The migration results revealed that Irgacure 819, Darocure 1173 and TPO, which had low migration rates, should be preferably selected by plastic food packaging manufacture for food safety.

<http://dx.doi.org/10.1016/j.polymertesting.2016.06.008>

## 248. Lipid Profiling Of Polarized Human Monocyte-Derived Macrophages

2016 - Prostaglandins & Other Lipid Mediators

Keywords: Cytokines, Immunology, Mass spectrometry, Phospholipases, Phospholipids

### Abstract

The highly orchestrated transcriptional and metabolic reprogramming during activation drastically transforms the main functions and physiology of human macrophages across the polarization spectrum. Lipids, for example, can modify protein function by acting remotely as signaling molecules but also locally by altering the physical properties of cellular membranes. These

changes play key roles in the functions of highly plastic immune cells due to their involvement in inflammation, immune responses, phagocytosis and wound healing processes. We report an analysis of major membrane lipids of distinct phenotypes of resting (M0), classically activated (M1), alternatively activated (M2a) and deactivated (M2c) human monocyte derived macrophages from different donors. Samples were subjected to supercritical fluid chromatography-ion mobility-mass spectrometry analysis, which allowed separations based on lipid class, facilitating the profiling of their fatty acid composition. Different levels of arachidonic acid mobilization as well as other fatty acid changes were observed for different lipid classes in the distinct polarization phenotypes, suggesting the activation of highly orchestrated and specific enzymatic processes in the biosynthesis of lipid signaling molecules and cell membrane remodeling. Thromboxane A2 production appeared to be a specific marker of M1 polarization. These alterations to the global composition of lipid bi-layer membranes in the cell provide a potential methodology for the definition and determination of cellular and tissue activation states.

<http://dx.doi.org/10.1016/j.prostaglandins.2016.11.002>

## 249. Tandem Mass Spectrometry Determined Maternal Cortisone To Cortisol Ratio And Psychiatric Morbidity During Pregnancy–Interaction With Birth Weight

2016 - Psychoneuroendocrinology

Keywords: Upsalla University, University of Groningen, Karolinska Institutet, 11- $\beta$ -hydroxysteroid dehydrogenase, cortisol, cortisone, Separation of steroids by ultra performance convergence chromatography (UPC<sup>2</sup> with Xevo TQS), health science

### Abstract

Maternal serum cortisol has been suggested to be influenced by psychiatric morbidity, and may also influence fetal growth. However, several studies found equal cortisol levels in depressed and healthy pregnant women. Placental 11- $\beta$ -hydroxysteroid dehydrogenase type 2 (11 $\beta$ -HSD2) shields the fetus from maternal cortisol by conversion to cortisone, a function that may be compromised by maternal stress. We aimed to compare the serum ratio of cortisone to cortisol, in women with and without psychiatric morbidity during pregnancy. A secondary aim was to investigate whether fetal growth, approximated by infant birth weight, was associated with the cortisone to cortisol ratio. We performed tandem mass spectrometry analysis of serum cortisol and cortisone in late pregnancy in 94 women with antenatal psychiatric morbidity and 122 controls (cohort 1). We also compared the placental gene expression of HSD11B1 and 2 in another group of 69 women with psychiatric morbidity and 47 controls (cohort 2). There were no group differences in cortisol to cortisone ratio, absolute levels of cortisone and cortisol (cohort 1), or expression of HSD11B1 or 2 (cohort 2). However, cortisone to cortisol ratio was positively associated with birth weight in women with psychiatric morbidity, also after adjustment for gestational length, fetal sex, maternal height, smoking, SSRI use, and time of blood sampling (standardized  $\beta$ =0.35,  $p$ <0.001), with no association in the healthy controls. Thus, the maternal serum cortisone to cortisol ratio does not seem to be affected by psychiatric morbidity, but psychiatric morbidity may increase fetal exposure to cortisol or other metabolic factors influencing fetal growth.

**[doi:10.1016/j.psyneuen.2016.04.006](https://doi.org/10.1016/j.psyneuen.2016.04.006)**

## 250. Identifying The Tobacco Related Free Radicals By UPCC-QTOF-MS With Radical Trapping Method In Mainstream Cigarette Smoke

2016 - Talanta

Keywords: Tongji University, Shanghai, Shanghai Tobacco Group Corporation Limited, Ultra-performance convergence chromatography, Radicals, Cigarette smoke, Spin trapping

### Abstract

Tobacco related free radicals (TFRs) in the cigarette smoke are specific classes of hazardous compounds that merit concern. In this study, we developed a hybrid method to identify TFRs directly based on ultra-performance convergence chromatography with a quadrupole time-of-flight mass spectrometry (UPCC-QTOF MS) combined spin trapping technique. The short-lived TFRs were stabilized successfully *in situ* through spin trapping procedure and UPCC was applied to facilitate efficient separation of complex derivative products. Coupling of orthogonal partial least squares



discriminant analysis (OPLS-DA), UPCC-QTOF MS system enabled us to identify specific potential TFRs with exact chemical formula. Moreover, computational stimulations have been carried out to evaluate the optimized stability of TFRs. This work is a successful demonstration for the application of an advanced hyphenated technique for separation of TFRs with short detection time (less than 7 min) and high throughput.

<http://dx.doi.org/10.1016/j.talanta.2016.07.002>

## 251. Analysis Of Hydroxylated Polybrominated Diphenyl Ethers (OH-Bdes) By Supercritical Fluid Chromatography/Mass Spectrometry

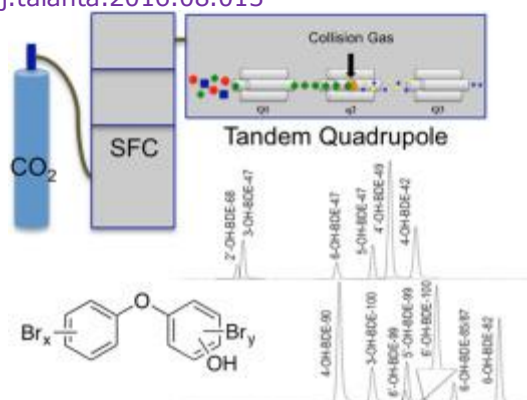
2016 - Talanta

KeyWords: The State University of New York, Waters Corporation, Hydroxylated Polybrominated Diphenyl Ethers (OH-BDEs), Supercritical Fluid Chromatography (SFC), Mass Spectrometry (MS), Metabolism, Human Serum

### Abstract

Hydroxylated polybrominated diphenyl ethers (OH-BDEs), which have anthropogenic and natural origins, have exhibited neurotoxic and endocrine disrupting effects in humans and wildlife. Therefore, there is an increased interest in the analysis of these compounds in biological matrices in order to assess their potential toxicological risks. Analysis of OH-BDEs is conventionally completed using liquid chromatography/mass spectrometry (LC/MS), or by gas chromatography/mass spectrometry (GC/MS) after derivatization. Issues with resolution in separating congeners have limited the analysis of OH-BDEs via LC/MS, with published methods only able to include 13 congeners in the analysis. On the other hand, while GC/MS analysis can analyze more OH-BDE congeners, derivatization of OH-BDEs to convert them to GC amenable compounds adds to sample preparation time and limits the column lifetime due to trace residues of highly reactive derivatization agents entering the column. Herein we report the development of a supercritical fluid chromatography/mass spectrometry (SFC/MS) method for the analysis of 22 OH-BDE congeners. Instrument limits of detection for the developed method ranged from 2 to 106 fg injected on column, which is lower than previously optimized LC/MS and GC/MS methods. The developed SFC/MS method was successfully applied towards the analysis of *in vitro* metabolism samples and human serum samples to demonstrate its applicability with different biological matrices.

<http://dx.doi.org/10.1016/j.talanta.2016.08.013>



## 252. Stereoselective Quantification Of Triconazole In Vegetables By Supercritical Fluid Chromatography

2016 - Talanta

Keywords: Triconazole, Enantioseparation, Supercritical fluid chromatography, Influence of organic modifier, Stereoselective quantification, QuEChERS pretreatment

### Abstract:

**A highly fast analytical method through supercritical fluid chromatography (SFC) has been developed to quantify triconazole enantiomers in cucumbers and tomatoes. Effects of organic modifier type and concentration on chiral separation and quantification of standard solution as well as matrix-matched standard solutions have**



been studied in detail. Among three organic modifiers, better separation of triticonazole racemate was achieved with 20% ethanol (v/v). The run time in SFC (ca 3 min) with CO<sub>2</sub>-ethanol (80:20, v/v) as the mobile phase was six-fold shorter than HPLC analysis (about 18 min). Then, QuEChERS (quick, easy, cheap, effective, rugged and safe) extraction procedure was used for triticonazole in vegetables. The residue analysis method was validated. Good linearity ( $R^2 \geq 0.9988$ ) and recoveries (81.62~106.21%,  $RSD \leq 7.30\%$ ) for the two enantiomers were achieved. This developed method described herein is convenient and reliable for enantioselective detection of triticonazole in vegetables, which might provide additional information for reliable risk assessment of chiral pesticides.

<http://dx.doi.org/10.1016/j.talanta.2016.08.077>

## 253. Ethynylogation Approach In Pharmacophore Design: From Alkynyl-To Butadiynyl-Carbinols Vs Antitumoral Cytotoxicity

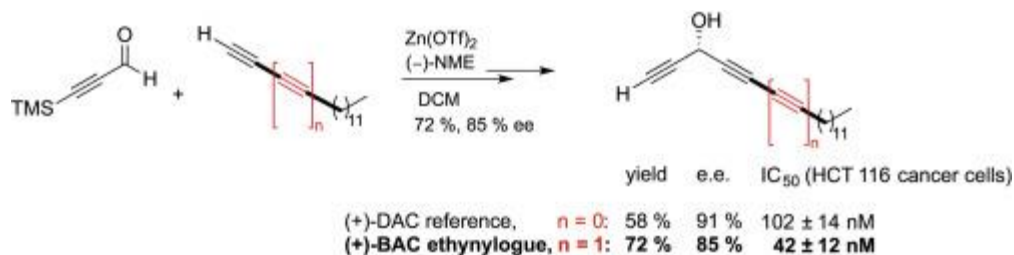
2016 - Tetrahedron

Keywords: Alkyne, Asymmetric synthesis, Antitumor agent, Cytotoxicity, Dialkynylcarbinol, 1,3-Diyne, Ethynylogation, Lipidic alkynylcarbinol

### Abstract:

Ethynylogation of a chiral lipidic dialkynylcarbinol (DAC), identified as a lead for cytotoxicity against HCT116 cancer cells, is shown to typify the butadiynyl-alkynylcarbinol (BAC) unit as a new pharmacophore. The enantiomers of the internal BAC have been synthesized with 72–75% yield and 85% ee through the use of a modified Carreira reaction shown here for the first time to be compatible with butadiyne and ynal substrates. One enantiomer of the internal BAC could be characterized by X-ray crystallography. In this particular case, the 'DAC to BAC' ethynylogation results in a slight enhancement of the eutomer potency with a preserved vanishing eudismic ratio ( $IC_{50}$  values from  $102 \pm 14$  nM to  $42 \pm 12$  nM for the (+) enantiomers).

<http://dx.doi.org/10.1016/j.tet.2016.09.001>



## 254. Pesticides Determination In Fruit Samples Using SFC-DAD

2016 - Toxicology Letters

Keywords: Pesticides, UPC2, QuEChERS, DisQue, Papaya, avocado, lime, banana, mango, melon

### Abstract:

The development of analytical methods for pesticides determination in fruits is an important task due to the toxicity of these compounds. To improve pesticides analysis in food matrices alternative chromatographic techniques can be used. Supercritical fluid chromatography (SFC) has barely been applied in this area. Atrazine (ATZ), ametryn (AME), carbofuran (CF), carbaryl (CAR) and methyl parathion (MeP), QuEChERS, DisQue kit, column Viridis BEH 2-EP (100 mm × 4.6 mm, 5 μm) and SFC-DAD system Acquity UPC2 (Waters). Fruits samples were subjected to QuEChERS AOAC Official Method. For chromatographic analysis, supercritical CO<sub>2</sub> and MeOH were used as mobile phase. The MeOH gradient was: 5% for 0.4 min, from 5 to 60% in 1.6 min and 60% for 3 min. Pressure, flow rate and column temperature was 1500 psi, 1.5 mL/min and 40 °C, respectively. MeP was detected at 265 nm and the others at 218 nm.

Pesticides were separated in 2.2 min with a resolution >1.5. The method was validated using papaya and avocado samples. From selectivity assess, interferences were no observed for the

studied pesticides in both fruits, except for CF. For papaya LODs and LOQs ranged from 0.13–0.38 and 0.22–0.64 g/g, respectively; recoveries varied from 72.8–94.6%; RSD was <3%; and the correlation coefficient (*r*) values were >0.99. While for avocado LODs and LOQs ranged from 0.12–0.45 and 0.28–0.80 g/g; respectively; RSD was <11%; recoveries varied from 50.0 to 94.2%; and the *r* values were >0.98. Matrix effect determined in both fruits was considered medium signal suppression. The method applicability was assessed for lime, banana, mango and melon samples. It was observed that this method can be used for the analysis of MeP and ATZ in the four fruits and for CAR and AME in mango and melon. A SFC-DAD method for pesticides analysis in papaya and avocado was developed. This method showed a good performance and satisfactory validation parameters. This method proved to be useful for other fruits.  
<http://dx.doi.org/10.1016/j.toxlet.2016.07.222>

## 255. The Emergence Of Low-Cost Compact Mass Spectrometry Detectors For Chromatographic Analysis

2016 - TrAC Trends in Analytical Chemistry

Keywords: Merck, Method development; High-throughput analysis; Pharmaceutical analysis; Process chemistry support

### Abstract

An overview of recent progress in the development of compact mass spectrometers for use as chromatographic detectors in chemical analysis is presented. As the applications of LC-MS technologies have grown in recent years there has been a continued expansion of the approach to new user groups. Within the pharmaceutical industry, the recent development of small, inexpensive and quiet MS detectors for LC has enabled the rollout of this important technology well beyond the initial user base of researchers in drug metabolism and bioanalysis to the direct support of research areas such as discovery chemistry, process chemistry, chemical engineering, manufacturing and formulation sciences, with comparable broadening of the MS user base occurring in other industries and in academia. In this review we survey recent developments and applications ranging from reaction monitoring, biomolecule analysis and high-throughput microplate analysis to the identification and analysis of impurities, degradation products and potential mutagens, offering thoughts on current limitations and future directions.  
[doi:10.1016/j.trac.2016.04.025](http://dx.doi.org/10.1016/j.trac.2016.04.025)

## 256. Metamorphosis Of Supercritical Fluid Chromatography To SFC – An Overview

2016 - TrAC Trends in Analytical Chemistry

Keywords: Waters, Tarafder, Method; Stationary phase; Application; Metabolite; Pharmaceutical; Forensic; Food

### Abstract

SFC is expanded as supercritical fluid chromatography, but the chromatography that is currently conducted under the name of SFC are not dependent on supercritical conditions. An SFC practitioner is mostly neither aware of the critical temperatures and pressures of the solvents, nor even require to take any measures to maintain supercriticality. Because according to the current author, SFC has decisively shifted its focus from using mobile phase in supercritical conditions to using carbon dioxide as mobile phase, mixed with other co-solvents. SFC has discovered the benefits of using compressed CO<sub>2</sub> as solvent, which opened up some distinctly different and significantly wide application possibilities for chromatographic analyses as a whole. Here an overview will be provided on how supercritical fluid chromatography metamorphosed to SFC and why SFC may no longer be considered as a technique with some special application scope, rather a complementary tool to some widely accepted analytical techniques e.g. reversed-phase chromatography.  
[doi:10.1016/j.trac.2016.01.002](http://dx.doi.org/10.1016/j.trac.2016.01.002)

## 257. Supercritical Fluids – The Current State And Outlook

2016 – Book - SUPERCRITICAL FLUID APPLICATIONS

Keywords: RESEARCH ON THE APPLICATION OF SUPERCRITICAL FLUIDS, EXTRACTION, FRACTIONATION, FOAMS, NANOPARTICLES

### **Summary**

The main results of the research in the Laboratory of Supercritical Fluids of the Institute of Chemical Process Fundamentals in Prague involve mathematical models for the kinetics of supercritical fluid extraction from plants, distinguished according to the plants and extracted substances, preparations based on CO<sub>2</sub> extracts for the application as botanical insecticides, and enzymatic reactions of oil in supercritical CO<sub>2</sub> medium. The contemporary research is focused on the online fractionation of CO<sub>2</sub> extracts, pressurized liquid extraction, CO<sub>2</sub> assisted foaming of polymers, and recrystallization of the films of metal oxides in watermodified supercritical CO<sub>2</sub>.  
<http://ins.pulawy.pl/icsfta/res/icsfta-2017.pdf>

## 2015 Publications

### 258. Direct Analysis Of Lipophilic Antioxidants Of Olive Oils Using Bicontinuous Microemulsions

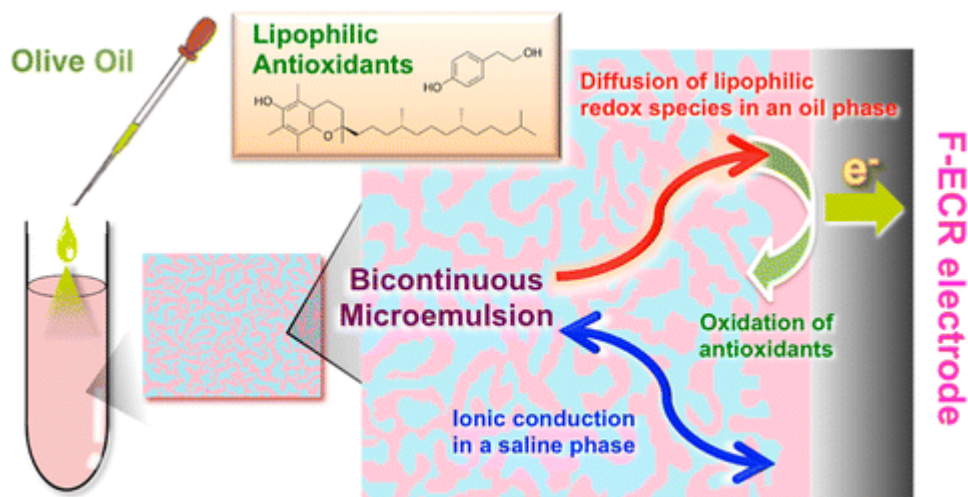
2015 - Analytical Chemistry

Keywords: Olive oil phenolics, lipophilic antioxidants, antioxidant capacity of EVOO

#### Abstract

Quantitative analyses of olive oil for lipophilic antioxidants, such as  $\alpha$ -tocopherol and phenolics, by simple electrochemical measurements were conducted in a bicontinuous microemulsion (BME), which was bicontinuously composed of saline and toluene microphases with a surfactant system. Lipophilic antioxidants in oils were directly monitored in BME solutions using a lipophilic, fluorinated nanocarbon-film electrode (F-ECR). The combination of a well-balanced BME and extremely biased electrodes, such as strongly hydrophilic indium/tin oxide and strongly lipophilic (hydrophobic) F-ECR, allowed individual monitoring of hydrophilic and lipophilic antioxidants in the same BME solution without any required extraction. Furthermore, values for the charge  $Q$ , integrated from observed currents, showed good linear relationships with the results of conventional assays for antioxidant activity, namely, total phenolics and oxygen radical absorbance capacity assays, even with practical food samples. This proposed methodology provided a very simple, rapid, easily serviceable, and highly reproducible analysis that possesses great potential for applications to a wide range of chemical mixtures, in terms of analyte and media, beyond food oils.

<http://dx.doi.org/10.1021/acs.analchem.5b03445>



#### Electrochemical Analysis of Antioxidants in Olive Oils

### 259. Enantioselective Simultaneous Analysis Of Selected Pharmaceuticals In Environmental Samples By Ultrahigh Performance Supercritical Fluid Based Chromatography Tandem Mass Spectrometry

2015 - Analytica Chimica Acta

Keywords: University of Bath, Norwegian Institute for Water Research, NIVA, chiral pharmaceutically active compounds, influent, effluent, amylose column, cellulose column, environmental

#### Abstract

In order to assess the true impact of each single enantiomer of pharmacologically active compounds (PACs) in the environment, highly efficient, fast and sensitive analytical methods are needed. For the first time this paper focuses on the use of ultrahigh performance supercritical fluid based chromatography coupled to a triple quadrupole mass spectrometer to develop multi-residue

enantioselective methods for chiral PACs in environmental matrices. This technique exploits the advantages of supercritical fluid chromatography, ultrahigh performance liquid chromatography and mass spectrometry. Two coated modified 2.5  $\mu\text{m}$ -polysaccharide-based chiral stationary phases were investigated: an amylose tris-3,5-dimethylphenylcarbamate column and a cellulose tris-3-chloro-4-methylphenylcarbamate column. The effect of different chromatographic variables on chiral recognition is highlighted. This novel approach resulted in the baseline resolution of 13 enantiomers PACs (aminorex, carprofen, chloramphenicol, 3-*N*-dechloroethylifosfamide, flurbiprofen, 2-hydroxyibuprofen, ifosfamide, imazalil, naproxen, ofloxacin, omeprazole, praziquantel and tetramisole) and partial resolution of 2 enantiomers PACs (ibuprofen and indoprofen) under fast-gradient conditions (<10 min analysis time). The overall performance of the methods was satisfactory. The applicability of the methods was tested on influent and effluent wastewater samples. To the best of our knowledge, this is the first feasibility study on the simultaneous separation of chemically diverse chiral PACs in environmental matrices using ultrahigh performance supercritical fluid based chromatography coupled with tandem mass spectrometry.

<http://dx.doi.org/10.1016/j.aca.2016.05.051>

## 260. Development And Optimization Of Ultra-High Performance Supercritical Fluid Chromatography Mass Spectrometry Method For High-Throughput Determination Of Tocopherols And Tocotrienols In Human Serum

2015 - Analytica Chimica Acta

Keywords: Charles University, Palacky University, Research Institute of Brewing and Malting, vitamin E, pharmaceutical

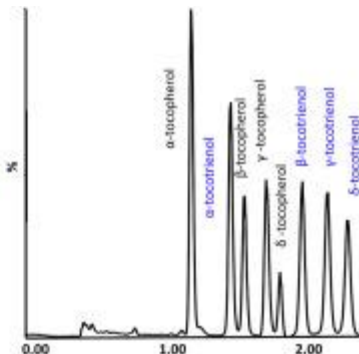
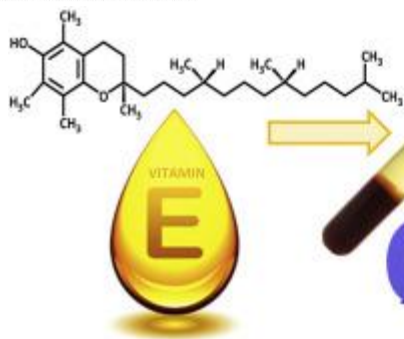
### Abstract

The goal of this study was to develop an effective supercritical fluid chromatography method using single quadrupole MS for analysis of all isomeric forms of vitamin E. Finally, two fast and effective methods, the high resolution one and the high speed one, for the determination of 8 vitamin E isomers in human serum were developed.

Rapid high-throughput liquid-liquid extraction was selected as a sample preparation step. Sample pretreatment of 100  $\mu\text{L}$  human serum was consisted of protein precipitation with 200  $\mu\text{L}$  ethanol and liquid-liquid extraction by 400  $\mu\text{L}$  hexane/dichloromethane (80/20, v/v). The separation was performed on BEH 2-EP (3.0  $\times$  100 mm, 1.7  $\mu\text{m}$ ) stationary phase, using isocratic elution with carbon dioxide and 10 mM ammonium formate in methanol in the ratio 98:2 for high resolution method with run time 4.5 min and in the ratio 95:5 for high speed method, where the run time was 2.5 min. The method development included optimization of key parameters: the choice of the suitable stationary phase and the composition of mobile phase, where an influence of various modifiers, their ratio and additives were tested, and optimization of fine tuning parameters including BPR pressure, flow-rate and column temperature. Quantification of all isomeric forms was performed using SIM (single ion monitoring) experiments in ESI positive ion mode. Both high speed and high resolution chromatographic methods were validated in terms of precision, accuracy, range, linearity, LOD, LOQ and matrix effects using the same LLE procedure. The high resolution method provided more sensitive results (LOD: 0.017–0.083  $\mu\text{g mL}^{-1}$ ) and better linearity ( $r^2 > 0.9930$ ) than the high speed one (LOD: 0.083–0.25  $\mu\text{g mL}^{-1}$ ,  $r^2 > 0.9877$ ) at the cost of double time of analysis.

<http://dx.doi.org/10.1016/j.aca.2016.06.008>

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## 261. Simultaneous Enantioselective Determination Of Triadimefon And Its Metabolite Triadimenol In Edible Vegetable Oil By Gel Permeation Chromatography And Ultraperformance Convergence Chromatography / Tandem Mass Spectrometry

2015 - Analytical and Bioanalytical Chemistry

Keywords: Zhejiang University, Shanghai Institute of Organic Chemistry, stereoisomeric separation, triadimenol, triadimefonyes, , vegetable oil, food

### Abstract

A novel, sensitive, and efficient enantioselective method for the determination of triadimefon and its metabolite triadimenol in edible vegetable oil, was developed by gel permeation chromatography and ultraperformance convergence chromatography/tandem triple quadrupole mass spectrometry. After the vegetable oil samples were prepared using gel permeation chromatography, the eluent was collected, evaporated, and dried with nitrogen gas. The residue was redissolved by adding methanol up to a final volume of 1 mL. The analytes of six enantiomers were analyzed on Chiralpak IA-3 column (150 × 4.6 mm) using compressed liquid CO<sub>2</sub>-mixed 14 % co-solvents, comprising ethanol / acetonitrile / isopropanol = 20/20/60 (v/v/v) in the mobile phase at 30 °C, and the total separation time was less than 4 min at a flow rate of 2 mL/min. Quantification was achieved using matrix-matched standard calibration curves. The overall mean recoveries for six enantiomers from vegetable oil were 90.1–97.3 %, with relative standard deviations of 0.8–5.4 % intra-day and 2.3–5.0 % inter-day at 0.5, 5, and 50 µg/kg levels. The limits of quantification were 0.5 µg/kg for all enantiomers based on five replicate extractions at the lowest fortified level in vegetable oil. Moreover, the absolute configuration of six enantiomers had been determined based on comparisons of the vibrational circular dichroism experimental spectra with the theoretical curve obtained by density functional theory calculations. Application of the proposed method to the 40 authentic vegetable oil samples from local markets suggests its potential use in enantioselective determination of triadimefon and triadimenol enantiomers.

<http://link.springer.com/article/10.1007/s00216-015-9046-y>

## 262. Analytical Method Development For The Determination Of Emerging Contaminants In Water Using Super-Critical Fluid Chromatography Coupled With Diode-Array Detection

2015 - Analytical and Bioanalytical Chemistry

Keywords: Universidad de Colima, emerging contaminants, Viridis BEH 2-EP, water samples, endocrine disruptors, triclosan, diuran, glyburide, carbamazepine, estradiol, ethinyl estradiol, bisphenol A, environmental

### Abstract

An analytical method using supercritical-fluid chromatography coupled with diode-array detection for the determination of seven emerging contaminants—two pharmaceuticals (carbamazepine and glyburide), three endocrine disruptors (17 $\alpha$ -ethinyl estradiol, bisphenol A, and 17 $\beta$ -estradiol), one bactericide (triclosan), and one pesticide (diuron)—was developed and validated. These contaminants were chosen because of their frequency of use and their toxic effects on both humans and the environment. The optimized chromatographic separation on a Viridis BEH 2-EP



column achieved baseline resolution for all compounds in less than 10 min. This separation was applied to environmental water samples after sample preparation. The optimized sample treatment involved a preconcentration step by means of solid-phase extraction using C18-OH cartridges. The proposed method was validated, finding recoveries higher than 94 % and limits of detection and limits of quantification in the range of 0.10–1.59  $\mu\text{g L}^{-1}$  and 0.31–4.83  $\mu\text{g L}^{-1}$ , respectively. Method validation established the proposed method to be selective, linear, accurate, and precise. Finally, the method was successfully applied to environmental water samples.

<http://dx.doi.org/10.1007/s00216-015-8581-x>

## 263. Analysis Of Glucuronide And Sulfate Steroids In Urine By Ultra-High-Performance Supercritical-Fluid Chromatography Hyphenated Tandem Mass Spectrometry

2015 - Analytical and Bioanalytical Chemistry

Keywords: LUNAM University, LABERCA, steroid profiling, conjugated steroids, glucuronide, sulfate steroids, anabolic steroids, steroid isomers, hormones, veterinary drug residue, bovine urine, food

### Abstract

Profiling conjugated urinary steroids to detect anabolic-steroid misuse is recognized as an efficient analytical strategy in both chemical-food-safety and anti-doping fields. The relevance and robustness of such profiling rely on the analysis of glucuronide and sulfate steroids, which is expected to have properties including accuracy, specificity, sensitivity, and, if possible, rapidity. In this context, the ability of ultra-high-performance supercritical-fluid chromatography (UHPSFC) hyphenated tandem mass spectrometry (MS–MS) to provide reliable and accurate phase II analysis of steroids was assessed. Four stationary phases with sub-2  $\mu\text{m}$  particles (BEH, BEH 2-ethyl-pyridine, HSS C18 SB, and CSH fluorophenyl) were screened for their capacity to separate several conjugated steroid isomers. Analytical conditions including stationary phase, modifier composition and percentage, back pressure, column temperature, and composition and flow rate of make-up solvent were investigated to improve the separation and/or the sensitivity. Thus, an analytical procedure enabling the analysis of eight glucuronide and 12 sulfate steroids by two different methods in 12 and 15 min, respectively, was optimized. The two procedures were evaluated, and UHPSFC–MS–MS analysis revealed its ability to provide sensitive (limits of quantification: 0.1  $\text{ng mL}^{-1}$  and 0.5  $\text{ng mL}^{-1}$  for sulfate and glucuronide steroids, respectively) and reliable quantitative performance ( $R^2 > 0.995$ ,  $\text{RSD} < 20\%$ , and  $\text{bias} < 30\%$ ) through the use of suitable labeled internal standards. Comparison with UHPLC–MS–MS was performed, and UHPSFC–MS–MS obtained better performance in terms of sensitivity. Finally, as a proof of concept, this so-called green technology was used in a chemical-food-safety context to profile steroid conjugates in urine samples from bovines treated with estradiol.

<http://dx.doi.org/10.1007/s00216-015-8573-x>

## 264. High-Throughput And Comprehensive Lipidomic Analysis Using Ultrahigh-Performance Supercritical Fluid Chromatography–Mass Spectrometry

2015 - Analytical Chemistry

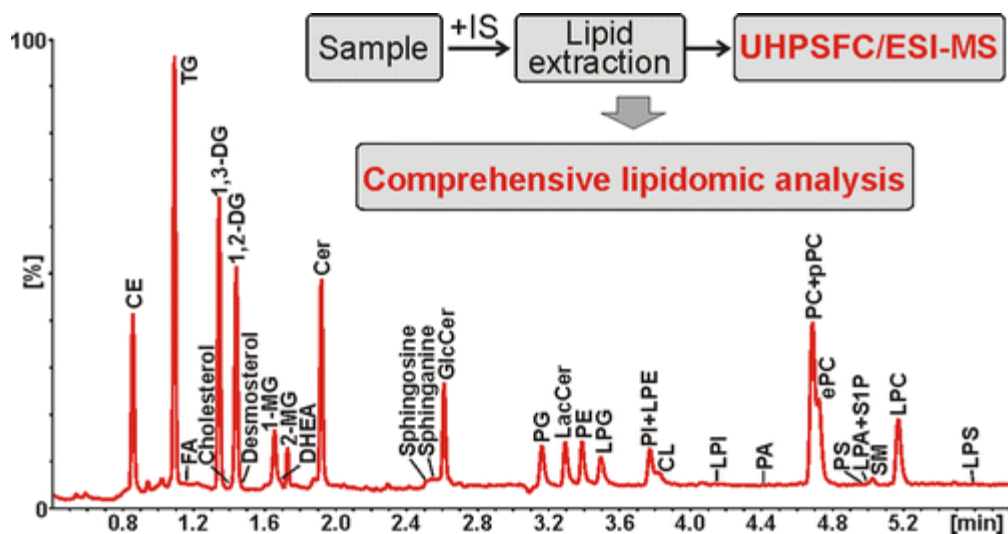
Keywords: Lipid class separations, ESI-MS, non-polar and polar lipid classes, fatty acyls, glycerolipids, glycerophospholipids, sphingolipids, sterols, and prenols, biological matrices

### Abstract

New analytical approach for high-throughput and comprehensive lipidomic analysis of biological samples using ultrahigh-performance supercritical fluid chromatography (UHPSFC) with electrospray ionization-mass spectrometry (ESI-MS) is presented in this work as an alternative approach to established shotgun MS or high-performance liquid chromatography-MS. The lipid class separation is performed by UHPSFC method based on 1.7  $\mu\text{m}$  particle-bridged ethylene hybrid silica column with a gradient of methanol–water–ammonium acetate mixture as a modifier. All parameters of UHPSFC conditions are carefully optimized and their influence on the chromatographic behavior of lipids is discussed. The final UHPSFC/ESI-MS method enables a fast separation of 30 nonpolar and polar lipid classes within 6 min analysis covering 6 main lipid categories including fatty acyls, glycerolipids, glycerophospholipids, sphingolipids, sterols, and prenols. Individual lipid species within lipid classes are identified based on positive and negative-

ion full-scan and tandem mass spectra measured with high mass accuracy and high resolving power. Developed UHPSFC/ESI-MS method is applied for the analysis of porcine brain extract as a complex lipidomic sample, where 24 lipid classes containing 436 lipid species are identified. The method is validated for the quantitative analysis of lipid species in biological tissues using internal standards for each lipid class. This high-throughput, comprehensive and accurate UHPSFC/ESI-MS method is suitable for the lipidomic analysis of large sample sets in the clinical research.

<http://dx.doi.org/10.1021/acs.analchem.5b01054>



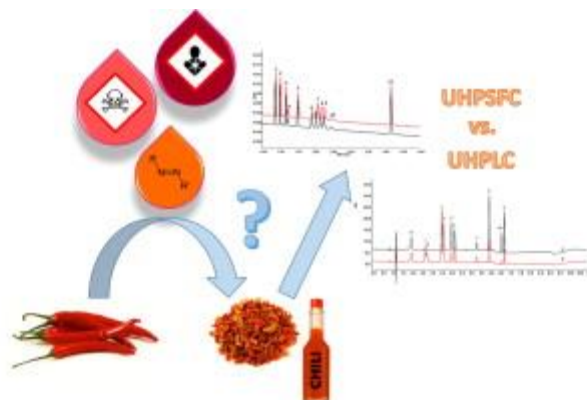
## 265. Development And Validation Of Ultra-High Performance Supercritical Fluid Chromatography Method For Determination Of Illegal Dyes And Comparison To Ultra-High Performance Liquid Chromatography Method

2015 - Analytica Chimica Acta

Keywords: Charles University, red dye, sudan red, spices, CSH, food

### Abstract

A novel simple, fast and efficient ultra-high performance supercritical fluid chromatography (UHPSFC) method was developed and validated for the separation and quantitative determination of eleven illegal dyes in chili-containing spices. The method involved a simple ultrasound-assisted liquid extraction of illegal compounds with tetrahydrofuran. The separation was performed using a supercritical fluid chromatography system and CSH Fluoro-Phenyl stationary phase at 70 °C. The mobile phase was carbon dioxide and the mixture of methanol:acetonitrile (1:1, v/v) with 2.5% formic acid as an additive at the flow rate 2.0 mL min<sup>-1</sup>. The UV-vis detection was accomplished at 500 nm for seven compounds and at 420 nm for Sudan Orange G, Butter Yellow, Fast Garnet GBC and Methyl Red due to their maximum of absorbance. All eleven compounds were separated in less than 5 min. The method was successfully validated and applied using three commercial samples of chili-containing spices – Chili sauce (Indonesia), Feferony sauce (Slovakia) and Mojo sauce (Spain). The linearity range of proposed method was 0.50–9.09 mg kg<sup>-1</sup> ( $r \geq 0.995$ ). The detection limits were determined as signal to noise ratio of 3 and were ranged from 0.15 mg kg<sup>-1</sup> to 0.60 mg kg<sup>-1</sup> (1.80 mg kg<sup>-1</sup> for Fast Garnet) for standard solution and from 0.25 mg kg<sup>-1</sup> to 1.00 mg kg<sup>-1</sup> (2.50 mg kg<sup>-1</sup> for Fast Garnet, 1.50 mg kg<sup>-1</sup> for Sudan Red 7B) for chili-containing samples. The recovery values were in the range of 73.5–107.2% and relative standard deviation ranging from 0.1% to 8.2% for within-day precision and from 0.5% to 8.8% for between-day precision. The method showed potential for being used to monitor forbidden dyes in food constituents. The developed UHPSFC method was compared to the UHPLC-UV method. The orthogonality of Sudan dyes separation by these two methods was demonstrated. Benefits and drawbacks were discussed showing the reliability of both methods for monitoring of studied illegal dyes in real food constituents.



## 266. Ultra High Performance Supercritical Fluid Chromatography Coupled With Tandem Mass Spectrometry For Screening Of Doping Agents. I: Investigation Of Mobile Phase And MS Conditions

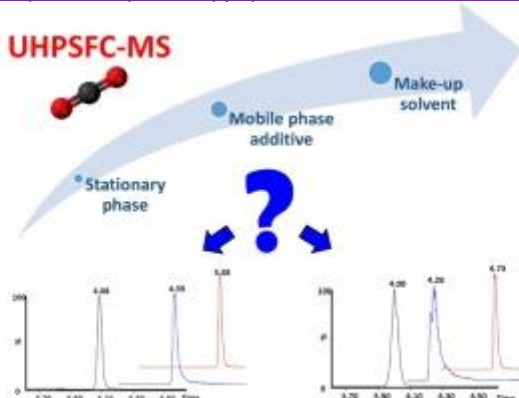
2015 - Analytica Chimica Acta

Keywords: Doping agents; Make-up solvent; Mobile phase; Ultra high performance liquid chromatography; Ultra high performance supercritical fluid chromatography

### Abstract

The conditions for the analysis of selected doping substances by UHPSFC-MS/MS were optimized to ensure suitable peak shapes and maximized MS responses. A representative mixture of 31 acidic and basic doping agents was analyzed, in both ESI+ and ESI- modes. The best compromise for all compounds in terms of MS sensitivity and chromatographic performance was obtained when adding 2% water and 10mM ammonium formate in the CO<sub>2</sub>/MeOH mobile phase. Beside mobile phase, the nature of the make-up solvent added for interfacing UHPSFC with MS was also evaluated. Ethanol was found to be the best candidate as it was able to compensate for the negative effect of 2% water addition in ESI- mode and provided a suitable MS response for all doping agents. Sensitivity of the optimized UHPSFC-MS/MS method was finally assessed and compared to the results obtained in conventional UHPLC-MS/MS. Sensitivity was improved by 5-100-fold in UHPSFC-MS/MS vs. UHPLC-MS/MS for 56% of compounds, while only one compound (bumetanide) offered a significantly higher MS response (4-fold) under UHPLC-MS/MS conditions. In the second paper of this series, the optimal conditions for UHPSFC-MS/MS analysis will be employed to screen >100 doping agents in urine matrix and results will be compared to those obtained by conventional UHPLC-MS/MS

<http://www.sciencedirect.com/science/article/pii/S0003267014012379>



## 267. Ultra High Performance Supercritical Fluid Chromatography Coupled With Tandem Mass Spectrometry For Screening Of Doping Agents. II: Analysis Of Biological Samples

2015 - Analytica Chimica Acta

Keywords: Charles University, University of Geneva, doping agents, Swiss Laboratory for Doping Analyses, urine, health science

### Abstract

The potential and applicability of UHPSFC–MS/MS for anti-doping screening in urine samples were tested for the first time. For this purpose, a group of 110 doping agents with diverse physicochemical properties was analyzed using two separation techniques, namely UHPLC–MS/MS and UHPSFC–MS/MS in both ESI+ and ESI– modes. The two approaches were compared in terms of selectivity, sensitivity, linearity and matrix effects. As expected, very diverse retentions and selectivities were obtained in UHPLC and UHPSFC, proving a good complementarity of these analytical strategies. In both conditions, acceptable peak shapes and MS detection capabilities were obtained within 7 min analysis time, enabling the application of these two methods for screening purposes. Method sensitivity was found comparable for 46% of tested compounds, while higher sensitivity was observed for 21% of tested compounds in UHPLC–MS/MS and for 32% in UHPSFC–MS/MS. The latter demonstrated a lower susceptibility to matrix effects, which were mostly observed as signal suppression. In the case of UHPLC–MS/MS, more serious matrix effects were observed, leading typically to signal enhancement and the matrix effect was also concentration dependent, i.e., more significant matrix effects occurred at the lowest concentrations.

<http://dx.doi.org/10.1016/j.aca.2014.10.007>



## 268. Rapid Separation Of Hexabromocyclododecane Diastereomers Using A Novel Method Combining Convergence Chromatography And Tandem Mass Spectrometry

2015 - Analytical Methods

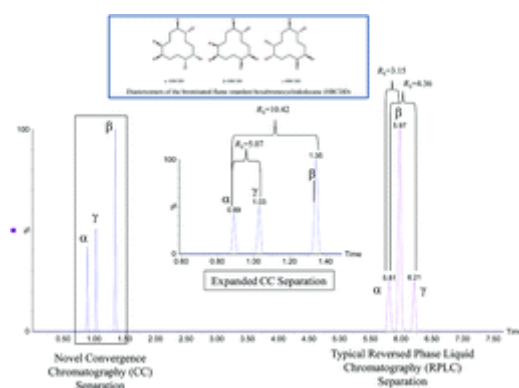
Keywords: Waters, Orebro University, diastereomers, brominated flame retardants, HSS, whale blubber, human serum, environmental

### Abstract

Analysis of the brominated flame retardant hexabromocyclododecane (HBCDD) is characterized by the separation of its three predominant diastereomers. This analysis is typically performed using reversed phase liquid chromatography (RPLC) coupled with mass spectrometric (MS) detection with analysis times in the order of 10 minutes or greater. Here we describe a rapid method using supercritical CO<sub>2</sub> and methanol to baseline separate the three most abundant HBCDD diastereomers within a three minute run time using a High Strength Silica (HSS) C18 1.8 μm particle size column. A unique elution order of the α-, β- and γ-HBCDD diastereomers using supercritical CO<sub>2</sub> was observed, and can be used as an orthogonal separation for further confidence in diastereomer identification when used in conjunction with RPLC. A tandem quadrupole mass spectrometer with negative mode electrospray ionization was used for detection, operating

in multiple reaction monitoring (MRM) mode. Ionization was enhanced by the addition of a make-up flow, which was introduced to the post-column effluent. Method limit of detection (LOD) and limit of quantification (LOQ) for  $\alpha$ -,  $\beta$ - and  $\gamma$ -HBCDD were based on peak-to-peak signal to noise ratios of greater than 3 or 10, respectively. The LOD for all HBCDD diastereomers as solvent standards was 100 fg on-column, and LOQs 500 fg on-column for  $\alpha$ - and  $\gamma$ -HBCDD and 250 fg on-column for  $\beta$ -HBCDD. In order to test the efficiency of this method, small subsets of complex human serum and whale blubber extracts were analyzed using this method, resulting in positive detections in samples of  $\alpha$ -HBCDD.

<http://dx.doi.org/10.1039/C4AY02923B>



## 269. Lipidomics: Novel Insight Into The Biochemical Mechanism Of Lipid Metabolism And Dysregulation-Associated Disease

2015 - Chemico-Biological Interactions

Keywords: Northwest University, State Food and Drug Administration, lipid metabolism, lipids, lipidomics, biomarkers, health science

### Abstract

The application of lipidomics, after genomics, proteomics and metabolomics, offered largely opportunities to illuminate the entire spectrum of lipidome based on a quantitative or semi-quantitative level in a biological system. When combined with advances in proteomics and metabolomics high-throughput platforms, lipidomics provided the opportunity for analyzing the unique roles of specific lipids in complex cellular processes. Abnormal lipid metabolism was demonstrated to be greatly implicated in many human lifestyle-related diseases. In this review, we focused on lipidomic applications in brain injury disease, cancer, metabolic disease, cardiovascular disease, respiratory disease and infectious disease to discover disease biomarkers and illustrate biochemical metabolic pathways. We also discussed the analytical techniques, future perspectives and potential problems of lipidomic applications. The application of lipidomics in disease biomarker discovery provides the opportunity for gaining novel insights into biochemical mechanism.

<http://dx.doi.org/10.1016/j.cbi.2015.09.005>

## 270. Determination Of 11 Fat Soluble Vitamins (A, D, E, K) And Their Derivatives In Vitamin Tablets By Ultra Performance Convergence Chromatography

2015 - Chinese Journal of Analytical Chemistry

Keywords: Ultra performance convergence chromatography; Vitamin tablets; Stereoisomers; Chiral separation

### Abstract

A new method was developed for the determination of 11 fat soluble vitamins (A, D, E and K) and its derivatives in vitamin tablets by ultra performance convergence chromatography (UPC<sup>2</sup>). The mobile phase was the mixture of supercritical CO<sub>2</sub> and acetonitrile at a flow rate of 1 mL/min. The separation was carried out on the Waters Acquity UPC<sup>2</sup> HSS C18 SB 100 mm × 3.0 mm i.d., 1.8



$\mu\text{m}$  column. The UV detector was set at a wavelength of 284 nm. The limits of detection (LOD) were 1.5 - 2.0 mg/L, and the calibration linear for VK1 , VK2 , VK3 and VB3 was 3-300 mg/L, linear for VA, VA palmitate, VA formic acid, VE, VE acetate, VD2 and VD3 was 5-300 mg/L, respectively. Its spiked recoveries were 97.31% - 98.76%, and the relative standard deviations (RSD's) were 0.41% - 0.96%. The method is applicable for the determination of fat soluble vitamins (A, D, E and K) and their derivatives in vitamin tablets.

<http://pesquisa.bvsalud.org/oncologiauy/resource/en/wprim-868374>

## 271. Determination Of Bifenthrin In Tea By Ultra Performance Convergence Chromatography And Gas Chromatography-Mass Spectrometry

2015 - Chinese Journal of Analytical Chemistry

Keywords: Ultra performance convergence chromatography; Bifenthrin; Tea, GC-MS

### Abstract

A method was developed for the determination of bifenthrin in tea by ultra performance convergence chromatography (UPC<sup>2</sup>). The samples were extracted with petroleum ether and cleaned up with Waters Sep-Pak<sup>®</sup> Carbon NH<sub>2</sub>, and then detected by UPC<sup>2</sup>. The mobile phase was the mixture of supercritical CO<sub>2</sub> and acetonitrile at a flow rate of 1.5 mL/min. The separation was conducted on a column of ACQUITY UPC<sup>2</sup>™ BEH (100 mm×3.0 mm, 1.7  $\mu\text{m}$ ). The UV detector was set at a wavelength of 220 nm. The detection limit was 20  $\mu\text{g/L}$ . The linear range of bifenthrin was 0.32-10.30 mg/L. The recoveries ranged from 88.7% to 98.2%. The relative standard deviations (RSD) were from 1.4% to 2.8%. The result showed that the UPC<sup>2</sup> was more efficient, rapid and low-cost than GC-MS. The method can meet the testing requirements of bifenthrin in tea. The efficacy of UPC<sup>2</sup> on testing the concentration of bifenthrin in tea was compared with GC-MS based on National Proficiency Testing and the results were satisfactory.

<http://pesquisa.bvsalud.org/oncologiauy/resource/en/wprim-882301>

## 272. Rapid Detection Of Five Common Fatty Acids In Industrial Oleic Acid Based On Ultra Performance Convergence Chromatography - Mass Spectrometry

2015 - Chinese Journal of Analytical Chemistry

Keywords: Ultra performance convergence chromatography; fatty acids; oleic acid, fruit matrix

### Abstract

A rapid method was developed for the determination of 5 common fatty acids, palmitic acid, stearic acid, oleic acid, linoleic acid and linolenic acid in industrial oleic acid based on ultra performance convergence chromatography-mass spectrometry (UPC<sub>MS</sub>). The sample was dissolved by n-hexane, followed by clean\_up of extract using 0.22  $\mu\text{m}$  organic phase filter. The fatty acids were separated in 3 min on the column of Acquity UPC<sub>2</sub> BEH 2<sub>EP</sub> by gradient elution with carbon dioxide and methanol/acetonitrile (1:1, V/V) system, and finally detected by MS detector in ESI- mode. Through the optimization of UPC<sub>2</sub>\_MS condition, the reasonable linearity was achieved for all the analytes over the range of 0.5-100 mg/L with the correlation coefficients (R<sup>2</sup>) greater than 0.9985. The recoveries for five fatty acids at three spiked levels were in the range from 89.3% to 106.67% with relative standard deviations of 0.8%-3.0%. The limits of detection for target compounds in the method ranged from 0.07 mg/L to 0.26 mg/L. The real sample analysis showed that this method was simple, fast and had a good separation effect. There was no need of derivatization for fatty acid samples. This work would provide a fast and effective detection method for UPC<sub>2</sub> technology in oil related research field.

<http://pesquisa.bvsalud.org/oncologiauy/resource/en/wprim-868386>

## 273. A Silica-Supported Solid Dispersion Of Bifendate Using Supercritical Carbon Dioxide Method With Enhanced Dissolution Rate And Oral Bioavailability

2015 - Drug Development and Industrial Pharmacy



Keywords: Shenyang Pharmaceutical University, bifendate, bioavailability, pharmacokinetics, veterinary, pharmaceuticals

#### Abstract

In this study, to enhance the dissolution rate and oral bioavailability of bifendate, a silica-supported solid dispersion (SD) of bifendate was prepared using supercritical carbon dioxide (ScCO<sub>2</sub>) technology. The properties of bifendate-silica SD were characterized by differential scanning calorimetry (DSC), X-ray diffraction (X-RD) and scanning electron microscopy. The pharmacokinetic study was carried out in beagle dogs using commercial bifendate dropping pills as a reference which is a conventional SD formulation of bifendate and PEG6000. A novel method of Ultra Performance Convergence Chromatography-tandem mass spectrometry (UPC<sup>2</sup><sup>TM</sup>-MS/MS) method was applied to determine bifendate concentration in plasma. The amorphous state of bifendate in bifendate-silica SD was revealed in X-RD and DSC when the ratios of bifendate and silica were 1:15 and 1:19, respectively. *In vitro* dissolution rate was significantly improved with cumulative release of 67% within 20 min relative to 8% for the physical mixture of bifendate and silica, and which was also higher than the commercial dropping pill of 52%. After storage at 75% relative humidity (RH) for 10 d, no recrystallization was found and reduced dissolution rate was obtained due to the absorption of moisture. In pharmacokinetic study,  $C_{max}$  and  $AUC_{0-t}$  for bifendate-silica SD were 153.1 ng/ml and 979.8 ng h/ml, respectively.  $AUC_{0-t}$  of bifendate-silica SDs was ~1.6-fold higher than that of the commercial dropping pills. These results suggest that adsorbing bifendate onto porous silica via ScCO<sub>2</sub> technique could be a feasible method to enhance oral bioavailability together with a higher dissolution rate.

<http://www.tandfonline.com/doi/abs/10.3109/03639045.2015.1071833#.VcDcwvIvHbc>

## 274. Determination Of A Selection Of Synthetic Cannabinoids And Metabolites In Urine By UHPSFC-MS/MS And By UHPLC-MS/MS

2015 - Drug Testing and Analysis

Keywords: Norwegian Institute of Public Health, synthetic cannabinoids, metabolites in urine, forensic toxicology

#### Abstract

Two different analytical techniques, ultra-high performance supercritical fluid chromatography-tandem mass spectrometry (UHPSFC-MS/MS) and reversed phase ultra-high performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS), were used for the determination of two synthetic cannabinoids and eleven metabolites in urine; AM-2201 N-4-OH-pentyl, AM-2233, JWH-018 N-5-OH-pentyl, JWH-018 N-pentanoic acid, JWH-073 N-4-OH-butyl, JWH-073 N-butanoic acid, JWH-122 N-5-OH-pentyl, MAM-2201, MAM-2201 N-4-OH-pentyl, RCS-4 N-5-OH-pentyl, UR-144 degradant N-pentanoic acid, UR-144 N-4-OH-pentyl, and UR-144 N-pentanoic acid. Sample preparation included a liquid-liquid extraction after deconjugation with  $\beta$ -glucuronidase. The UHPSFC-MS/MS method used an Acquity UPC<sup>2</sup><sup>TM</sup> BEH column with a mobile phase consisting of CO<sub>2</sub> and 0.3% ammonia in methanol, while the UHPLC-MS/MS method used an Acquity UPLC® BEH C<sub>18</sub> column with a mobile phase consisting of 5 mM ammonium formate (pH 10.2) and methanol. MS/MS detection was performed with positive electrospray ionization and two multiple reaction monitoring transitions. Deuterated internal standards were used for six of the compounds. Limits of quantification (LOQs) were between 0.04 and 0.4  $\mu$ g/L. Between-day relative standard deviations at concentrations  $\geq$  LOQ were  $\leq$ 20%, with biases within  $\pm$ 19%. Recoveries ranged from 40 to 90%. Corrected matrix effects were within 100  $\pm$  10%, except for MAM-2201 with UHPSFC-MS/MS, and for UR-144 N-pentanoic acid and MAM-2201 N-4-OH-pentyl with UHPLC-MS/MS. Elution order obtained by UHPSFC-MS/MS was almost opposite to that obtained by UHPLC-MS/MS, making this instrument setup an interesting combination for screening and confirmation analyses in forensic cases. The UHPLC-MS/MS method has, since August 2014, been successfully used for confirmation of synthetic cannabinoids in urine samples revealing a positive immunoassay screening result.

<http://dx.doi.org/10.1002/dta.1844>

## 275. Evaluation Of Ultrahigh-Performance Supercritical Fluid Chromatography–Mass Spectrometry As An Alternative Approach For The Analysis Of Fatty Acid Methyl Esters In Aviation Turbine Fuel

2015 - Energy Fuels

### Abstract

The current international reference method (IP585/10) for the determination of rapeseed methyl ester (RME) in jet fuel [aviation turbine fuel (AVTUR), current specifications U.S. ASTM 1655 and DEF STAN 91-91] uses gas chromatography–mass spectrometry (GC–MS). The fuel matrix requirements demand that a slow temperature gradient method (50 min) must be used. The fuel matrix also limits the application of this approach in relation to the detection and quantification of low-carbon-number fatty acid methyl esters (FAMES), e.g., coconut methyl ester (CME), C8–C14 from coconut oil, a feedstock for FAME production in the Pacific Rim region. A 3 min ultrahigh-performance supercritical fluid chromatography–mass spectrometry (UHPSFC–MS) method has been developed for the analysis of RME and CME. This is compared to the existing reference method and an adapted form of the reference GC–MS method for the detection of low-carbon-number FAMES. The UHPSFC–MS method is approximately 20 times faster than the ASTM reference method, affords a comparable linear dynamic range for the detection of total FAME content up to 100 ppm with a linear correlation ( $R^2 > 0.99$  for RME), and is more suitable for the detection and quantification of lower chain length methyl esters.

<http://dx.doi.org/10.1021/acs.energyfuels.5b00103>

## 276. Analytical Advances In Pharmaceutical Impurity Profiling

2015 - European Journal of Pharmaceutical Sciences

Keywords: H. Lundbeck A/S, GlaxoSmithKline, pharmaceutical

### Abstract

Impurities will be present in all drug substances and drug products, i.e. nothing is 100% pure if one looks in enough depth. The current regulatory guidance on impurities accepts this, and for drug products with a dose of less than 2 g/day identification of impurities is set at 0.1% levels and above (ICH Q3B(R2), 2006). For some impurities, this is a simple undertaking as generally available analytical techniques can address the prevailing analytical challenges; whereas, for others this may be much more challenging requiring more sophisticated analytical approaches. The present review provides an insight into current development of analytical techniques to investigate and quantify impurities in drug substances and drug products providing discussion of progress particular within the field of chromatography to ensure separation of and quantification of those related impurities. Further, a section is devoted to the identification of classical impurities, but in addition, inorganic (metal residues) and solid state impurities are also discussed. Risk control strategies for pharmaceutical impurities aligned with several of the ICH guidelines, are also discussed.

[doi:10.1016/j.ejps.2015.12.007](https://doi.org/10.1016/j.ejps.2015.12.007)

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## 277. Stereoselective Determination Of Tebuconazole In Water And Zebrafish By Supercritical Fluid Chromatography Tandem Mass Spectrometry

2015 - Journal of Agricultural and Food Chemistry

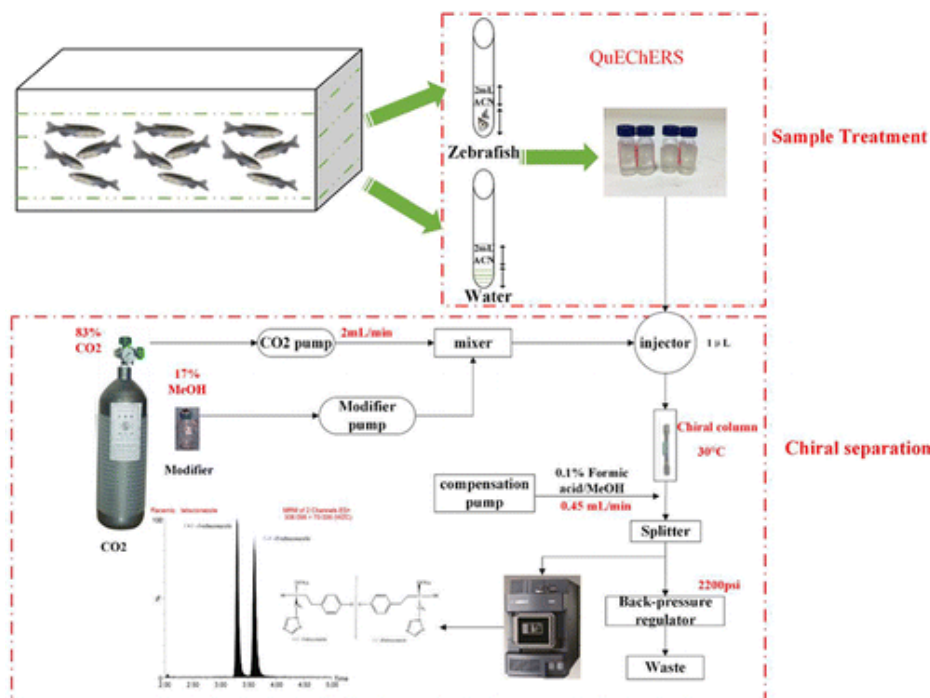
Keywords: Shenyang Agricultural University, tebuconazole enantiomers, zebrafish, food

### Abstract

A simple and sensitive method for the enantioselective determination of tebuconazole enantiomers in water and zebrafish has been established using supercritical fluid chromatography (SFC)-MS/MS. The effects of the chiral stationary phases, mobile phase, auto back pressure regulator (ABPR) pressure, column temperature, flow rate of the mobile phase, and compensation pump solvent were evaluated. Finally, the optimal SFC-MS/MS working conditions were determined to include a CO<sub>2</sub>/MeOH mobile phase (87:13, v/v), 2.0 mL/min flow rate, 2200 psi ABPR, and 30 °C column temperature using a Chiralpak IA-3 chiral column under electrospray ionization positive mode. The modified QuEChERS method was applied to water and zebrafish samples. The mean recoveries for the tebuconazole enantiomers were 79.8–108.4% with RSDs ≤ 7.0% in both

matrices. The LOQs ranged from 0.24 to 1.20 µg/kg. The developed analytical method was further validated by application to the analysis of authentic samples.

<http://dx.doi.org/10.1021/acs.jafc.5b02450>



## 278. A Rapid Method For The Separation Of Vitamin D And Its Metabolites By Ultra-High Performance Supercritical Fluid Chromatography–Mass Spectrometry

2015 - Journal of Chromatography A

Keywords: Lund University, vitamin\_D2, vitamin\_D3, plasma, health science

### Abstract

In this study, a new supercritical fluid chromatography-mass spectrometry (SFC-MS) method has been developed for the separation of nine vitamin D metabolites within less than eight minutes. This is the first study of analysis of vitamin D and its metabolites carried out by SFC-MS. Six columns of orthogonal selectivity were examined, and the best separation was obtained by using a 1-aminoanthracene (1-AA) column. The number and the position of hydroxyl groups in the structure of the studied compounds as well as the number of unsaturated bonds determine the physicochemical properties and, thus the separation of vitamin D metabolites that is achieved on this column. All D2 and the D3 forms were baseline separated with resolution values >1.5. The effects of pressure, temperature, flow rate and different gradient modes were studied. Electrospray ionization (ESI) and atmospheric pressure chemical ionization (APCI) were compared in positive mode, both by direct infusion and after SFC separation. The results showed that the sensitivity in APCI(+) was higher than in ESI(+) using direct infusion. In contrast, the sensitivity in APCI(+) was 6-fold lower than in ESI(+) after SFC separation. The SFC-MS method was validated between 10 and 500ng/mL for all analytes with coefficient of determination  $(R^2) \geq 0.999$  for all calibration curves. The limits of detection (LOD) were found to range between 0.39 and 5.98ng/mL for 24,25-dihydroxyvitamin D3 (24,25(OH)2D3) and 1-hydroxyvitamin D2 (1OHD2), respectively. To show its potential, the method was applied to human plasma samples from healthy individuals. Vitamin D3 (D3), 25-hydroxyvitamin D3 (25OHD3) and 24,25(OH)2D3 were determined in plasma samples and the concentrations were  $6.6 \pm 3.0$ ng/mL,  $23.8 \pm 9.2$ ng/mL and  $5.4 \pm 2.7$ ng/mL, respectively.

[doi:10.1016/j.chroma.2016.02.043](https://doi.org/10.1016/j.chroma.2016.02.043)

## 279. Application Of Ultra-High Performance Supercritical Fluid Chromatography For The Determination Of Carotenoids In Dietary Supplements

2015 - Journal of Chromatography A

Keywords: Beijing Center for Disease Control and Prevention, food

### Abstract

A quick and simple ultra-high performance supercritical fluid chromatography-photodiode array detector method was developed and validated for the simultaneous determination of 9 carotenoids in dietary supplements. The influences of stationary phase, co-solvent, pressure, temperature and flow rate on the separation of carotenoids were evaluated. The separation of the carotenoids was carried out using an Acquity UPC<sup>2</sup> HSS C18 SB column (150 mm × 3.0 mm, 1.8 μm) by gradient elution with carbon dioxide and a 1:2 (v:v) methanol/ethanol mixture. The column temperature was set to 35 °C and the backpressure was 15.2 MPa. Under these conditions, 9 carotenoids and the internal standard, β-apo-8'-carotenal, were successfully separated within 10 min. The correlation coefficients ( $R^2$ ) of the calibration curves were all above 0.997, the limits of detection for the 9 carotenoids were in the range of 0.33–1.08 μg/mL, and the limits of quantification were in the range of 1.09–3.58 μg/mL. The mean recoveries were from 93.4% to 109.5% at different spiking levels, and the relative standard deviations were between 0.8% and 6.0%. This method was successfully applied to the determination of 9 carotenoids in commercial dietary supplements. <http://dx.doi.org/10.1016/j.chroma.2015.11.029>

## 280. Evaluation Of Scale-Up From Analytical To Preparative Supercritical Fluid Chromatography

2015 - Journal of Chromatography A

Keywords: Karlstadt University, AstraZeneca, SFC; Chiral separation; Transfer of method; Scale-up; Operational parameters; Design of experiments

### Abstract

An approach for reliable transfer from analytical to preparative scale supercritical fluid chromatography was evaluated. Here, we accounted for the conditions inside the columns as well as to the fact that most analytical instruments are volume-controlled while most preparative scale units are mass-controlled. The latter is a particular problem when performing pilot scale experiments and optimizations prior to scaling up to production scale. This was solved by measuring the mass flow, the pressure and the temperature on the analytical unit using external sensors. Thereafter, it was revealed with a design of experiments approach that the methanol fraction and the pressure are the two most important parameters to control for preserved retention throughout the scale-up; for preserved selectivity the temperature was most important in this particular system. Using this approach, the resulting chromatograms from the preparative unit agreed well with those from the analytical unit while keeping the same column length and particles size. A brief investigation on how the solute elution volume varies with the volumetric flow rate revealed a complex dependency on pressure, density and apparent methanol content. Since the methanol content is a parameter of great importance to control during the scale up, we must be careful when changing operational and column design conditions which generates deviations in pressure, density and methanol content between different columns. <http://dx.doi.org/10.1016/j.chroma.2015.11.001>

## 281. Fast Separation Of Selected Cathinones And Phenylethylamines By Supercritical Fluid Chromatography

2015 - Journal of Chromatography A

Keywords: Palacky University in Olomouc, University of Texas, Institute of Microbiology, v.v.i., designer drugs, BEH silica, BEH 2-ethylpyridine, CSH Fluoro-Phenyl, and HSS C18SB, Cathinones; Phenylethylamines; New designer drugs; Supercritical fluid chromatography; Electrospray ionization mass spectrometry

### Abstract

The chromatographic behaviour of eleven synthetic cathinones and four phenylethylamines under supercritical/subcritical fluid conditions was investigated. Four stationary phases with sub-2  $\mu\text{m}$  particles (Waters Acquity UPC<sup>2</sup> BEH silica, BEH 2-ethylpyridine, CSH Fluoro-Phenyl, and HSS C18SB) were evaluated in terms of isomer resolution, chromatographic peak shape, and analysis time. Methanol, water, formic acid, ammonium hydroxide, ammonium acetate, and ammonium formate were mixed with carbon dioxide to test their influence on analyte retention and peak shapes. Methanol and ammonium cations were essential for successful separations. Efficient separations of four isomeric pairs ( $R > 1$ ), and most of the remaining analytes, were achieved in less than 3.3 min on BEH and Fluoro-Phenyl columns with gradient of methanolic ammonium hydroxide in  $\text{CO}_2$ . Drugs were detected by positive electrospray ionization–triple quadrupole mass spectrometry in selected reaction monitoring mode. Added detection specificity and faster separation of isomers on the BEH column using a steep gradient and high flow rate reduced analysis time of the mixture of 15 drugs to 1.6 min.

<http://dx.doi.org/10.1016/j.chroma.2015.10.061>

## 282. Method Development Approaches In Supercritical Fluid Chromatography Applied To The Analysis Of Cosmetics

2015 - Journal of Chromatography A

Keywords: U. Orleans, Groupe Yves Rocher, column screening, stationary phase, sunscreens, eye liner, eye serum, glyceryl caprylate, caffeine, UV filters, chemical materials

### Abstract

Analyses of complex samples of cosmetics, such as creams or lotions, are generally achieved by HPLC. These analyses are often multistep gradients, due to the presence of compounds with a large range of polarity. For instance, the bioactive compounds may be polar, while the matrix contains lipid components that are rather non-polar, thus cosmetic formulations are usually oil-water emulsions. Supercritical fluid chromatography (SFC) uses mobile phases composed of carbon dioxide and organic co-solvents, allowing for good solubility of both the active compounds and the matrix excipients. Moreover, the classical and well-known properties of these mobile phases yield fast analyses and ensure rapid method development. However, due to the large number of stationary phases available for SFC and to the varied additional parameters acting both on retention and separation factors (co-solvent nature and percentage, temperature, backpressure, flow rate, column dimensions and particle size), a simplified approach can be followed to ensure a fast method development. First, suited stationary phases should be carefully selected for an initial screening, and then the other operating parameters can be limited to the co-solvent nature and percentage, maintaining the oven temperature and back-pressure constant. To describe simple method development guidelines in SFC, three sample applications are discussed in this paper: UV-filters (sunscreens) in sunscreen cream, glyceryl caprylate in eye liner and caffeine in eye serum. Firstly, five stationary phases (ACQUITY UPC(2)) are screened with isocratic elution conditions (10% methanol in carbon dioxide). Complementary of the stationary phases is assessed based on our spider diagram classification which compares a large number of stationary phases based on five molecular interactions. Secondly, the one or two best stationary phases are retained for further optimization of mobile phase composition, with isocratic elution conditions or, when necessary, two-step gradient elution. The developed methods were then applied to real cosmetic samples to assess the method specificity, with regards to matrix interferences, and calibration curves were plotted to evaluate quantification. Besides, depending on the matrix and on the studied compounds, the importance of the detector type, UV or ELSD (evaporative light-scattering detection), and of the particle size of the stationary phase is discussed.

<http://dx.doi.org/10.1016/j.chroma.2015.10.053>

## 283. Application Of Cinchona Alkaloid-Based Zwitterionic Chiral Stationary Phases In Supercritical Fluid Chromatography For The Enantioseparation Of N(Alpha)-Protected Proteinogenic Amino Acids

2015 - Journal of Chromatography A

Keywords: University of Szeged, University of Vienna, enantiomer, Zwitterionic chiral stationary phases; Na-Fmoc-protected proteinogenic amino acids; Temperature effect, water

### Abstract



Stereoselective supercritical fluid chromatographic separations of the enantiomers of a large set of Na-Fmoc proteinogenic amino acids were carried out on the recently developed Cinchona alkaloid-based zwitterionic chiral stationary phases Chiralpak ZWIX(+)<sup>TM</sup> and ZWIX(-)<sup>TM</sup> with protic solvents as co-solvents. The effects of the mobile phase composition, the natures and concentrations of the acid or base additives, the co- and counter-ions and temperature on the separations were investigated. The retention time in most cases slightly increased, while the separation factor decreased with increasing temperature. The changes in standard enthalpy,  $\Delta(\Delta H^\circ)$ , entropy,  $\Delta(\Delta S^\circ)$ , and free energy,  $\Delta(\Delta G^\circ)$ , were calculated from the linear van't Hoff plots derived from the  $\ln a$  vs  $1/T$  curves in the studied temperature range (20-60°C). The values of the thermodynamic parameters depended on the natures of the selectors and the structures of the analytes. On both ZWIX(+)<sup>TM</sup> and ZWIX(-)<sup>TM</sup> columns, enthalpically-driven separations were observed. The elution sequence was determined in all cases and was observed to be opposite on ZWIX(+)<sup>TM</sup> and ZWIX(-)<sup>TM</sup> which acted for the presented applications as chiral anion exchanger.  
<http://dx.doi.org/10.1016/j.chroma.2015.08.058>

## 284. An Attempt To Estimate Ionic Interactions With Phenyl And Pentafluorophenyl Stationary Phases In Supercritical Fluid Chromatography

2015 - Journal of Chromatography A

Keywords: University of Orleans, method development, solvation parameter model, column classifications, separations science

### Abstract

In several metabolomic studies, it has already been demonstrated that capillary electrophoresis hyphenated to mass spectrometry (CE-MS) can detect an important group of highly polar and ionized metabolites that are overseen by techniques such as NMR, LC-MS and GC-MS, providing complementary information. In this work, we present a strategy for anionic metabolite profiling by CE-MS using a cationic capillary coating. The polymer, abbreviated as PTH, is composed of a poly-(N,N,N',N'-tetraethyldiethylenetriamine, N-(2-hydroxypropyl) methacrylamide, TEDETAMA-co-HPMA (50:50) copolymer. A CE-MS method based on PTH-coating was optimized for the analysis of a group of 16 standard anionic metabolites. Separation was achieved within 12min, with high separation efficiency (up to 92,000 theoretical plates per meter), and good repeatability, namely, relative standard deviation values for migration times and peak areas were below 0.2 and 2.1%, respectively. The optimized method allowed the detection of 87 metabolites in orange juice and 142 metabolites in red wine, demonstrating the good possibilities of this strategy for metabolomic applications.

<http://dx.doi.org/10.1016/j.chroma.2015.08.009>

## 285. Performance Of The Same Column In Supercritical Fluid Chromatography And In Liquid Chromatography

2015 - Journal of Chromatography A

Keywords: University of Pecs, mass transfer, stochastic model, moment analysis, separation science

### Abstract

We have studied the chromatographic behavior of the homologous series of alkylbenzenes (ranging from octylbenzene to octadecylbenzene) on the same C18 reversed-phase column in supercritical fluid chromatography (SFC) and reversed phase liquid chromatography (RPLC) at various experimental conditions, such as different eluent compositions, flow-rates, and mobile phase densities. The first and the second moments of the peaks were used to estimate the overall mass-transfer processes in both chromatographic modes using the stochastic model of chromatography. The results confirm that in SFC - as the density of the mobile phase is influenced by the flow-rate - there is a broader variation of mass-transfer properties than in liquid chromatography. As expected, the optimum mobile phase velocity is higher in SFC, but there is no real difference in the minimum value of plate height, i.e. in the optimum efficiency

<http://dx.doi.org/10.1016/j.chroma.2015.07.056>



## 286. Sum-Of-Ranking-Differences To Rank Stationary Phases Used In Packed Column Supercritical Fluid Chromatography

2015 - Journal of Chromatography A

Keywords: University of Orleans, University of Prague, Hungarian Academy of Sciences, column classification, method development, stationary phases, selectivity, separation science

### Abstract

The identification of a suitable stationary phase in supercritical fluid chromatography (SFC) is a major source of difficulty for those with little experience in this technique. Several protocols have been suggested for column classification in high-performance liquid chromatography (HPLC), gas chromatography (GC), and SFC. However, none of the proposed classification schemes received general acceptance. A fair way to compare columns was proposed with the sum of ranking differences (SRD). In this project, we used the retention data obtained for 86 test compounds with varied polarity and structure, analyzed on 71 different stationary phases encompassing the full range in polarity of commercial packed columns currently available to the SFC chromatographer, with a single set of mobile phase and operating conditions (carbon dioxide-methanol mobile phase, 25°C, 150bar outlet pressure, 3ml/min). First, a reference column was selected and the 70 remaining columns were ranked based on this reference column and the retention data obtained on the 86 analytes. As these analytes previously served for the calculation of linear solvation energy relationships (LSER) on the 71 columns, SRD ranks were compared to LSER methodology. Finally, an external comparison based on the analysis of 10 other analytes (UV filters) related the observed selectivity to SRD ranking. Comparison of elution orders of the UV filters to the SRD rankings is highly supportive of the adequacy of SRD methodology to select similar and dissimilar columns.

<http://dx.doi.org/10.1016/j.chroma.2015.07.071>

## 287. Response Surface Methodology For The Enantioseparation Of Dinotefuran And Its Chiral Metabolite In Bee Products And Environmental Sample By Supercritical Fluid Chromatography/Tandem Mass Spectrometry

2015 - Journal of Chromatography A

Keywords: Institute of Plant Protection, Chinese Academy of Agricultural Sciences, Institute for the Control of Agrochemicals, Ministry of Agriculture, chiral separation, enantiomers, environmental

### Abstract

Tracing the enantiomers of dinotefuran and its metabolite in bee products and relevant environmental matrices is vital because of the high toxicity of their racemates to bees. In this study, a statistical optimization strategy using three-dimensional response surface methodology for the enantioseparation of dinotefuran and its metabolite UF was developed by a novel supercritical fluid chromatography/tandem mass spectrometry (SFC-MS/MS) technique. After direct evaluation of the chromatographic variables - co-solvent content, mobile phase flow rate, automated backpressure regulator pressure (ABPR), and column temperature - involved in the separation mechanism and assessment of the interactions among these variables, the optimal SFC-MS/MS working conditions were selected as a CO<sub>2</sub>/2% formic acid-methanol mobile phase, 1.9mL/min flow rate, 2009.8psi ABPR, and 26.0°C column temperature using an amylose tris-(3,5-dimethylphenyl)carbamate chiral stationary phase under electrospray ionization positive mode. Baseline resolution, favorable retention, and high sensitivity of the two pairs of enantiomers were achieved in pollen, honey, water, and soil matrices within 4.5min. Additionally, the parameters affecting the dispersive solid-phase extraction procedure, such as the type and content of extractant or purification sorbents, were systematically screened to obtain better extraction yields of the enantiomers. Mean recoveries were between 78.3% and 100.2% with relative standard deviations lower than 8.0% in all matrices. The limits of quantification ranged from 1.0µg/kg to 12.5µg/kg for the dinotefuran and UF enantiomers. Furthermore, the developed method was effectively applied to authentic samples from a market, an irrigation canal, and a trial field, and the enantioselective dissipation of dinotefuran and UF in soil was demonstrated.

<http://dx.doi.org/10.1016/j.chroma.2015.07.067>

## 288. Rapid Chiral Separation Of Atenolol, Metoprolol, Propranolol, And The Zwitterionic Metoprolol Acid Using Supercritical Fluid Chromatography-Tandem Mass Spectrometry – Application To Wetland Microcosms

2015 - Journal of Chromatography A

Keywords: Uppsala University, National Veterinary Institute, Medical Products Agency, University of California – Berkeley, enantiomeric separation, chiralpak, separation science

### Abstract

A method for enantiomeric separation of the three  $\beta$ -blocking agents atenolol, metoprolol, propranolol and the zwitterionic metoprolol acid, a major metabolite of both metoprolol and in environmental matrices also atenolol, has been developed. By use of supercritical fluid chromatography and the polysaccharide-based Chiralpak(®) IB-3, all four compounds were simultaneously enantiomerically separated ( $R_s > 1.5$ ) within 8min. Detection was performed using tandem mass spectrometry, and to avoid isobaric interference between the co-eluting metoprolol and metoprolol acid, the achiral column Acquity(®) UPC(2) BEH 2-EP was attached ahead of to the chiral column. Carbon dioxide with 18% methanol containing 0.5% (v/v) of the additives trifluoroacetic acid and ammonia in a 2:1 molar ratio were used as mobile phase. A post column make-up flow (0.3mL/min) of methanol containing 0.1% (v/v) formic acid was used to enhance the positive electrospray ionization. Detection was carried out using a triple quadrupole mass spectrometer operating in the selected reaction monitoring mode, using one transition per analyte and internal standard. The method was successfully applied for monitoring the enantiomeric fraction change over time in a laboratory scale wetland degradation study. It showed good precision, recovery, sensitivity and low effect of the sample matrix.

<http://dx.doi.org/10.1016/j.chroma.2015.07.075>

## 289. Development Of An Achiral Supercritical Fluid Chromatography Method With Ultraviolet Absorbance And Mass Spectrometry Detection For Impurity Profiling Of Drug Candidates. Part 2: Selection Of An Orthogonal Set Of Stationary Phases

2015 - Journal of Chromatography A

Keywords: University of Orleans, Servier Research Institute, column selection, method development, column screening, Nucleoshell, drugs, pharmaceuticals, acquity hsss, column rankings

### Abstract

Impurity profiling of organic products that are synthesized as possible drug candidates requires complementary analytical methods to ensure that all impurities are identified. Supercritical fluid chromatography (SFC) is a very useful tool to achieve this objective, as an adequate selection of stationary phases can provide orthogonal separations so as to maximize the chances to see all impurities. In this series of papers, we have developed a method for achiral SFC-MS profiling of drug candidates, based on a selection of 160 analytes issued from Servier Research Laboratories. In the first part of this study, focusing on mobile phase selection, a gradient elution with carbon dioxide and methanol comprising 2% water and 20mM ammonium acetate proved to be the best in terms of chromatographic performance, while also providing good MS response [1]. The objective of this second part was the selection of an orthogonal set of ultra-high performance stationary phases, that was carried out in two steps. Firstly, a reduced set of analytes (20) was used to screen 23 columns. The columns selected were all 1.7-2.5 $\mu$ m fully porous or 2.6-2.7 $\mu$ m superficially porous particles, with a variety of stationary phase chemistries. Derringer desirability functions were used to rank the columns according to retention window, column efficiency evaluated with peak width of selected analytes, and the proportion of analytes successfully eluted with good peak shapes. The columns providing the worst performances were thus eliminated and a shorter selection of columns (11) was obtained. Secondly, based on 160 tested analytes, the 11 columns were ranked again. The retention data obtained on these columns were then compared to define a reduced set of the best columns providing the greatest orthogonality, to maximize the chances to see all impurities within a limited number of runs. Two high-performance columns were thus selected: ACQUITY UPC<sup>2</sup> HSS C18 SB and Nucleoshell HILIC.

<http://dx.doi.org/10.1016/j.chroma.2015.07.035>

## 290. Development Of An Achiral Supercritical Fluid Chromatography Method With Ultraviolet Absorbance And Mass Spectrometry Detection For Impurity Profiling Of Drug Candidates. Part 1: Optimization Of Mobile Phase Composition

2015 - Journal of Chromatography A

Keywords: University of Orleans, Servier Research Institute, column selection, method development, column screening, Nucleoshell, drugs, pharmaceuticals, acquity hsss, column rankings

### Abstract

Supercritical fluid chromatography (SFC) is a very useful tool in the purpose of impurity profiling of drug candidates, as an adequate selection of stationary phases can provide orthogonal separations so as to maximize the chances to see all impurities. The purpose of the present work is to develop a method for chemical purity assessment. The first part, presented here, focuses on mobile phase selection to ensure adequate elution and detection of drug-like molecules, while the second part focuses on stationary phase selection for optimal separation and orthogonality.

The use of additives in the carbon dioxide – solvent mobile phase in SFC is now commonplace, and enables in particular to increase the number of eluted compounds and to improve peak shapes. The objective of this first part was to test different additives (acids, bases, salts and water) for their chromatographic performance assessed in gradient elution with a diode-array detector, but also for the mass responses obtained with a single-quadrupole mass detector, equipped with an electrospray ionization source (Waters ACQUITY QDa).

In this project, we used a selection of one hundred and sixty compounds issued from Servier Research Laboratories to screen a set of columns and additives in SFC with a Waters ACQUITY UPC2 system. The selected columns were all high-performance columns (1.7–1.8  $\mu\text{m}$  with totally porous particles or 2.6–2.7  $\mu\text{m}$  with superficially porous particles) with a variety of stationary phase chemistries.

Initially, eight additives dissolved in the methanol co-solvent were tested on a UPC2 ACQUITY UPC2 HSS C18 SB column. A Derringer desirability function was used to classify the additives according to selected criteria: elution capability, peak shapes, UV baseline drift, and UV and mass responses (signal-to-noise ratios). Following these tests, the two best additives (ammonium acetate and ammonium hydroxide) were tested on a larger number of columns (10) where the two additives appeared to provide very comparable overall scores. However, ammonium acetate was selected for slightly better chromatographic quality.

In a second step, we investigated the effects of ammonium acetate concentration (between 0 and 25 mM in the methanol co-solvent) on retention and peak efficiency. Two types of silica supports were tested by working with ACQUITY UPC2 HSS C18 SB and BEH columns. 20 mM ammonium acetate in methanol with 2% water was finally selected as the best co-solvent composition.

<http://dx.doi.org/10.1016/j.chroma.2015.07.037>

## 291. Potential And Limitations Of On-Line Comprehensive Reversed Phase Liquid Chromatography $\times$ Supercritical Fluid Chromatography For The Separation Of Neutral Compounds: An Approach To Separate An Aqueous Extract Of Bio-Oil

2015 - Journal of Chromatography A

Keywords: University of Lyons, IFP Energies Nouvelles, Waters SAS, bio oil, biomass, 2d chromatography, ACQUITY BEH, Hpercarb, chemical materials

### Abstract

On-line comprehensive Reversed Phase Liquid Chromatography  $\times$  Supercritical Fluid Chromatography (RPLC $\times$ SFC) was investigated for the separation of complex samples of neutral compounds. The presented approach aimed at overcoming the constraints involved by such a coupling. The search for suitable conditions (stationary phases, injection solvent, injection volume, design of interface) are discussed with a view of ensuring a good transfer of the compounds between both dimensions, thereby allowing high effective peak capacity in the second dimension. Instrumental aspects that are of prime importance in on-line 2D separations, were also tackled (dwell volume, extra column volume and detection). After extensive preliminary studies, an on-

line RPLCxSFC separation of a bio-oil aqueous extract was carried out and compared to an on-line RPLCxRPLC separation of the same sample in terms of orthogonality, peak capacity and sensitivity. Both separations were achieved in 100 min. For this sample and in these optimized conditions, it is shown that RPLCxSFC (with Hypercarb and Acquity BEH-2EP as stationary phases in first and second dimension respectively) can generate a slightly higher peak capacity than RPLCxRPLC (with Hypercarb and Acquity CSH phenyl-hexyl as stationary phases in first and second dimension respectively) (620 vs 560). Such a result is essentially due to the high degree of orthogonality between RPLC and SFC which may balance for lesser peak efficiency obtained with SFC as second dimension. Finally, even though current limitations in SFC instrumentation (i.e. large extra-column volume, large dwell volume, no ultra-high pressure) can be critical at the moment for on-line 2D-separations, RPLCxSFC appears to be a promising alternative to RPLCxRPLC for the separation of complex samples of neutral compounds.  
<http://dx.doi.org/10.1016/j.chroma.2015.05.005>

## 292. Use Of Isopycnic Plots To Understand The Role Of Density In SFC, Which Is Now A Misnomer. In This Report We Intentionally Refrained From Using The Expansion Anywhere To Avoid Any Technical Inaccuracy. - I. Effect Of Pressure Variation On Retention Factors

2015 - Journal of Chromatography A

Keywords: Waters, pressure dependence, retention factor, separation science

### Abstract

This paper aims to demonstrate the effect of pressure variations in modifying analyte retention behavior in SFC. There is a general understanding that in SFC increasing pressure decreases the retention factor ( $k'$ ), and vice versa. What is not clearly discussed or explained in any recent literature is that these variations can be very different at different operating pressures, temperatures and modifier concentrations. It is important to have a clearer understanding on these variabilities during method development and results analysis. In this paper the nature of  $k'$  variation with pressure, at different temperatures and modifier concentrations, will be explained with the help of isopycnic plots of CO<sub>2</sub> and CO<sub>2</sub>+methanol mixtures.

<http://dx.doi.org/10.1016/j.chroma.2015.05.052>

## 293. A Closer Study Of Peak Distortions In Supercritical Fluid Chromatography As Generated By The Injection

2015 - Journal of Chromatography A

Keywords: Karlstadt University, University of Western Sydney, viscous fingering, solvent strength, modeling, tracer peak, adsorption isotherms, separation science

### Abstract

In SFC the sample cannot be dissolved in the mobile phase, so it is often dissolved in pure modifier, or another liquid, sometimes resulting in serious distortions of the eluted peak profiles already at moderately high injection volumes. It is suspected the reasons for these effects are solvent strength mismatch and/or viscosity mismatch. This study presents a systematic and fundamental investigation of the origin of these peak deformations due to the injection solvent effects in SFC, using both systematic experiments and numerical modeling. The first set of experiments proved that the injection volume and the elution strength of the sample solution had a major impact of the shapes of the eluted peaks. Secondly, the sample band elution profile was numerically modeled on a theoretical basis assuming both un-retained and retained co-solvent injection plugs, respectively. These calculations quantitatively confirmed our first set of experiments but also pointed out that there is also an additional significant effect. Third, viscous fingering experiments were performed using viscosity contrast conditions imitating those encountered in SFC. These experiments clearly proved that viscous fingering effects play a significant role. A new method for determination of adsorption isotherms of solvents was also developed, called the "Retention Time Peak Method" (RTPM). The RTPM was used for fast estimation of the adsorption isotherms of the modifier and required using only two experiments.

<http://dx.doi.org/10.1016/j.chroma.2015.04.059>

## 294. Chromatographic Resolution Of Atropisomers For Toxicity And Biotransformation Studies In Pharmaceutical Research

2015 - Journal of Chromatography A

Keywords: Pfizer, chiral chromatography, stability testing, energy barrier calculation, absolute configuration, human plasma, pharmaceutical

### Abstract

Atropisomerism can be a complex concept for those who have not encountered it before. This paper discusses the experiments for identification, isolation, thermal stability, toxicity and biotransformation of various species. The identified atropisomers are a series of rotational hindered biaryl, rotational hindered amide, ring flip, and macrocycles atropisomers identified using supercritical fluid chromatography (SFC) and high performance liquid chromatography (HPLC). These technologies offered the advantage of separating various atropoenantiomers, atropdiastereomers and mixed atropisomers with other forms of stereoisomers in both analytical and preparative scales. With ultra-performance convergence chromatography (UPC(2)), the detection of N-oxide atropisomer metabolites can be obtained at very low level thus enabling the observation of conversion in human plasma possible. As the resolution of atropisomers are related to the energy barriers on the rotational axis, a calculated computational protocol was developed to predict the formation. A threshold of 10kcal/mol was established for possible detection of the atropisomers' existence with chromatographic technologies at room temperature or above. The atropisomer with higher energy barrier (>20kcal/mol) were isolated via preparative chromatography and the isolates studied in vitro and in vivo for evaluation of their stability in human plasma. The detailed analytical method development to analyze the biotransformation of the atropisomers in human plasma are also discussed in this paper.

<http://dx.doi.org/10.1016/j.chroma.2015.04.023>

## 295. Exploring The Enantioseparation Of Amino-Naphthol Analogues By Supercritical Fluid Chromatography

2015 - Journal of Chromatography A

Keywords: University of Szeged, University of Orleans, Betti bases, chiral stationary phases, enantiomer separation, diethanolamine, immobilized polysaccharide, Chiralpak, separation science

### Abstract

The direct separation of the enantiomers of 1-( $\alpha$ -aminoarylmethyl)-2-naphthol, 1-( $\alpha$ -aminoalkyl)-2-naphthol, 2-( $\alpha$ -aminoarylmethyl)-1-naphthol analogues and 2-(1-amino-2-methylpropyl)-1-naphthol) was investigated in supercritical fluid chromatography. Five commercially available chiral stationary phases based on immobilized polysaccharide chiral selectors (Chiralpak IA, IB, IC, ID and IE) were evaluated. Chiralpak IB was by far the most efficient to achieve the separation of these racemates and was further selected for optimization of elution conditions. The effects of column temperature (varying between 5 and 45 °C) and co-solvent added to carbon dioxide (methanol, ethanol, isopropanol and dichloromethane) were investigated. A particular attention was paid to mobile-phase additives. Several of them, acids, bases or salts (namely water, formic acid, acetic acid, trifluoroacetic acid, diethylamine, diethanolamine, triethylamine, triethanolamine, dimethylethanolamine, ammonia and ammonium acetate), were tested in order to improve peak shapes while maintaining selectivity. With the help of other achiral naphthol derivatives, the additive effects were examined.

<http://dx.doi.org/10.1016/j.chroma.2015.01.084>

## 296. Search For Improved Fluorinated Stationary Phases For Separation Of Fluorine-Containing Pharmaceuticals From Their Desfluoro Analogs

2015 - Journal of Chromatography A

Keywords: Merck Research Laboratories, ES Industries Inc., desfluorinated impurities, fluorine containing drugs, pentafluorophenyl, fluororous stationary phases, Hypersil, Poroshell, pharmaceutical

### Abstract

Evaluation of several fluorine-containing stationary phases for the chromatographic separation of fluorine-containing pharmaceuticals from their corresponding desfluoro analogs revealed a number of perfluoroaryl and perfluoroalkyl stationary phases that afford good separations. These fluororous



stationary phases exhibit greater retention for the fluorine-containing compounds relative to the H-containing analogs, consistent with a fluorophilic retention mechanism. While both perfluoroalkyl and perfluoroaryl stationary phases afford adequate resolution, the perfluoroaryl columns generally exhibit superior separation factor ( $\alpha$ ) and peak efficiency ( $N$ ), resulting in faster baseline separations, with the Hypersil Gold PFP and Poroshell 120 PFP columns providing the best overall performance for the test group studied.

<http://dx.doi.org/10.1016/j.chroma.2014.12.025>

## 297. The Many Faces Of Packed Column Supercritical Fluid Chromatography – A Critical Review

2015 - Journal of Chromatography A

Keywords: University of Orleans, elution strength, retention mechanisms, achiral separations, chiral separations. separation science

### Abstract

Packed column sub- and supercritical fluid chromatography (SFC) is a versatile separation method: on the one hand the number of parameters acting on the quality of a separation is very large, and the effects of these parameters can be complex (and not always fully understood). But on another hand, due to numerous advantageous properties of CO<sub>2</sub>-based mobile phases, method development is a fast task. This paper is a review of the main features of SFC, focusing essentially on achiral separations. However, several fundamental aspects discussed here are also relevant to chiral SFC separations. This is not intended to be an extensive review, as the way to practice SFC has somewhat evolved with time. We rather wished to provide an expert opinion on the characteristics of the method, pointing at the sources of difficulty and displaying the wide possibilities that it offers. A large number of selected applications concerning several different areas are also presented.

<http://dx.doi.org/10.1016/j.chroma.2014.12.083>

## 298. Expanding The Potential Of Chiral Chromatography For High-Throughput Screening Of Large Compound Libraries By Means Of Sub-2 Mm Whelk-O 1 Stationary Phase In Supercritical Fluid Conditions

2015 - Journal of Chromatography A

Keywords: University of Rome, Novartis, University of Ferrara, University of Naples, Regis Technologies, chiral separations, enantioselective screening. separation science

### Abstract

With the aim of exploring the potential of ultra-fast chiral chromatography for high-throughput analysis, the new sub-2 micron Whelk-O 1 chiral stationary phase (CSP) has been employed in supercritical fluid conditions to screen 129 racemates, mainly of pharmaceutical interest. By using a 5-cm long column (0.46cm internal diameter), a single co-solvent (MeOH) and a 7-min gradient elution, 85% of acidic and neutral analytes considered in this work have been successfully resolved, with resolution ( $R_s$ ) larger than 2 in more than 65% of cases. Moreover, almost a half of basic samples that, for their own characteristics, are known to be difficult to separate on Whelk-O 1 CSP, have shown  $R_s$  greater than 0.3. The screening of the entire library could be accomplished in less than 24h (single run) with 63% of positive score. For well-resolved enantiomers ( $R_s$  roughly included between 1 and 3), we show that method transfer from gradient to isocratic conditions is straightforward. In many cases, isocratic ultra-fast separations (with analysis time smaller than 60s) have been achieved by simply employing, as isocratic mobile phase, the eluent composition at which the second enantiomer was eluted in gradient mode. By considering the extension and variety of the library in terms of chemico-physical and structural properties of compounds and numerosness, we believe that this work demonstrates the real potential of the technique for high-throughput enantioselective screening.

<http://dx.doi.org/10.1016/j.chroma.2015.01.042>

## 299. Possibilities Of Retention Modeling And Computer Assisted Method Development In SFC

2015 - Journal of Chromatography A



Keywords: Vrije Universiteit Brussels, University of Geneva, method development, retention modeling, retention prediction, separation science

**Abstract**

The multi-modal retention mechanism in supercritical fluid chromatography (SFC) results in a non-linear dependency of  $\log(k)$  on the fraction of organic solvent  $\phi$  and  $\log(\phi)$ . In the present study, the possibility of retention modeling for method development purposes in SFC was investigated, considering several non-linear isocratic relationships. Therefore, both isocratic and gradient runs were performed, involving different column chemistries and analytes possessing diverse physico-chemical properties. The isocratic retention data of these compounds could be described accurately using the non-linear retention models typically used in HILIC and reversed-phase LC. The interconversion between isocratic and gradient retention data was found to be less straightforward than in RPLC and HILIC because of pressure effects. The possibility of gradient predictions using gradient scouting runs to estimate the retention parameters was investigated as well, showing that predictions for other gradients with the same starting conditions were acceptable (always below 5%), whereas prediction errors for gradients with a different starting condition were found to be highly dependent on the compound. The second part of the study consisted of the gradient optimization of two pharmaceutical mixtures (one involving atorvastatin and four related impurities, and one involving a 16 components mixture including eight drugs and their main phase I metabolites). This could be done via individual retention modeling based on gradient scouting runs. The best linear gradient was found via a grid search and the best multi-segment gradient via the previously published one-segment-per-component search. The latter improved the resolution between the critical pairs for both mixtures, while still giving accurate prediction errors (using the same starting concentrations as the gradient scouting runs used to build the model). The optimized separations were found in less than 3 h and 8 h of analysis time (including equilibration times), respectively.

<http://dx.doi.org/10.1016/j.chroma.2014.12.077>

### 300. Study Of Ultrahigh Performance Supercritical Fluid Chromatography To Measure Free Fatty Acids Without Fatty Acid Ester Preparation

2015 - Journal of Chromatography B

Keywords: Virginia Tech, Waters, free fatty acids, evaporative light scattering, fish oil, fatty acid ester derivatization, food

**Abstract**

Most lipids are best characterized by their fatty acids which may differ in (a) chain length, (b) degree of unsaturation, (c) configuration and position of the double bonds, and (d) the presence of other functionalities. Thus, a fast, simple, and quantitative analytical technique to determine naturally occurring free fatty acids (FFA) in different samples is very important. Just as for saponified acylglycerols, the determination of FFA's has generally been carried out by high resolution gas chromatography (HRGC). The use of an open tubular capillary column coupled with a flame ionization or mass spectrometric detector provides for both high resolution and quantification of FFA's but only after conversion of all free fatty acids to fatty acid methyl esters (FAME) or pentafluorobenzyl esters. Unfortunately, volatilization of labile ester derivatives of mono- and poly-unsaturated FFA's can cause both thermal degradation and isomerization of the fatty acid during HRGC. The employment of a second generation instrument (here referred to as UltraHigh Performance Supercritical Fluid Chromatograph, UHPSFC) with high precision for modified flow and repeated back pressure adjustment in conjunction with sub-2 $\mu$ m various bonded silica particles (coupled with evaporative light scattering, ELSD, and mass spectrometric, MS, detection) for separation and detection of the following mixtures is described: (a) 31 free fatty acids, (b) isomeric FFA's, and (c) lipophilic materials in two real world fish oil samples. Limits of detection for FFA's via UHPSFC/MS and UHPSFC/ELSD versus detection of FAME's via HRGC/MS are quantitatively compared.

<http://dx.doi.org/10.1016/j.jchromb.2015.05.031>

### 301. Simultaneous Determination Of Seven Gestagens In Kidney Fats By Ultraperformance Convergence Chromatography Tandem Mass Spectrometry

Keywords: Huazhong Agricultural University, Wageningen University, gestagens, kidney fat, health science

**Abstract**

An ultra-performance convergence chromatography (UPC2) system coupled tandem mass spectrometry was successfully utilised to analyse chlormadinone acetate, delmadinone acetate, fluorogestone acetate, medroxyprogesterone acetate, megestrol acetate, melengestrol acetate, chlortestosterone acetate in bovine and porcine kidney fat. This novel approach obtained an improved resolution in comparison to previously reported chromatographic methods combined with MS detector in a shorter analytical time. All the acetylgestagen compounds were well separated on a ACQUITY UPC(2) HSS C18 column (3.0 × 100 mm, 1.7 μm) by applying methanol and carbon dioxide (2/98). The LOQ of delmadinone acetate, melengestrol acetate, medroxyprogesterone acetate and megestrol acetate are 0.5 μg/kg, fluorogestone acetate, chlormadinone acetate and chlortestosterone acetate 1.0 μg/kg. The recoveries of gestagens spiked in kidney fats at a concentration range of 0.5 to 4 μg/kg were above 86.1% with relative standard deviations (RSD) less than 13.1%. These rapid and reliable methods can be used to efficiently separate, characterize and quantify the residues of gestagens in kidney fats with advantages of shorter time, more sensitive and environmental friendly.  
<http://dx.doi.org/10.1016/j.jchromb.2015.02.034>

### 302. Ultrahigh Performance Supercritical Fluid Chromatography Of Lipophilic Compounds With Application To Synthetic And Commercial Biodiesel

2015 - Journal of Chromatography B

Keywords: Virginia Tech, Waters, tobacco seed oil, biodiesel, soybean oil, bound and free glycerols, chemical materials

**Abstract**

Ultrahigh performance supercritical fluid chromatography (UHPSFC) in combination with sub-2μm particles and either diode array ultraviolet (UV), evaporative light scattering, (ELSD), or mass spectrometric (MS) detection has been shown to be a valuable technique for the determination of acylglycerols in soybean, corn, sesame, and tobacco seed oils. Excellent resolution on an un-encapped single C18 column (3.0mm×150mm) with a mobile phase gradient of acetonitrile and carbon dioxide in as little as 10min served greatly as an improvement on first generation packed column SFC instrumentation. Unlike high resolution gas chromatography and high performance liquid chromatography with mass spectrometric detection, UHPSFC/MS was determined to be a superior analytical tool for both separation and detection of mono-, di-, and tri-acylglycerols as well as free glycerol itself in biodiesel without derivatization. Baseline separation of residual tri-, di-, and mono-acylglycerols alongside glycerol at 0.05% (w/w) was easily obtained employing packed column SFC. The new analytical methodology was applied to both commercial B100 biodiesel (i.e. fatty acid methyl esters) derived from vegetable oil and to an "in-house" synthetic biodiesel (i.e. fatty acid ethyl esters) derived from tobacco seed oil and ethanol both before and after purification via column chromatography on bare silica.  
<http://dx.doi.org/10.1016/j.jchromb.2014.12.012>

### 303. Supercritical Fluid Chromatography With Diode-Array Detection For Emerging Contaminants Determination In Water Samples. Method Validation And Estimation Of The Uncertainty

2015 - Journal of Chromatography Separation Techniques

Keywords: Universidad Colima, Viridis, Bond Elut, wastewater, pesticide, bactericide, pharmaceuticals

**Abstract**

Here we present a communication about the article "Salvatierra-Stamp VC, Ceballos-Magaña SG, Gonzalez J, Ibarra-Galván V, Muñoz-Valencia R (2015) Analytical method development for the determination of emerging contaminants in water using supercritical-fluid chromatography coupled with diode-array detection. Analytical and Bioanalytical Chemistry 407:4219-4226". In this paper, a selective, linear, accurate and precise supercritical-fluid chromatography coupled with diode-

array detection method was developed and validated for the determination of seven emerging contaminants: two pharmaceuticals, three endocrine disruptors, one bactericide and one pesticide. The compounds were base-line separated in around 10 minutes. Also, the method involved a sample treatment optimization by means of C18-OH solid phase extraction cartridges. The developed method was validated. In this sense, the correlation coefficient and recovery was higher than 0.9997 and 94%, respectively. Limit of detection and quantification was in the range of 0.10-1.59 µg/L and 0.31-4.83 µg/L, respectively. The measurement uncertainty was evaluated using the top-down model considering six sources of uncertainty. For all compounds, the uncertainty associated with accuracy and linearity regression was the main contribution to the combined uncertainty. Expanded uncertainties for each compound in method analysis were lower than 10.8%. Finally the method was successfully applied to environmental water samples.

<http://dx.doi.org/10.4172/2157-7064.100029>

### 304. Development Of A Sensitive And Rapid Method For Rifampicin Impurity Analysis Using Supercritical Fluid Chromatography

2015 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: China Pharmaceutical University, Ministry of Education, Anhui Institute for Food and Drug Control, impurities, pharmaceutical

#### Abstract

A novel simple, fast and efficient supercritical fluid chromatography (SFC) method was developed and compared with RPLC method for the separation and determination of impurities in rifampicin. The separation was performed using a packed diol column and a mobile phase B (modifier) consisting of methanol with 0.1% ammonium formate (w/v) and 2% water (v/v). Overall satisfactory resolutions and peak shapes for rifampicin quinone (RQ), rifampicin (RF), rifamycin SV (RSV), rifampicin N-oxide (RNO) and 3-formylrifamycinSV (3-FR) were obtained by optimization of the chromatography system. With gradient elution of mobile phase, all of the impurities and the active were separated within 4 min. Taking full advantage of features of SFC (such as particular selectivity, non-sloping baseline in gradient elution, and without injection solvent effects), the method was successfully used for determination of impurities in rifampicin, with more impurity peaks detected, better resolution achieved and much less analysis time needed compared with conventional reversed-phase liquid chromatography (RPLC) methods.

<http://dx.doi:10.1016/j.jpba.2015.06.012>

### 305. Method Development For Impurity Profiling In SFC: The Selection Of A Dissimilar Set Of Stationary Phases

2015 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: Vrije University, achiral SFC, chemometrics, column selection, orthogonal column selection, pharmaceutical

#### Abstract

Supercritical fluid chromatography (SFC) is drawing considerable interest as separation technique in the pharmaceutical industry. The technique is already well established in chiral separations both analytically and on a preparative scale. The use of SFC as a technique for drug impurity profiling is examined here. To define starting conditions in method development for drug impurity profiling, a set of dissimilar stationary phases is screened in parallel. The possibility to select a set of dissimilar columns using the retention factors (k-values) for a set of 64 drugs measured on 27 columns in SFC was examined. Experiments were carried out at a back-pressure of 150 bar and 25 °C with a mobile phase consisting of CO<sub>2</sub> and methanol with 0.1% isopropylamine (5-40% over 10 min) at a flow rate of 3 mL/min. These k-values were then used to calculate correlation coefficients on the one hand and to perform a principal component analysis on the other. The Kennard and Stone algorithm, besides dendrograms and correlation-coefficient colour maps were used to select a set of 6 dissimilar stationary phases. The stationary phase characterization results from this study were compared to those from previous studies found in the literature. Retention mechanisms for compounds possessing different properties were also evaluated. The dissimilarity

of the selected subset of 6 stationary phases was validated using mixtures of compounds with similar properties and structures, as one can expect in a drug impurity profile.

<http://dx.doi.org/10.1016/j.jpba.2014.12.043>

### 306. Supercritical Fluid Chromatography For The Separation Of Isoflavones

2015 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: University of Innsbruck, isoflavones, soy, red glover, kudzu, food

#### Abstract

The first protocol for the analysis of isoflavones by supercritical fluid chromatography is reported. Optimum results were obtained on an Acquity UPC(2) BEH 1.7  $\mu\text{m}$  column, using a solvent gradient of supercritical carbon dioxide and methanol (with phosphoric acid as additive) for elution. The method enables the baseline separation of nine isoflavones (aglyca and glycosides) in 8 min, and is suitable for their quantitative determination in dietary supplements containing soy (*Glycine max*), red glover (*Trifolium pratense*) and kudzu (*Pueraria lobata*). Method validation confirmed that the assay is selective, linear ( $R(2) \geq 0.9994$ ), accurate (recovery rates from 97.6 to 102.4%), as well as precise on the short- and long-term level (intra-day precision  $\leq 2.1\%$ ), and shows an on-column detection limit of 0.2 ng and below. This, together with an excellent performance shown in the analysis of real samples, indicates that SFC is well suited for the fast and accurate determination of isoflavones in complex matrices. Disadvantages compared to the established approaches were not observed, so that SFC has to be considered in this case as an (at least) equivalent analytical alternative.

<http://dx.doi.org/10.1016/j.jpba.2015.01.013>

### 307. Supercritical Fluid Chromatography In Pharmaceutical Analysis

2015 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: University of Geneva, Charles University, chiral separations, biofluids, impurity profiling, pharmaceuticals

#### Abstract

In the last few years, there has been a resurgence of supercritical fluid chromatography (SFC), which has been stimulated by the introduction of a new generation of instruments and columns from the main providers of chromatographic instrumentation, that are strongly committed to advancing the technology. The known limitations of SFC, such as weak UV sensitivity, limited reliability and poor quantitative performance have been mostly tackled with these advanced instruments. In addition, due to the obvious benefits of SFC in terms of kinetic performance and its complementarity to LC, advanced packed-column SFC represents today an additional strategy in the toolbox of the analytical scientist, which may be particularly interesting in pharmaceutical analysis. In the present review, the instrumentation and experimental conditions (i.e. stationary phase chemistry and dimensions, mobile phase nature, pressure and temperature) to perform "advanced SFC" are discussed. The applicability of SFC in pharmaceutical analysis, including the determination of drugs in formulations and biofluids is critically discussed.

<http://dx.doi.org/10.1016/j.jpba.2015.03.007>



### 308. Advances In The Analytical Methodologies: Profiling Steroids In Familiar Pathways-Challenging Dogmas

2015 - The Journal of Steroid Biochemistry and Molecular Biology

Keywords: University of Stellenbosch, 11 $\beta$ HSD, PCOS, LNCaP prostate cancer, H295R adrenal cell, steroid metabolites, steroidogenesis, health science

#### Abstract

The comprehensive evaluation of the adrenal steroidogenic pathway, given its complexity, requires methodology beyond the standard techniques currently employed. Advances in LC-MS/MS, coupled with in vitro cell models that produce all the steroid metabolites of the mineralo-, glucocorticoid and androgen arms, present a powerful approach for the comprehensive evaluation of adrenal steroidogenesis in response to compounds of interest including bioactives, drug treatments and endocrine disrupting compounds. UHPLC-MS/MS analysis of steroid panels in forskolin, angiotensin II and K<sup>+</sup> stimulated H295R cells provides a snapshot of their effect on intermediates and end products of adrenal steroidogenesis. The impact of full steroid panel evaluations by LC- and GC-MS/MS extends to clinical profiling with the characterization of normal pediatric steroid reference ranges in sexual development and of disease-specific profiles improving diagnosis and sub classification. Comprehensive analyses of steroid profiles may potentially improve patient outcomes together with the application of treatments specifically suited to clinical subgroups. LC-MS/MS and GC-MS/MS applications in the analyses of comprehensive steroid panels are demonstrated in clinical conditions such as congenital adrenal hyperplasia in newborns requiring accurate diagnoses and in predicting metabolic risk in polycystic ovary syndrome patients. Most notable perhaps is the impact of LC-MS/MS evaluations on our understanding of the basic biochemistry of steroidogenesis with the detection of the long forgotten adrenal steroid, 11 $\beta$ -hydroxyandrostenedione, at significant levels. The characterization of its metabolism to androgen receptor ligands in the LNCaP prostate cancer cell model, specifically within the context of recurring prostate cancer, lends new perspectives to old dogmas. We demonstrate that UHPLC-MS/MS has enabled the analyses of novel metabolites of the enzymes, SRD5A, 11 $\beta$ HSD and 17 $\beta$ HSD, in LNCaP cells. Undoubtedly, the continuous advances in the analytical methodologies used for steroid profiling and quantification will give impetus to the unraveling of the remaining enigmas, old and new, of both hormone biosynthesis and metabolism.

<http://dx.doi.org/10.1016/j.jsbmb.2015.04.009>

### 309. Rapid And Simultaneous Analysis Of Sesquiterpene Pyridine Alkaloids From *Tripterygium Wilfordii* Hook. F. Using Supercritical Fluid Chromatography-Diode Array Detector-Tandem Mass Spectrometry

2015 - The journal of Supercritical Fluids

Keywords: East China University, Sesquiterpene pyridine alkaloids, *Tripterygium wilfordii* Hook. f, component profiling, natural products, tcm, health science

**Abstract**

Sesquiterpene pyridine alkaloids are considered to be the active components of *Tripterygium wilfordii* Hook. f. A rapid method was developed for comprehensive profiling of sesquiterpene pyridine alkaloids from an extract of root bark of *T. wilfordii* using supercritical fluid chromatography-diode array detector-tandem mass spectrometry (SFC-DAD-MS/MS). Alkaloids were separated on a BEH 2EP column within 10 min, eluted by CO<sub>2</sub>-methanol as mobile phase with a back pressure of 13.8 Mpa and a column temperature of 45 °C. MS/MS analysis of [M + H]<sup>+</sup> ion of each alkaloid standard showed that all the pyridine alkaloids produced very similar fragmentation patterns. The product-ions at *m/z* 206 and 204 were identified as the diagnostic fragments while mass region of 200–500 Da was assigned as the characteristic region. As a result, 71 components in the extract were identified as sesquiterpene pyridine alkaloids, including 40 wilfordate/evoninate type alkaloids, 13 iso-wilfordate/evoninate type alkaloids and 19 hydroxyl-wilfordate/evoninate type alkaloids. The results proved the feasibility of SFC-DAD-MS/MS method for the rapid and high-throughput analysis of sesquiterpene pyridine alkaloids in complex samples.  
<http://dx.doi.org/10.1016/j.supflu.2015.05.006>

### 310. Applicability Of Ultra Performance Convergence Chromatography - A New Generation Of Supercritical Fluid Chromatography For The Analysis Of Pesticide Residues

2015 - Periodica Polytechnica Chemical Engineering

Keywords: Corvinus University of Budapest, Budapest University of Technology and Economics, food safety, quechers, food

**Abstract**

Monitoring and controlling wide variety of pesticide residues is a crucial challenge of food safety. In our study ultra-performance convergent chromatography (UPC<sup>2</sup>), as the new generation of supercritical fluid chromatography coupled with ESI-MS/MS system was applied to separate a set of pesticides to investigate their chromatographic behavior under various UPC<sup>2</sup> conditions. 30 components were selected representing the GC and LC measurable components. Capacity factors obtained from LC and GC runs UPC<sup>2</sup>-PDA were compared. Based on our data UPC<sup>2</sup> should be considered as an alternative chromatographic approach with separation mechanisms not yet fully characterized. Interestingly the type of mobile phase modifier influences the ionization in an ESI-MS system.

<http://dx.doi.org/10.3311/PPch.8363>

### 311. Exploring The Complexity Of Oil Sands Process-Affected Water By High Efficiency Supercritical Fluid Chromatography/Orbitrap Mass Spectrometry

2015 - Rapid Communications in Mass Spectrometry

Keywords: University of Alberta, dissolved organic compounds, water contamination, water treatment, naphthenic acid, environmental

**Abstract**

Approximately 1 billion m<sup>3</sup> of oil sands process-affected water (OSPW) is currently stored in tailings ponds in Northern Alberta, Canada. The dissolved organic compounds in OSPW have been termed a *supercomplex* mixture of bitumen-derived substances and continuing efforts to understand its underlying chemical composition are important for evaluating its environmental hazards. This combination of high efficiency chromatography and ultra-high mass resolution detection resulted in a powerful method with capabilities for characterizing or 'fingerprinting' unknown species with little interference. The method has great promise for environmental monitoring and forensics in the oil sands region, as well as for further studies on the composition of dissolved organic compounds in OSPW.

<http://dx.doi.org/10.1002/rcm.7156>



### 312. Quantitative Analysis Of Five Toxic Alkaloids In *Aconitum Pendulum* By Ultra-Performance Convergence Chromatography (UPC<sup>2</sup>) Coupled With Mass Spectrometry

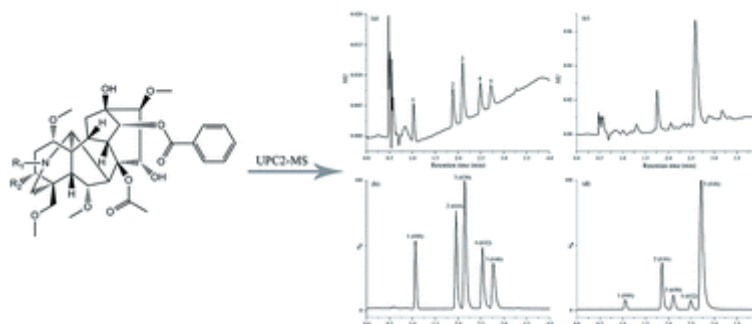
2015 - RSC Advances

Keywords: Lanzhou Institute of Chemical Physics, tcm, biobotanicals, herbal supplements, medicinal herbs, method development, method validation, food

#### Abstract

A rapid and efficient ultra-performance convergence chromatography (UPC<sup>2</sup>) method coupled with electrospray ionization single quadrupole mass spectrometry (ESI-MS) was developed and validated for the simultaneous quantification of five diester diterpenoid alkaloid constituents (3-acetylaconitine, hypaconitine, deoxyaconitine, mesaconitine, aconitine) in *Aconitum pendulum*. Optimum separation was achieved on a BEH 2-EP C<sub>18</sub> column (2.1 × 150 mm i.d., 1.7 μm particle) with a gradient elution of a mixture of A (supercritical CO<sub>2</sub>) and B (methanol containing 10 mmol L<sup>-1</sup> ammonium acetate) and at a flow rate of 0.8 mL min<sup>-1</sup> within 3 minutes. Quantification was performed using mass spectrometry in a positive ion ionization mode and selected ion recording (SIR) mode. The influences of column, modifier, additive, column temperature, and back pressure were investigated. The five alkaloids were identified and quantified using a comparison of retention time, ultraviolet spectrum, molecular ion peak (obtained from a selective ion recording mode) and peak areas with the reference compounds. The method was validated through linearity, limits of detection, limits of quantification, precision, stability, repeatability, and accuracy. The validated method was applied to analyze *A. pendulum*, which provided a reference for the quality evaluation of *A. pendulum*.

<http://dx.doi.org/10.1039/C5RA21233B>



### 313. Analysis Of Anthraquinones In Rhubarb (*Rheum Palmatum* And *Rheum Officinale*) By Supercritical Fluid Chromatography

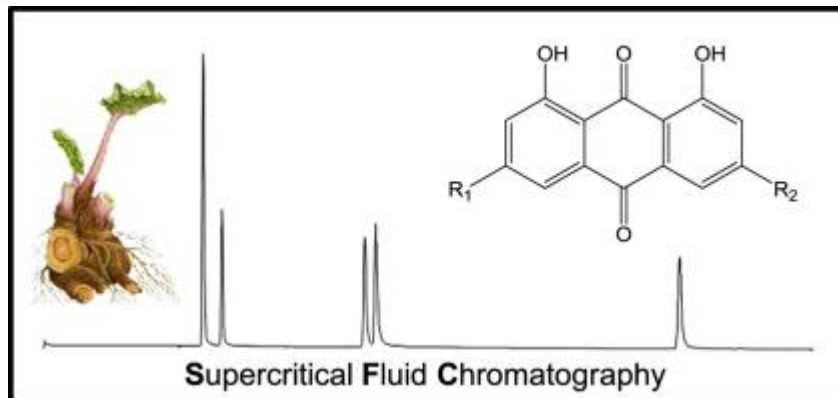
2015 - Talanta

Keywords: University of Innsbruck, chrysophanol, physcion, emodin, aloemodin, and rhein, Rhubarb; Anthraquinone, food

#### Abstract

The first report on the separation of five anthraquinones (chrysophanol, physcion, emodin, aloemodin, and rhein) from rhubarb by supercritical fluid chromatography indicates that this technique is an interesting analytical alternative not just for non-polar substances. Within less than five minutes the compounds could be baseline resolved, using a mobile phase comprising supercritical carbon dioxide and methanol with 0.05% diethylamine. The optimum stationary phase showed to be an Acquity UPC<sup>2</sup> HSS C18 SB 1.8 μm column, operated at a flow rate of 2 ml/min and a temperature of 30 °C. Method validation confirmed that the developed procedure is selective, linear ( $R^2 \geq 0.999$ ), accurate (recovery rates: 95.4% to 103.1%), and precise (intra-day  $\leq 6.9\%$ , inter-day  $\leq 4.7\%$ ); the limit of detection was below 0.5 ng on-column. The analysis of plant extracts was feasible with acceptable repeatability ( $\sigma_{rel} \leq 3.8\%$ ), and it determined 0.3 to 0.7% of free aglyca in the native samples. After hydrolysis according to the European Pharmacopoeia, a rise in the total content up to 2.1% was observed, with rhein being the most dominant derivative in nearly all specimens.

<http://dx.doi.org/10.1016/j.talanta.2015.08.011>



### 314. Extended Structural Modulation Of Bio-Inspired Chiral Lipidic Alkynylcarbinols As Antitumor Pharmacophores

2015 - Tetrahedron

Keywords: LCC (Laboratoire de Chimie de Coordination), Universite de Toulouse, Université Paul Sabatier, Taras Shevchenko National University of Kyiv, alkyne, antitumor agent, asymmetric synthesis, cytotoxicity, Lipidic alkynylcarbinol, health science

#### Abstract

The chiral alkynylcarbinol motif typically found in natural marine products, has been the subject of intense research activity for its pharmacophoric properties, in particular cytotoxicity against tumor cell lines. In a chemical synthesis-driven four-parameter structure–activity relationship (SAR) study from the (*S,E*)-eicos-4-en-1-yl-3-ol natural reference 1, the (*S*)-dialkynylcarbinol unit of the non-natural dehydro derivative 2 emerged as an unprecedented anti-tumoral pharmacophore. An extended study of lipidic alkynylcarbinol pharmacophores is presented, addressing additional structural parameters: *Z*→*E* isomerization of the alkenyl carbinol substituent of 1, variation of the lipidic chain length of 2 ( $C_{3n}$ ,  $n=3, 4, 6$ ), oxidation or substitution of the carbinol unit of 2 (to ketone, tertiary methylcarbinol, or methylether), cyclomethylenation of the double bond of 1. The synthesis of these analogues is described, including the preparation of enantio-enriched chiral alkynylcarbinol derivatives using a modified Carreira procedure for Zn-mediated addition of (trialkylsilyl)acetylene substrates to ynals in the presence of (–)- or (+)-*N*-methylephedrine. Preliminary cytotoxicity evaluation of 12 new products against the HCT 116 tumor cell line are finally reported and the results compared with those obtained for 1 and 2. These observations support and refine the relevance of the pharmacophoric character of secondary DAC units.  
<http://dx.doi.org/10.1016/j.tet.2015.08.003>

### 315. Advances In Sample Preparation And Analytical Techniques For Lipidomics Study Of Clinical Samples

2015 - TrAC Trends in Analytical Chemistry

Keywords: Bioprocessing Technology Institute, Agency for Science Technology and Research (A\*STAR), Chromatography; Clinical lipidomics; Clinical sample analysis; Disease mechanism; Disease treatment; Lipid; Lipid extraction; Lipidomics; Mass spectrometry; Sample preparation, health science

#### Abstract

Lipids play multiple key roles in biological systems, including acting as secondary energy reserves, being components of cellular membranes and participating in cell-signaling pathways. As a result, lipid defects have been implicated in the development of diseases. Consequently, the detailed analysis of lipids found in clinical samples, known as clinical lipidomics, is crucial for improving our understanding of disease mechanisms and progression, and the development of potential treatment strategies. This review documents the lipidomics workflow, beginning with a description of approaches to preparation of samples of lipids. We also describe progress in mass spectrometry technologies that led to the development of several widely-used techniques of lipid analysis. The

review concludes with a discussion on the major challenges that exist in clinical lipidomics studies and looks at potential solutions that can address them.

<http://dx.doi.org/10.1016/j.trac.2014.10.010>

### 316. Qualitative And Quantitative Analysis Of Bushen Jiannao Grains By Ultra Performance Convergence Chromatography

2015 - Chinese Journal of Analytical Chemistry

Keywords: Bushen Jiannao Grains; Ultra performance convergence chromatography; echinacoside

#### Abstract

An ultra performance convergence chromatographic (UPC<sup>2</sup>) method was established for the attribution analysis of the main peaks as well as the quantitative determination of echinacoside and  $\beta$ -ecdysterone in Bushen Jiannao Grains. The samples were extracted with ethanol and separated on Waters ACQUITY UPC<sup>2</sup> BEH column (100 mm  $\times$  3.00 mm, 1.7  $\mu$ m), with a gradient supercritical CO<sub>2</sub> - 0.05% phosphoric acid-methanol solvent system at 40 °C. The flow rate was 0.8 mL/min, the detection wavelength was set at 248 nm and the injection volume was 1  $\mu$ L. Results showed that all the main peaks in the fingerprint were clearly attributed. The peak named 12 was  $\beta$ -ecdysterone with the content of 380 $\mu$ g/g and the peak named 15 was echinacoside with the content of 9.562 mg/g. The method was simple, eco-friendly, accurate and reliable compared with HPLC and UPLC.

<http://pesquisa.bvsalud.org/oncologiauy/resource/en/wprim-873751>

### 317. Fast Analysis Of Common Fatty Acids In Edible Vegetable Oils By Ultra-Performance Convergence Chromatography-Mass Spectrometry

2015 - Chinese Journal of Analytical Chemistry

Keywords: Fatty Acids; Plant Oils; Vegetables; Chromatography; Mono-unsaturated; Tandem Mass Spectrometry; UPC<sup>2</sup>

#### Abstract

A fast analytical method for five common fatty acids in six edible vegetable oils was developed by ultra-performance convergence chromatography-mass spectrometry (UPC<sup>2</sup>-MS). The five fatty acids are palmitic acid, stearic acid, oleic acid, linoleic acid and linolenic acid. Their contents in the corn oil, sunflower oil, soybean oil, tea oil, rapeseed oil and peanut oil were compared. The chromatographic separation was performed on an ACQUITY UPC<sup>2</sup> BEH 2-EP column (100 mm  $\times$  2.1 mm, 1.7  $\mu$ m) using the mobile phases of carbon dioxide and methanol/acetonitrile (1:1, v/v) with gradient elution. The separated compounds were detected by negative electrospray ionization ESF-MS. The results showed that the reasonable linearities were achieved for all the analytes over the range of 0.5-100 mg/L with the correlation coefficients (R<sup>2</sup>) of 0.9985-0.9998. The limits of quantification (S/N  $\geq$  10) of the five fatty acids were 0.15-0.50 mg/L. The recoveries of the five fatty acids at three spiked levels were in the range of 89.61%-108.50% with relative standard deviations of 0.69%-3.01%. The developed method showed high performance, good resolution and fast analysis for the underivatized fatty acids. It has been successfully used to detect the five fatty acids from corn oil, sunflower oil, soybean oil, tea oil rapeseed oil and peanut oil.

<http://pesquisa.bvsalud.org/oncologiauy/resource/en/mdl-26292410>

## 2014 Publications

### 318. Alkaloids Analysis Using An Off-Line Two-Dimensional Supercritical Fluid Chromatography × Ultra-High Performance Liquid Chromatography

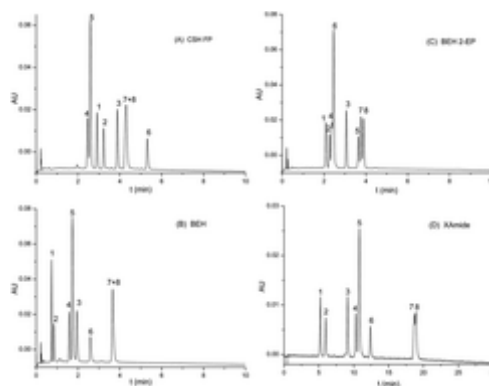
2014 - Analyst

Keywords: East China University, alkaloids, BEH, BEH 2-EP, XAmide, CSH FP, HSS T3, pharmaceutical

#### Abstract

In this study, an off-line two-dimensional (2-D) supercritical fluid chromatography (SFC) × ultra-high performance liquid chromatography (UHPLC) method with high orthogonality was developed for the analysis of the practical amide alkaloids fraction from *P. longum* L. The effects of SFC parameters such as column type, organic modifier, temperature and back-pressure on separation were systematically evaluated. Different selectivity was observed for different columns (BEH, BEH 2-EP, XAmide and CSH FP). An investigation was then carried out of the orthogonality of different columns and systems following a geometric approach with a set of amide alkaloid samples. The orthogonality between a CSH FP column and a BEH column reached 50.79%, which was much higher than that for the other columns. While the orthogonality between SFC and UHPLC based on an XAmide column and an HSS T3 column reached 69.84%, which was the highest of all the combinations. At last, the practical amide alkaloids fraction was analyzed with an off-line 2-D chromatography SFC × UHPLC system. In total, at least 340 peaks were detected by this method. Rapid separation in these two dimensions and easy post treatment of SFC facilitated this 2-D system for the separation of complex samples.

<http://dx.doi.org/10.1039/C4AN00438H>



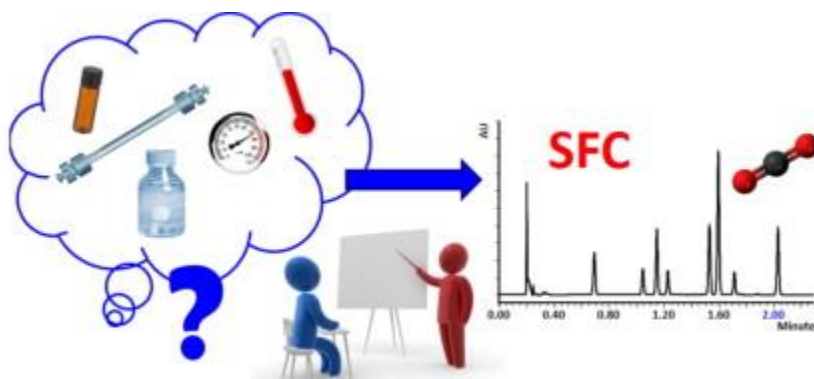
### 319. Modern Analytical Supercritical Fluid Chromatography Using Columns Packed With Sub-2 Mm Particles: A Tutorial

2014 - Analytica Chimica Acta

Keywords: Charles University, University of Geneva, Waters Corporation, lipophilic, hydrophilic, basic drugs, tutorial, pharmaceutical

#### Abstract

This tutorial provides an overview of the possibilities, limitations and analytical conditions of modern analytical supercritical fluid chromatography (SFC) using columns packed with sub-2  $\mu\text{m}$  particles. In particular, it gives a detailed overview of commercially available modern SFC instrumentation and the detectors that can be employed (UV, MS, ELSD, FID, etc.). Some advice on the choice of the stationary phase dimensions and chemistries, the nature of the mobile phase (choice of organic modifier and additives) and its flow rate as well as the backpressure and temperature are also provided. Finally, several groups of potentially problematic compounds, including lipophilic compounds, hydrophilic substances and basic drugs, are discussed in detail. All these families of analytes can be resolved with SFC but require specific analytical conditions.



### 320. Analysis Of Paclitaxel In Pharmaceutical Injection By Ultra Performance Convergence Chromatography

2014 - Advanced Materials Research

Keywords: Paclitaxel, Chinese Academy of Tropical Agricultural Sciences, Shannxi University, chemotherapy, BEH -2EP, impurity profiling, pharmaceutical

#### Abstract

A simple and sensitive ultra-performance convergence chromatography system coupled with a diode array detector for analysis of paclitaxel, 10-deacetyl-7-epipaclitaxel and cephalomannine in paclitaxel injection was developed. The analyses were carried out on a Waters Acquity UPC2 BEH 2-EP using the mobile phase of mixture of supercritical CO<sub>2</sub> and methanol with a linear gradient elution from 92:8 to 82:18 at 50 °C. The method offers good linearity, higher resolution, and good repeatability. LOD and LOQ were 0.45 and 1.32 ng, respectively.

<http://dx.doi.org/10.4028/www.scientific.net/AMR.989-994.1060>

### 321. Stereoselective Separation And Pharmacokinetic Dissipation Of The Chiral Neonicotinoid Sulfoxaflor In Soil By Ultrapformance Convergence Chromatography / Tandem Mass Spectrometry

2014 - Analytical and Bioanalytical Chemistry

Keywords: Chinese Academy of Agricultural Sciences, sulfoxaflor, stereoisomeric separation, enantioselective degradation, Chiralpak IA-3, soil, environmental

#### Abstract

Ultrapformance convergence chromatography/tandem triple quadrupole mass spectrometry (UPC<sup>2</sup>-MS/MS) is a novel tool in separation science that combines the advantages of supercritical fluid chromatography with ultrapformance liquid chromatography/MS/MS technology. The use of nontoxic CO<sub>2</sub> fluid and a postcolumn additive to complement MS/MS allows better control of analyte retention for chiral separation and high-sensitivity determination with different chiral stationary phases. This paper reports the stereoselective separation and determination of the chiral neonicotinoid sulfoxaflor in vegetables and soil by UPC<sup>2</sup>-MS/MS. Baseline resolution ( $R_s \geq 1.56$ ) of and high selectivity ( $LOQ \leq 1.83 \mu\text{g}/\text{kg}$ ) for the four stereoisomers were achieved by postcolumn addition of 1 % formic acid-methanol to a Chiralpak IA-3 using CO<sub>2</sub>/isopropanol/acetonitrile as the mobile phase at 40 °C, 2,500 psi, and for 6.5 min in electrospray ionization positive mode. Rearranged Van't Hoff equations afforded the thermodynamic parameters  $\Delta H^\circ$  and  $\Delta S^\circ$ , which were analyzed to promote understanding of the enthalpy-driven separation of sulfoxaflor stereoisomers. The interday mean recovery, intraday repeatability, and interday reproducibility varied from 72.9 to 103.7 %, from 1.8 to 9.2 %, and from 3.1 to 9.4 %, respectively. The proposed method was used to study the pharmacokinetic dissipation of sulfoxaflor stereoisomers in soil under greenhouse conditions. The estimated half-life

ranged from 5.59 to 6.03 d, and statistically nonsignificant enantioselective degradation was observed. This study not only demonstrates that the UPC<sup>2</sup>-MS/MS system is an efficient and sensitive method for sulfoxaflor stereoseparation, but also provides the first experimental evidence of the pharmacokinetic dissipation of sulfoxaflor stereoisomers in the environment. <http://dx.doi.org/10.1007/s00216-014-8089-9>

### 322. Investigating Sub-2 Mm Particle Stationary Phase Supercritical Fluid Chromatography Coupled To Mass Spectrometry For Chemical Profiling Of Chamomile Extracts

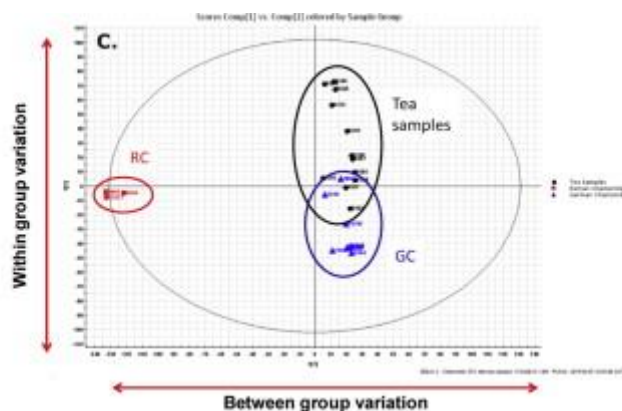
2014 - Analytica Chimica Acta

Keywords: Waters, University of Mississippi, Kings College, chamomile, tea extracts, food

#### Abstract

Roman and German chamomile are widely used throughout the world. Chamomiles contain a wide variety of active constituents including sesquiterpene lactones. Various extraction techniques were performed on these two types of chamomile. A packed-column supercritical fluid chromatography-mass spectrometry method was designed for the identification of sesquiterpenes and other constituents from chamomile extracts with no derivatization step prior to analysis. Mass spectrometry detection was achieved by using electrospray ionization. All of the compounds of interest were separated within 15 min. The chamomile extracts were analyzed and compared for similarities and distinct differences. Multivariate statistical analysis including principal component analysis and orthogonal partial least squares-discriminant analysis (OPLS-DA) were used to differentiate between the chamomile samples. German chamomile samples confirmed the presence of cis- and trans-tonghaosu, chrysosplenols, apigenin diglucoside whereas Roman chamomile samples confirmed the presence of apigenin, nobilin, 1,10-epioxynobilin, and hydroxyisonobilin.

<http://dx.doi.org/10.1016/j.aca.2014.06.031>



### 323. Chromatographic Evidence Of Silyl Ether Formation (SEF) In Supercritical Fluid Chromatography

2014 - Analytical Chemistry

Keywords: Waters Corporation, silyl ether formation, surface chemistry, particle chemistry, separation science

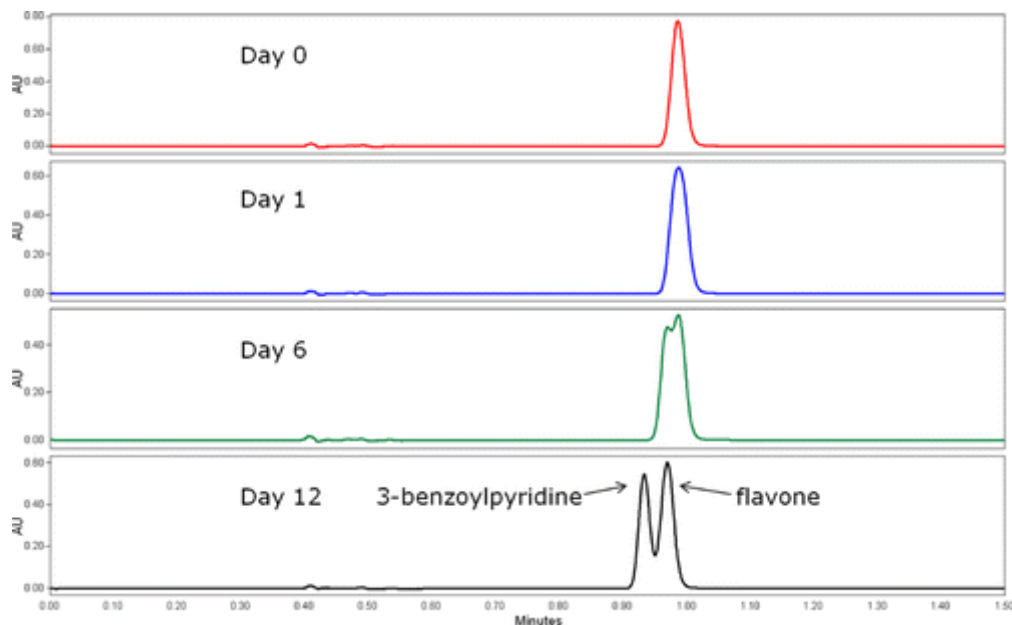
#### Abstract

In this article, we propose that silyl ether formation (SEF) is a major contribution to retention and selectivity variation over time for supercritical fluid chromatography (SFC). In the past, the variations were attributed to instrumentation, but high performance SFC systems have shed new light on the source of variation. As silyl ethers form on the particle surface, the hydrophilicity is decreased, significantly altering the retention and selectivity observed. SEF is expected to occur with any chromatographic particle containing silanols but is slowed on hybrid inorganic/organic particles. The SEF reaction is between alcohols on the particle surface and in the mobile phase solvent. We have found that storage conditions of a column are paramount, which can either prevent or accelerate the process. Because SEF exists as an equilibrium between the liquid phase



and the particle surface, the process is also reversible. The silanols can be hydroxylated (regenerated) to their original state upon exposure to water. The next generation of stationary phases will either advantageously utilize SEF or effectively mitigate its effects. Mitigation of SEF would be a significant improvement in SFC that has the potential to vault their performance to levels of similar reproducibility and reliability observed for high performance liquid chromatography (HPLC). Further research in SEF may lead to a better understanding of the mechanism of interaction between the solutes and chromatographic surface.

<http://dx.doi.org/10.1021/ac5035709>



### 324. Supercritical Fluid Chromatography As A Tool For Enantioselective Separation – A Review

2014 - Analytica Chimica Acta

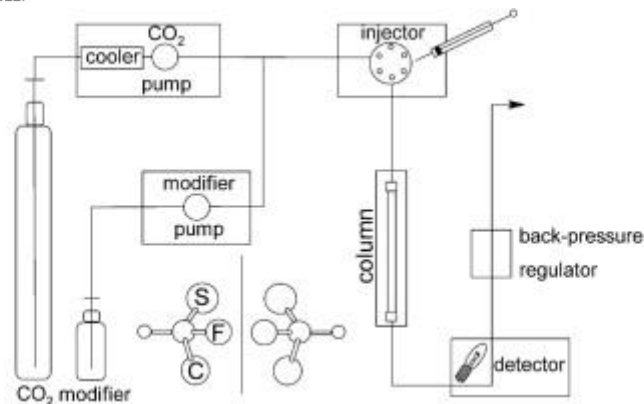
Keywords: Charles University, enantioselective separation, enantiomers, chiral separations, review

#### Abstract

Supercritical fluid chromatography (SFC) has become popular in the field of enantioselective separations. Many works have been reported during the last years. This review covers the period from 2000 till August 2013. The article is divided into three main chapters. The first one comprises a basic introduction to SFC. The authors provide a brief explanation of general principles and possibilities of this method. The advantages and drawbacks are also listed. Next part deals with chiral separation systems available in SFC, namely with the commonly used chiral stationary phases. Properties and interaction possibilities of the chiral separation systems are described. Recent theoretical papers are emphasized in this chapter. The last part of the paper gives an overview of applications of enantioselective SFC in analytical chemistry, in both analytical and preparative scales. Separation systems and conditions are summed up in tables so that they provide a helpful tool for analysts who search for a particular method of analysis.

- <http://dx.doi.org/10.1016/j.aca.2014.02.036>

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### 325. Rapid Profiling Of Triacylglycerols For Identifying Authenticity Of Edible Oils Using Supercritical Fluid Chromatography-Quadruple Time-Of-Flight Mass Spectrometry Combined With Chemometric Tools

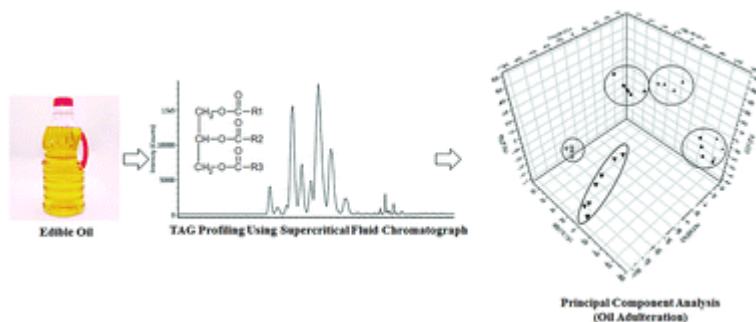
2014 - Analytical Methods

Keywords: Beijing University of Chemical Technology, food authentication, food authenticity, food

#### Abstract

Triacylglycerol (TAG) as the major ingredient of oil is a key indicator for the identification of oil adulteration due to its characteristic distributions in different oils. In this research, a high-throughput method for rapidly detecting acylglycerols in various edible oils was established by applying supercritical fluid chromatography (SFC) coupled with quadruple time-of-flight mass spectrometry (Q-TOF-MS), without any sample pretreatment procedure. The retention mechanism of TAGs on different columns were comprehensively evaluated including the previous work on an ODS column, as well as our study on HSS C<sub>18</sub>SB, BEH and BEH 2-EP columns. Distinctive retention of our method allows the separation of certain pairs of TAGs which remains difficult by traditional methods, and the analysis time is greatly reduced. SFC-MS data were subsequently analysed by principal component analysis (PCA) to make a clear classification between six different kinds of vegetable oils, showing its potential in differentiating the fakes quickly. Considering the high-price of olive oil, further quantification of olive oil adulteration was studied by estimating known and unknown compositions of blend oils according to the curves of areas of selected TAG markers *versus* adulterant concentrations. Good consistencies with the labeled content of olive oil in commercial blend oils demonstrated the reliability of the quantitative method, and these blend oils were differentiated distinctly from pure olive oils in the score plot of a PCA model. To the best of our knowledge, it was the first time that the retention of TAGs using different stationary phases in a SFC system was discussed, and that SFC was applied to quantify oil adulteration. This fast and effective method is of great advantage to authenticate edible oils.

<http://dx.doi.org/10.1039/C6AY00970K>



### 326. Rapid Analysis Of Non-Steroidal Anti-Inflammatory Drugs In Tap Water And Drinks By Ionic Liquid Dispersive Liquid–Liquid Microextraction Coupled To Ultra-High Performance Supercritical Fluid Chromatography

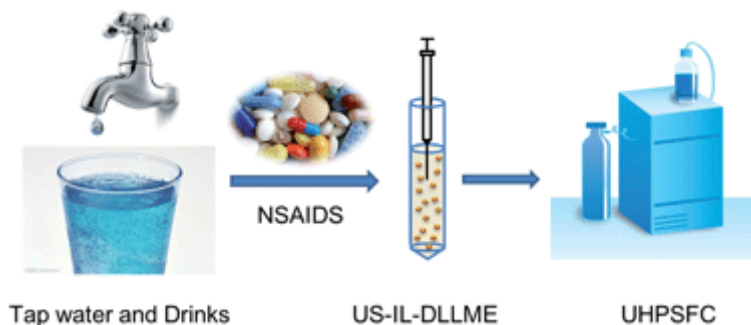
2014 - Analytical Methods

Keywords: Beijing University of Chemical Technology, tap water, drinking water, non-steroidal anti-inflammatory drugs, nabumetone, ibuprofen, naproxen and diclofenac, NSAIDs, environmental

#### Abstract

A novel rapid analytical method for the determination of four non-steroidal anti-inflammatory drugs (NSAIDs) – nabumetone, ibuprofen, naproxen and diclofenac – in tap water and drinks is presented. The method is based on ultrasound-assisted ionic liquid dispersive liquid–liquid microextraction (US-IL-DLLME) followed by ultra-high performance supercritical fluid chromatography (UHPSFC) coupled to a photo-diode array detector (PDA). The ionic liquid 1-octyl-3-methylimidazolium hexafluorophosphate ( $[C_8MIM][PF_6]$ ) and methanol were used as the extraction and dispersion solvents for the DLLME procedure other than using a toxic chlorinated solvent. Plackett–Burman and Box–Behnken designs were applied as the experimental design strategies to screen and optimize the experimental variables such as the volume of the ionic liquid, the volume of the disperser solvent, sample pH, ionic strength, ultrasonication time and centrifugation time which affected the extraction efficiency. Separation conditions of UHPSFC, such as column screening, modifiers, column temperature, back pressure and flow rate, were also optimized in this study. 4 NSAIDs were simultaneously separated and determined in 2.1 minutes. The optimized US-IL-DLLME-UHPSFC-PDA method showed good enrichment factors (126–132) and recoveries (81.37–107.47%) for the rapid extraction of nabumetone, ibuprofen, naproxen and diclofenac in tap water and drinks. The method's limits of detection for nabumetone, ibuprofen, naproxen and diclofenac were 1.56, 7.69, 0.62, and 7.37  $ng\ mL^{-1}$  with excellent linearity ( $R > 0.9957$ ).

<http://dx.doi.org/10.1039/c4ay01305k>



### 327. Analysis Of Chemical Constituents In Jackfruit Peel By UPC<sup>2</sup> / Q-TOF-MS Method

2014 - Applied Mechanics and Materials

Keywords: Chinese Academy of Tropical Agricultural Sciences, Northeast Agricultural University, Hainan University, jackfruit peel, HSS, food

#### Abstract

A new method for the analysis chemical constituents in jackfruit peel by ultra performance convergence chromatography (UPC<sup>2</sup>) was developed for the first time. The extraction of jackfruit peel was carried out under classical heating with ultrasonic wave and extracted with ethyl ether. The analytes were separated on an ACQUITY UPC<sup>2</sup> HSS C18 SB column with a gradient elution (80:20 to 99.8:0.2) of mobile phase consisting of CO<sub>2</sub> and methanol. The result indicated that UPC<sup>2</sup>/Q-TOF-MS is a simple, rapid, reliable and effective method to analyze the biochemical compounds in jackfruit peel. A total of 65 compounds were identified, including acids, esters, alcohols, and pyrazine, etc.

<http://dx.doi.org/10.4028/www.scientific.net/AMM.556-562.607>

### 328. Organocatalytic Cascade Reactions: Diversity-Oriented Synthesis For The Construction Of Hydroisoquinoline Scaffolds

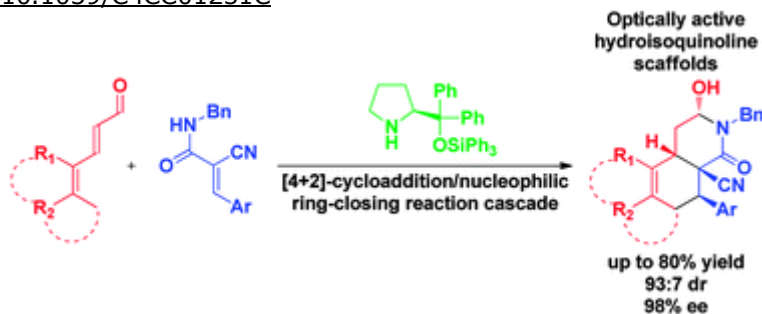
2014 - Chemical Communications

Keywords: Aarhus University, enantioselective synthesis, hydroisoquinilines, separation science

#### Abstract

Novel hydrophobized hyaluronan (HA) derivatives, containing  $\omega$ -phenylalkanoic acids ( $\omega$ -PAA, 4-phenylbutyric acid, 6-phenylhexanoic, 8-phenyloctanoic or 11-tolylundecanoic acids) were prepared by esterification. Mixed anhydrides obtained after reaction of the carboxyl acid moiety and benzoyl chloride were found to be active acylating agents, affording hydrophobized HA in good yield and under mild conditions. The reactivity of the aromatic fatty acids towards esterification has decreased with the increasing length of the aliphatic spacer between the aromatic substituent and carboxylic acid moiety. The novel HA derivatives self-assembled from very low concentrations and were found to be non-cytotoxic. The potential use of  $\omega$ -phenylalkanoic acids grafted-HA towards drug delivery applications was demonstrated by hydrophobic drugs (resveratrol and retinyl palmitate) encapsulation. The drug loading capacity of the novel HA derivatives was significantly improved most likely because of  $\pi$ - $\pi$  interactions between the micelle core and loaded hydrophobic aromatic compound.

<http://dx.doi.org/10.1039/C4CC01231C>



### 329. Organocatalytic Cascade Reactions: Towards The Diversification Of Hydroisochromenes And Chromenes Through Two Different Activation Modes

2014 - Chemistry, A European Journal

Keywords: Aarhus University, hydroisochromenes, chromenes, organocatalysis, separation science

#### Abstract

The organocatalytic enantioselective syntheses of functionalized hydroisochromenes and chromenes by trienamine-mediated [4+2]-cycloaddition/nucleophilic ring-closing and iminium-ion/aminal-mediated oxa-Michael/Michael/nucleophilic ring-closing with 2-nitroallylic alcohols are presented. The corresponding cycloadducts, with up to five stereocenters, are formed in good yield and excellent enantioselectivities. The synthetic applications of the obtained products have been demonstrated.

<http://dx.doi.org/10.1002/chem.201403505>

### 330. Fast Separation Method Development For Supercritical Fluid Chromatography Using An Autoblending Protocol

2014 - Chromatographia

Keywords: Chengdu Institute of Biology, method development, enantioseparations, health science

#### Abstract

Supercritical fluid chromatography (SFC) is a powerful separation technique particularly in the area of enantioseparations. With rapid analysis speed, wide polarity compatibility, higher column efficiency and lower cost of the mobile phase, SFC is regarded as a better choice than high-performance liquid chromatography for drug discovery. In the development of separation method, the choice of modifier and/or additive is the key point of optimum separation. However, such screening of SFC is typically time-consuming. In this study, an autoblending protocol was introduced to speed up the modifier and/or additive screening process, which was performed on a separate programmable gradient proportioning system. The protocol prepares mobile phases on the fly to speed up the screening of modifiers and/or additives and reduces the waste of solutions. Furthermore, by switching mobile phase in the same run, separation of different types of compounds could also be achieved. This system was successfully applied to screen modifier-additive combinations of three alkaloids and three polyphenols by switching to two mobile phase conditions, as well as by a ternary additive mobile phase on an SFC system. The proposed protocol allows fast separation method development of SFC, which was proved to be rapid, simple, and reproducible.

<http://dx.doi.org/10.1007/s10337-014-2684-y>

### 331. Separation Of Pharmaceuticals By SFC Using Mono And Di-Hydroxy Substituted Phenyl Stationary Phases

2014 - Chromatography Today

Keywords: Pfizer Global Research, sfc stationary phases, pharmaceutical

#### Abstract

Supercritical Fluid Chromatography (SFC) has gained significant momentum over the past 10 years as the technique of choice for analytical and preparative separation of small organic molecules. One of the main contributors to its success is the selectivity enhancements derived from multifunctional stationary phases above and beyond that achieved through mobile phase tuning. While the pyridine column has become a standard column in SFC by expanding the range of compounds amenable to SFC, the monofunctional pyridine phase may be too polar to be broadly applicable. Likewise, the C18 and phenyl columns may be too non-polar for many compounds. Therefore, in order to offer enhanced selectivity in SFC, these phases are often substituted. For instance, adding polar functional groups to the pyridine phase have produced alternatives phases such as hydroxylamino dipyridinyl column. In a similar approach, more polar functional groups can be added to the phenyl phase to increase its overall polarity and thus improve its selectivity and applicability. In this application note, we highlight selectivity changes observed when introducing mono- and di-hydroxy polar groups onto phenyl phases and comparing them to their unsubstituted counterpart.

[https://www.researchgate.net/publication/269037616\\_Separation\\_of\\_Pharmaceuticals\\_by\\_SFC\\_using\\_Mono-\\_and\\_Di-Hydroxy\\_Substituted\\_Phenyl\\_Stationary\\_Phases](https://www.researchgate.net/publication/269037616_Separation_of_Pharmaceuticals_by_SFC_using_Mono-_and_Di-Hydroxy_Substituted_Phenyl_Stationary_Phases)

### 332. Delivering The Promise Of SFC: A Case Study

2014 - Drug Discovery Today

Keywords: AstraZeneca, purification, case study, pharmaceutical

#### Abstract

During the past years there has been a rapid development in supercritical fluid chromatography (SFC) instrumentation making it a highly efficient and robust technique. Although much is written about the advantages of SFC over liquid chromatography (LC), there are not many direct comparisons detailing the gain in purification throughput, the savings in solvent consumption and the reduced environmental impact for large-scale SFC applications. We will show that a research scale separation laboratory built to handle multigram amounts can be used for kilogram separations when moving from LC to SFC.

<http://dx.doi.org/10.1016/j.drudis.2014.04.021>

### 333. A New Method For Determination Of A-Tocopherol In Tropical Fruits By Ultra Performance Convergence Chromatography With Diode Array Detector

2014 - Food Analytical Methods

Keywords: Agricultural Product Processing Research Institute, Chinese Academy of Tropical Agricultural Sciences, tocopherol, food

#### Abstract

A new method for the analysis of  $\alpha$ -tocopherol in tropical fruits by ultra performance convergence chromatography (UPC<sup>2</sup>) was developed for the first time. Five varieties of tropical fruit samples were separately saponified under classical heating and extracted with ether. The extracted  $\alpha$ -tocopherol was separated on a BEH column, with a mobile phase consisting of CO<sub>2</sub> and methanol, with a gradient elution (99:1 to 90:10), and detected with diode array detector at 293 nm. The limit of detection (LOD) and limit of quantification (LOQ) were about 60.0 and 103.3 ng, respectively. This method was considered to be simple, fast and reliable, and successfully applied to analysis of  $\alpha$ -tocopherol in tropical fruits. The values of  $\alpha$ -tocopherol in pitaya, jackfruit, durians, mango, and papaya ranged from 0.16 to 0.45 mg/100 g dry weight in edible portion. Recovery rates obtained by the standard addition method on these tropical fruit samples ranged from 95.4 to 101.4 % with high repeatability (RSD, 1.2–2.6 %).

<http://dx.doi.org/10.1007/s12161-014-9789-7>

### 334. Ultra-Performance Convergence Chromatography (UPC<sup>2</sup>) Method For The Analysis Of Biogenic Amines In Fermented Foods

2014 - Food Chemistry

Keywords: Agricultural Product Processing Research Institute, Chinese Academy of Tropical Agricultural Sciences, biogenic amines, fermented foods, yulu, sufu, food

#### Abstract

A rapid ultra-performance convergence chromatography (UPC(2)) method for the determination of eight biogenic amines (spermine, spermidine, putrescine, cadaverine, tryptamine, phenylethylamine, histamine and tyramine) in fermented foods was developed. The amines were pre-column derivatized with dansyl chloride and separated on UPC(2) system with a HSS C18 SB column (3.0 × 100 mm, 1.8  $\mu$ m) using gradient elution with a binary system of CO<sub>2</sub> and n-hexane:isopropanol:ammonium hydroxide (70:30:0.15, v/v/v), back pressure of 2,000 psi, flow rate of 2.0 ml/min and DAD detection at 254 nm. The result showed excellent linearity ( $r=0.9995-1.0000$ ). Limits of detection (LOD) and limits of quantification (LOQ) were 21-67 ng/L and 72-224 ng/L, respectively. Relative standard deviations (RSD) for repeatability and reproducibility were 0.21-0.87% and 1.98-4.02%, respectively. Furthermore, this method was successfully applied to analysis of biogenic amines in Yulu and Sufu samples.

<http://dx.doi.org/10.1016/j.foodchem.2014.04.063>

### 335. Chemical Profiling Of Triacylglycerols And Diacylglycerols In Cow Milk Fat By Ultra-Performance Convergence Chromatography Combined With Quadrupole Time-Of-Flight Mass Spectrometry

2014 - Food Chemistry

Keywords: Shanghai Jiao Tong University, triacylglycerols and diacylglycerols tags, dags, cow milk, food

#### Abstract

An ultra-performance convergence chromatography (UPC(2)) system coupled with quadrupole time-of-flight mass spectrometry (Q-TOF-MS) was successfully utilised to analyse triacylglycerols and diacylglycerols in cow milk fat. This novel approach obtained an improved resolution of triacylglycerols in comparison to previously reported chromatographic methods combined with MS detector in a shorter analytical time. A total of 49 triacylglycerols and 7 diacylglycerols were identified according to their secondary MS profiles and elementary composition. Furthermore, UPC(2) is an environmental friendly analytical method with a drastic reduction of organic solvent usage. The established UPC(2)-MS approach has potential application in lipidomics as an alternative method besides LC-MS and GC-MS.

<http://dx.doi.org/10.1016/j.foodchem.2013.07.114>



### 336. Preparation Of Bio-Based Surfactants From Glycerol And Dodecanol By Direct Etherification

2014 - Green Chemistry

Keywords: East China University of Science and Technology, surfactants, glycerol, dodecanol, chemical materials

#### Abstract

In this paper, we studied an original synthetic strategy to prepare bio-based surfactants by direct solvent-free etherification of glycerol with dodecanol using heterogeneous interfacial acidic catalysts dubbed Pickering Interfacial Catalysis. The conversion of dodecanol could be achieved to 60–71% with limited production of didodecyl ether (DE) as the main side product. The selectivity of the final product, alkylpolyglycerylether (AGEM), could be pushed to >80% with a water removal process at 150 °C, as a mixture of monolauryl polyglyceryl ethers, multilauryl polyglyceryl ethers and multilauryl cyclicpolyglyceryl ethers. AGEM could be isolated with a suitable work-up and was fully characterized by GC (MS), HPLC, SFC/HRMS, *etc.* The physicochemical properties of these new surfactants were evaluated, as well as their laundry performances. This solvent-free direct etherification process paves the way towards new value-added applications of glycerol.

<http://dx.doi.org/10.1039/C4GC00818A>

### 337. Green And Sensitive Supercritical Fluid Chromatographic–Tandem Mass Spectrometric Method For The Separation And Determination Of Flutriafol Enantiomers In Vegetables, Fruits, And Soil

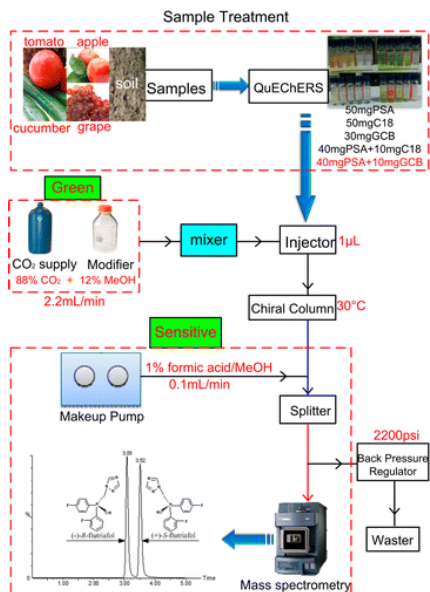
2014 - Journal of Agricultural and Food Chemistry

Keywords: Institute of Plant Protection, Chinese Academy of Sciences, flutriafol enantiomers, vegetables, fruit, soil, environmental, food

#### Abstract

A green and sensitive chiral analytical method was developed to determine flutriafol enantiomers in vegetables (tomato, cucumber), fruits (apple, grape), and soil by supercritical fluid chromatography–tandem mass spectrometry. The enantioseparation was performed within 3.50 min using Chiralpak IA-3 column with CO<sub>2</sub>/methanol (88:12, v/v) as the mobile phase at a 2.2 mL/min flow rate. The postcolumn compensation technology provided with 1% formic acid/methanol greatly improved the ionization efficiency of mass spectrometry. Column temperature, auto back pressure regulator pressure, and flow rate of compensation solvent were optimized to 30 °C, 2200 psi, and 0.1 mL/min, respectively. The simple and fast QuEChERS pretreatment method was adopted. Mean recoveries for flutriafol enantiomers were 77.2–98.9% with RSDs ≤ 9.6% in all matrices. The limits of quantification ranged from 0.41 to 1.18 µg/kg. Well-applied to analyze authentic samples, the developed method could act as a versatile strategy for the analysis of flutriafol enantiomers in food and environmental matrices.

<http://dx.doi.org/10.1021/jf504324t>



### 338. Catalytic Asymmetric Synthesis Of 4-Nitropyrzolidines: An Access To Optically Active 1,2,3-Triamines

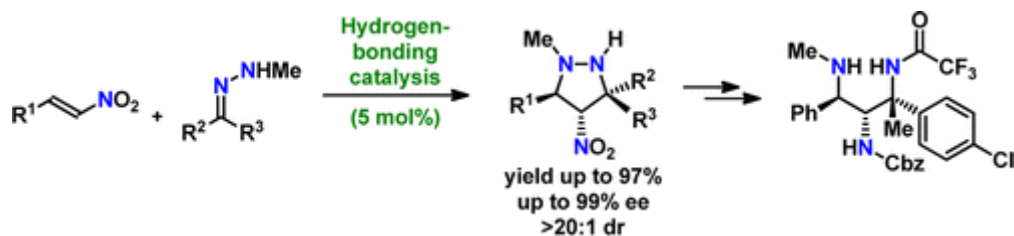
2014 - Journal of the American Chemical Society

Keywords: Aarhus University, enantioselective synthesis, diastereoselective synthesis, separation science

#### Abstract

The first catalytic enantio- and diastereoselective synthesis of 4-nitropyrzolidines is presented. Asymmetric hydrogen-bonding activation of nitro-olefins facilitated the 1,3-dipolar cycloaddition with hydrazones, affording optically active 4-nitropyrzolidines containing three continuous stereogenic centers as a single diastereomer in up to 99% ee. Furthermore, it is demonstrated that the optically active 4-nitropyrzolidines can be applied as precursors for the synthesis of highly interesting 1,2,3-triamines.

<http://dx.doi.org/10.1021/ja506694v>



### 339. Evaluation Of Co-Solvent Fraction, Pressure And Temperature Effects In Analytical And Preparative Supercritical Fluid Chromatography

2014 - Journal of Chromatography A

Keywords: Karlstadt University, chemometrics, design of experiments, separation science

#### Abstract

A chemometric approach is used for studying the combined effect of temperature, pressure and co-solvent fraction in analytical and preparative supercritical fluid chromatography (SFC). More specifically, by utilizing design of experiments coupled with careful measurements of the experimental conditions the interaction between pressure, temperature and co-solvent fraction was studied with respect to productivity, selectivity and retention in chiral SFC. A tris-(3,5-dimethylphenyl) carbamoyl cellulose stationary phase with carbon dioxide/methanol as mobile phase and the two racemic analytes trans-stilbene oxide (TSO) and 1,1'-bi-2-naphthol (BINOL) were investigated. It was found for the investigated model system that the co-solvent fraction and pressure were the parameters that most affected the retention factors and that the co-solvent fraction and column temperature were most important for controlling the selectivity. The productivity in the preparative mode of SFC was most influenced by the co-solvent fraction and temperature. Both high co-solvent fraction and temperature gave maximum productivity in the studied design space.

<http://dx.doi.org/10.1016/j.chroma.2014.11.045>

### 340. Comparison Of Liquid Chromatography And Supercritical Fluid Chromatography Coupled To Compact Single Quadrupole Mass Spectrometer For Targeted In Vitro Metabolism Assay

2014 - Journal of Chromatography A

Keywords: University of Geneva, method development, in vitro metabolism, column screening, phytochemical inhibitors, pharmaceutical

#### Abstract

The goal of this study was to evaluate the combination of powerful chromatographic methods and compact single quadrupole MS device for simple in vitro cytochrome P450 (CYP) inhibition assay, instead of more expensive triple quadrupole MS/MS detectors. For this purpose, two modern chromatographic approaches (ultra-high pressure liquid chromatography (UHPLC) and ultra-high performance supercritical fluid chromatography (UHPSFC)) were tested in combination with simple MS detector. To show the applicability for an in vitro CYP-mediated metabolism assay using the cocktail approach, a method was first developed in UHPLC-MS to separate a mixture of 8 probe substrates and 8 CYP-specific metabolites. A screening procedure was initially applied to determine the best combination of a column, an organic modifier and a mobile-phase pH, followed by fine tuning of the conditions (i.e., gradient profile, temperature and pH) using HPLC modelling software. A similar sequential method development procedure was also evaluated for UHPSFC-MS. For method development, where peak tracking is necessary, the use of single quadrupole MS was found to be extremely valuable for following the investigated analytes. Ultimately, a baseline separation of the 16 compounds was achieved in both UHPLC-MS and UHPSFC-MS with an analysis time of less than 7 min. In a second series of experiments, sensitivity was evaluated, and LOQ values were between 2 and 100 ng/mL in UHPLC-MS, while they ranged from 2 to 200 ng/mL in UHPSFC-MS. Based on the concentrations employed for the current in vitro phase I metabolism assay, these LOQ values were appropriate for this type of application. Finally, the two analytical methods were applied to in vitro CYP-dependent metabolism testing. Two well-known phytochemical inhibitors, yohimbine and resveratrol, were investigated, and reliable conclusions were drawn from these experiments with both UHPLC-MS and UHPSFC-MS. At the end, the proposed strategy of optimized chromatography combined with simple MS device has been shown to potentially compete with the widely used combination of generic chromatography and highly selective MS/MS device for simple in vitro CYP inhibition assays. In addition, our analytical method may be easier to use in a routine environment; the instrument cost is significantly reduced and the two developed methods fit for purpose.

<http://dx.doi.org/10.1016/j.chroma.2014.10.055>

### 341. Evolution Of Strategies To Achieve Baseline Separation Of Ten Anionic, Water-Soluble Sulfated Estrogens Via Achiral Packed Column Supercritical Fluid Chromatography

2014 - Journal of Chromatography A

Keywords: Pfizer, Waters, Virginia Tech, 2-ethylpyridine, sulfated estrogen salts, health science

### Abstract

Near baseline separation of ten sulfated sodium salts of various structurally related estrogens employing a variety of bonded stationary phase packed columns was obtained using a conventional supercritical fluid chromatograph coupled with UV detection. Critical pairs 2/3 (8,9-dehydroestrone/17 $\beta$ -dihydroequilin) and 6/7 (17 $\alpha$ -estradiol or 17 $\alpha$ -dihydroequilin/estrone), however, failed to baseline separate. In all preliminary separations, 10mM ammonium acetate and variable percentages of H<sub>2</sub>O were initially used as co-additives in conjunction with methanol as a modifier. Different modifier programs and temperatures were employed to optimize the separation in a timely manner. A 2-ethylpyridine column provided the best separation compared to bare silica, diol, and cyano-based bonded phase columns. The employment of both salt and water as additives to the methanol-modified CO<sub>2</sub> mobile phase suggested a mixed mode separation mechanism involving both ion pairing of each anionic sulfated estrogen with ammonium ion and hydrophilic interaction facilitated by partitioning of analyte between the aqueous solvated stationary phase and the aqueous component of the mobile phase. Upon more extensive study with either iso-propylamine or formic acid-ammonium formate buffer, the critical anionic pairs were 95% baseline resolved.

<http://dx.doi.org/10.1016/j.chroma.2014.10.021>

## 342. Evaluation Of The Quantitative Performances Of Supercritical Fluid Chromatography: From Method Development To Validation

2014 - Journal of Chromatography A

Keywords: University of Liege, quantitative performance, design space, pharmaceutical quality control, drugs, method validation

### Abstract

Recently, the number of papers about SFC increased drastically but scientists did not truly focus their work on quantitative performances of this technique. In order to prove the potential of UHPSFC, the present work discussed about the different steps of the analytical life cycle of a method: from development to validation and application. Moreover, the UHPSFC quantitative performances were evaluated in comparison with UHPLC, which is the main technique used for quality control in the pharmaceutical industry and then could be considered as a reference. The methods were developed using Design Space strategy, leading to the optimization of robust method. In this context, when the Design Space optimization shows guarantee of quality, no more robustness study is required prior to the validation. Then, the methods were geometrically transferred in order to reduce the analysis time. The UHPSFC and UHPLC methods were validated based on the total error approach using accuracy profile. Even if UHPLC showed better precision and sensitivity, UHPSFC method is able to give accurate results in a dosing range larger than the 80-120% range required by the European Medicines Agency. Consequently, UHPSFC results are valid and could be used for the control of active substance in a finished pharmaceutical product. Finally, UHPSFC validated method was used to analyse real samples and gave similar results than the reference method (UHPLC).

<http://dx.doi.org/10.1016/j.chroma.2014.01.046>

## 343. A Scaling Rule In Supercritical Fluid Chromatography. I. Theory For Isocratic Systems

2014 - Journal of Chromatography A

Keywords: Waters, method transfer, pressure drop, density variation, density modulation, preparative, scaling, scale-up, separation science

### Abstract

Scaling is regularly done in chromatography either to transfer a successfully designed method of analysis developed in one system to another system, or to scale-up a separation method developed in analytical scale to preparative scale. For liquid chromatography there are well-tested guidelines for scaling, which makes it a routine job. For supercritical fluid chromatography (SFC), on the other hand, neither do we have any well-understood principles behind scaling nor do we know how far the strategies applied in LC could be applicable to SFC. In this article, we have addressed these issues and proposed a rule applicable for scaling isocratic methods between different SFC systems and column dimensions under commonly used operating temperatures and

pressures. We have shown that the scale-up and method transfer techniques used in LC can be applied to SFC, provided we ensure that both the original and the target systems in SFC operate at the same average density. The current article will present the theory, discuss the extents of applicability of this rule, and outline its limitations. In an accompanying article implementation of this rule in various practical situations will be presented.

<http://dx.doi.org/doi:10.1016/j.chroma.2014.08.009>

### 344. Simultaneous Analysis For Water- And Fat-Soluble Vitamins By A Novel Single Chromatography Technique Unifying Supercritical Fluid Chromatography And Liquid Chromatography

2014 - Journal of Chromatography A

Keywords: Osaka University, fat soluble vitamins, water soluble vitamins, food

#### Abstract

Chromatography techniques usually use a single state in the mobile phase, such as liquid, gas, or supercritical fluid. Chromatographers manage one of these techniques for their purpose but are sometimes required to use multiple methods, or even worse, multiple techniques when the target compounds have a wide range of chemical properties. To overcome this challenge, we developed a single method covering a diverse compound range by means of a "unified" chromatography which completely bridges supercritical fluid chromatography and liquid chromatography. In our method, the phase state was continuously changed in the following order; supercritical, subcritical and liquid. Moreover, the gradient of the mobile phase starting at almost 100% CO<sub>2</sub> was replaced with 100% methanol at the end completely. As a result, this approach achieved further extension of the polarity range of the mobile phase in a single run, and successfully enabled the simultaneous analysis of fat- and water-soluble vitamins with a wide logP range of -2.11 to 10.12. Furthermore, the 17 vitamins were exceptionally separated in 4min. Our results indicated that the use of dense CO<sub>2</sub> and the replacement of CO<sub>2</sub> by methanol are practical approaches in unified chromatography covering diverse compounds. Additionally, this is a first report to apply the novel approach to unified chromatography, and can open another door for diverse compound analysis in a single chromatographic technique with single injection, single column and single system.

<http://dx.doi.org/doi:10.1016/j.chroma.2014.08.003>

### 345. Evaluation Of Stationary Phases Packed With Superficially Porous Particles For The Analysis Of Pharmaceutical Compounds Using Supercritical Fluid Chromatography

2014 - Journal of Chromatography A

Keywords: Osaka University, fat soluble vitamins, water soluble vitamins, food

#### Abstract

Superficially porous particles (SPP), or core shell particles, which consist of a non-porous silica core surrounded by a thin shell of porous silica, have gained popularity as a solid support for chromatography over the last decade. In the present study, five unbonded silica, one diol, and two ethylpyridine (2-ethyl and 4-ethyl) SPP columns were evaluated under SFC conditions using two mixtures, one with 17 drug-like compounds and the other one with 7 drug-like basic compounds. Three of the SPP phases, SunShell™ 2-ethylpyridine (2-EP), Poroshell™ HILIC, and Ascentis® Express HILIC, exhibited superior performances relative to the others (reduced theoretical plate height (h<sub>min</sub>) values of 1.9–2.5 for neutral compounds). When accounting for both achievable plate count and permeability of the support using kinetic plot evaluation, the Cortecs™ HILIC 1.6 μm and Ascentis® Express HILIC 2.7 μm phases were found to be the best choices among tested SPPs to reach efficiencies up to 30,000 plates in the minimum amount of time. For desired efficiencies ranging from 30,000 to 60,000 plates, the SunShell™ 2-EP 2.6 μm column clearly outperformed all other SPPs. With the addition of a mobile phase additive such as 10 mM ammonium formate, which was required to elute the basic components with sharp peaks, the Poroshell™ HILIC, SunShell™ Diol and SunShell™ 2-EP phases represent the most orthogonal SPP columns with the highest peak capacities. This study demonstrates the obvious benefits of using columns packed with SPP on current SFC instrumentation.

<http://dx.doi.org/doi:10.1016/j.chroma.2014.07.078>

### 346. Effect Of Particle Size On The Speed And Resolution Of Chiral Separations Using Supercritical Fluid Chromatography

2014 - Journal of Chromatography A

Keywords: Merck, Celgene, Chiralcel, pharmaceutical

#### Abstract

Fast chiral supercritical fluid chromatography (SFC) separations have become important due to the increasing use of high-throughput experimentation (HTE) in organic synthesis. These HTE experiments can generate hundreds of samples for chiral analysis that need to be assayed in a short time. In general, chiral SFC can provide much faster analysis times compared to liquid chromatography (LC). Additionally, columns packed with smaller particles can provide faster and more efficient separations. In this study, the effect of the particle size on the speed and resolution of chiral separations by SFC was evaluated. The performance of Chiralcel OD columns packed with either 5 or 3  $\mu\text{m}$  particles were compared using van Deemter or other kinetic plots. The benefits of using smaller particle columns for chiral SFC analysis are illustrated.

<http://dx.doi.org/10.1016/j.chroma.2014.07.010>

### 347. Enantioselective High Performance Liquid Chromatography And Supercritical Fluid Chromatography Separation Of Spirocyclic Terpenoid Flavor Compounds

2014 - Journal of Chromatography A

Keywords: Sanofi, University of Hamburg, chiral separations, chiral stationary phases, allylic oxidation, flavors, natural products, terpenes, food

#### Abstract

Chiral spirocyclic terpenoids are abundant natural flavors with significant impact particularly on the food industry. Chromatographic methods for analytical and preparative separation of these compounds are therefore of high interest to natural product chemists in academia and industry. Gas chromatography on chiral stationary phases is currently the standard method for the separation of volatile terpenoids, limiting the scale to analytical quantities. We report herein high performance liquid chromatography (HPLC) and supercritical fluid chromatography (SFC) protocols for the chiral separation of several racemic spirocyclic terpenoids such as the important flavors theaspirane and vitispirane. A screening of mobile phases and 16 commercially available chiral stationary phases (CSPs) largely based on polysaccharides led to identification of protocols for the separation of all terpenoids tested. SFC methods were found to be particularly useful for the separation of these spirocyclic flavors due to the volatility and low polarity of the compounds. The reported chiral HPLC and SFC protocols are scalable alternatives to gas chromatographic separations of volatile terpenoid flavors.

<http://dx.doi.org/10.1016/j.chroma.2014.07.001>

### 348. Insights Into Chiral Recognition Mechanism In Supercritical Fluid Chromatography III. Non-Halogenated Polysaccharide Stationary Phases

2014 - Journal of Chromatography A

Keywords: University of Orleans, Bristol Myers Squibb, chiral recognition, linear solvation energy relationship, polysaccharide, retention relationships, separation science

#### Abstract

The majority of published enantiomeric separations by supercritical fluid chromatography (SFC) utilize chiral stationary phases (CSP) based on chemically derivatized amylose or cellulose, coated or immobilized on silica. There is a large diversity among these polysaccharide-type CSP enhancing the scope of chiral separation applications. But on the other hand, identifying the appropriate support for a given separation problem is rather difficult. Hence, this study aims to provide insights on the difference and similarity among the non-halogenated polysaccharide CSP in terms of retention and selectivity at a molecular level. Firstly, the potential of the clones provided by different manufacturers is evaluated with carbon dioxide - methanol mobile phases. Then different aspects of the chiral recognition mechanism contributing to the separations on 16 different columns of five distinct chiral selectors will be explored based on a large amount of experimental data acquired with the help of modelling and chemometric techniques. We report the



influence of the ligand bonded to the polysaccharide on the non-enantio-specific interactions between the solute and the CSP, comparing phenylcarbamate to 3,5-dimethylphenylcarbamate, and 4-methylphenylester to 3,5-dimethylphenylcarbamate. In addition, we evaluate the impact of the silica treatment on the quality of the separation. The phases are characterized in terms of their retention characteristics assessed by the solvation parameter model and separation capabilities assessed by discriminant analysis.

<http://dx.doi.org/10.1016/j.chroma.2014.06.084>

### 349. Insights Into Chiral Recognition Mechanism In Supercritical Fluid Chromatography IV. Chlorinated Polysaccharide Stationary Phases

2014 - Journal of Chromatography A

Keywords: University of Orleans, Bristol Myers Squibb, chemometrics, chlorinated polysaccharides, chiral recognition, linear solvation energy relationship, polysaccharide, retention relationships, separation science

#### Abstract

The chiral recognition mechanism for a successful enantioseparation on polysaccharide stationary phases are still poorly understood. In this series of papers, we aim to provide some insight into the retention and separation mechanisms occurring in enantioselective supercritical fluid chromatography (SFC). This paper presents a thorough investigation on chlorinated polysaccharide chiral stationary phases (CSP) comprising five coated and three immobilized phases from different manufacturers. The columns are also compared to four non-chlorinated phases to unravel the most significant differences brought about by the introduction of electron-withdrawing atoms on the aromatic ligands. Chemometrics are used to (i) get an overview of all columns (cluster analysis), (ii) describe retention (modified solvation parameter model) and (iii) describe enantioseparation (discriminant analysis). Sample applications are provided to support the discussion.

<http://dx.doi.org/10.1016/j.chroma.2014.06.026>

### 350. Generic Chiral Method Development In Supercritical Fluid Chromatography And Ultra-Performance Supercritical Fluid Chromatography

2014 - Journal of Chromatography A

Keywords: Vrije Universiteit Brussel, Bristol Myers Squibb, method development, chiral separations, polysaccharide-based stationary phases, separation science

#### Abstract

The development of chiral separation methods in pharmaceutical industry is often a very tedious, labour intensive and expensive process. A trial-and-error approach remains frequently used, given the unpredictable nature of enantioselectivity. To speed-up this process and to maximize the efficiency of method development, a generic chiral separation strategy for SFC is proposed in this study. To define such strategy, the effect of different chromatographic parameters on the enantioselectivity is investigated and evaluated. Subsequently, optimization steps are defined to improve a chiral separation in terms of resolution, analysis time, etc. or to induce separation when initially not obtained. The defined strategy proved its applicability and efficiency with the successful separation of a novel 20-compound test set. In a second stage, the method transfer from a conventional to an ultra-performance SFC system is investigated for the screening step of the separation strategy. The method transfer proved to be very easy and straightforward. Similar enantioresolution values, but slightly shorter analysis times were obtained on the ultra-performance equipment. Nevertheless, even more benefit may be expected in ultra-performance SFC when customized sub-2  $\mu\text{m}$  chiral stationary phases will become available.

<http://dx.doi.org/10.1016/j.chroma.2014.06.011>

### 351. Determination Of The Average Volumetric Flow Rate In Supercritical Fluid Chromatography

2014 - Journal of Chromatography A

Keywords: University of Tennessee, average volumetric flow rate, nitrous oxide, hold-up volume, separation science

**Abstract**

This work reviews and discusses controversies and errors made in the determination of the average volumetric flow rate of a compressible mobile phase forced to flow through a chromatographic column. Proper estimates of the volumetric flow rate, which obviously changes along the column, are keys to understanding the retention mechanism that takes place inside the column and to achieve repeatable and reproducible separations. Each step of the calculation process will be discussed in detail, including how to estimate the variations of the pressure and the temperature along the column. The determination of the average volumetric flow rate requires the knowledge of the average density of the mobile phase and of its mass flow rate. The calculations were carried out under various experimental conditions, including different column temperatures and inlet pressures. The estimated values of the volumetric flow rate are validated by the conversion of the retention times to the retention volumes of nitrous oxide peaks, which is valid since this compound is assumed to be non retained, which makes it a hold-up time marker. <http://dx.doi.org/10.1016/j.chroma.2014.02.078>

### 352. Coupling State-Of-The-Art Supercritical Fluid Chromatography And Mass Spectrometry: From Hyphenation Interface Optimization To High-Sensitivity Analysis Of Pharmaceutical Compounds

2014 - Journal of Chromatography A

Keywords: University of Geneva, interfacing approach, detection sensitivity, pharmaceutical

**Abstract**

The recent market release of a new generation of supercritical fluid chromatography (SFC) instruments compatible with state-of-the-art columns packed with sub-2 $\mu$ m particles (UHPSFC) has contributed to the reemergence of interest in this technology at the analytical scale. However, to ensure performance competitiveness of this technique with modern analytical standards, a robust hyphenation of UHPSFC to mass spectrometry (MS) is mandatory. UHPSFC-MS hyphenation interface should be able to manage the compressibility of the SFC mobile phase and to preserve as much as possible the chromatographic separation integrity. Although several interfaces can be envisioned, each will have noticeable effects on chromatographic fidelity, flexibility and user-friendliness. In the present study, various interface configurations were evaluated in terms of their impact on chromatographic efficiency and MS detection sensitivity. An interface including a splitter and a make-up solvent inlet was found to be the best compromise and exhibited good detection sensitivity while maintaining more than 75% of the chromatographic efficiency. This interface was also the most versatile in terms of applicable analytical conditions. In addition, an accurate model of the fluidics behavior of this interface was created for a better understanding of the influence of chromatographic settings on its mode of operation. In the second part, the most influential experimental factors affecting MS detection sensitivity were identified and optimized using a design-of-experiment approach. The application of low capillary voltage and high desolvation temperature and drying gas flow rate were required for optimal ESI ionization and nebulization processes. The detection sensitivity achieved using the maximized UHPSFC-ESI-MS/MS conditions for a mixture of basic pharmaceutical compounds showed 4- to 10-fold improvements in peak intensity compared to the best performance achieved by UHPLC-ESI-MS/MS with the same MS detector. <http://dx.doi.org/10.1016/j.chroma.2014.03.006>

### 353. The Modeling Of Overloaded Elution Band Profiles In Supercritical Fluid Chromatography

2014 - Journal of Chromatography A

Keywords: University of Tennessee, average volumetric flow rate, equilibrium dispersive model, separation science

**Abstract**

Three methods were used to analyze elution bands of methanol on silica, using pure CO<sub>2</sub> as the eluent. The results of these analyses were applied to calculate overloaded elution band profiles in supercritical fluid chromatography. The results obtained are compared. To ensure that the mobile

phase density varies widely along the column bed, high volumetric flow rates of the mobile phase (CO<sub>2</sub>) were applied to two columns packed with neat, porous silica. Then, even a slight error made in the determination of the isotherm parameters or during the numerical calculations should be magnified compared to those obtained with a low pressure drop along the column. During the determination of the isotherms of adsorption of methanol from liquid carbon dioxide onto silica, the inlet and outlet pressure of the column, the mass flow rate and the temperature were monitored continuously. Based on these parameters, overloaded elution bands were calculated numerically using three calculation methods. The results are compared with experimental ones. <http://dx.doi.org/10.1016/j.chroma.2014.01.034>

### **354. Combined Size Exclusion Chromatography, Supercritical Fluid Chromatography And Electrospray Ionization Mass Spectrometry For The Analysis Of Complex Aliphatic Polyesters**

2014 - Journal of Chromatography A

Keywords: University of Stellenbosch, aliphatic polyesters, chemical materials

#### **Abstract**

Aliphatic polyesters are complex products of polycondensation that are distributed regarding the degree of polycondensation, the end group functionality and the molecular topology. To address the molecular heterogeneity of polyesters based on phthalic acid and propylene glycol, for the first time the combination of SEC, SFC and ESI-MS have been used. In a first set of experiments, samples were fractionated by SEC and the collected fractions analyzed by SFC for a tentative assignment of the degrees of polycondensation. More conclusive results were obtained by semi-preparative SFC fractionation of the bulk samples and the subsequent analysis of the collected fractions by ESI-MS. The ESI-MS spectra of the SFC fractions provided detailed information on the presence of linear and cyclic oligomers, their degrees of polycondensation and their end groups. Information on the presence of propylene oxide oligomers was also obtained and it was shown how they were inserted in the polymer structures. Compared to previous work, the present approach provides significantly more detailed information on the molecular complexity of aliphatic polyesters. This is mainly due to the fact that SFC has been used as the second chromatographic dimension which is known to have superior separation capabilities.

<http://dx.doi.org/10.1016/j.chroma.2014.01.018>

### **355. Comparative Assessment Of Achiral Stationary Phases For High Throughput Analysis In Supercritical Fluid Chromatography**

2014 - Journal of Chromatography A

Keywords: Bristol Myers Squibb, residual silanols, ammonium acetate, separation science

#### **Abstract**

Supercritical fluid chromatography (SFC) using open bed fraction collection is becoming more widely used for purification of diverse collections of compounds for drug discovery. This application requires predictable chromatography on scale up from analytical to preparative conditions. We have discovered that the selectivities of many columns used for SFC change over time when ammonium acetate additive is present in the mobile phase as a result of changes in silanophilic interactions. This makes scale up predictions difficult. To address this challenge we have developed a nontraditional comprehensive column ranking. Our system is based on the long-term retention repeatability of basic drugs in ammonium acetate containing mobile phase. The decreases in retention over time were used as a measure of changing silanophilicity of the stationary phases and became the basis for a column ranking system. This system, along with results for 24 commonly used silica-based columns, is presented in this paper.

<http://dx.doi.org/10.1016/j.chroma.2014.01.060>

### **356. Ultra High Resolution SFC - MS As A High Throughput Platform For Metabolic Phenotyping: Application To Metabolic Profiling Of Rat And Dog Bile**

2014 - Journal of Chromatography B

Keywords: Waters, Imperial College, King's College, metabolic profiling, metabonomics, metabolomics, bile acids, bile metabolites, health science

**Abstract**

Ultra high resolution SFC-MS (on sub-2 $\mu$ m particles) coupled to mass spectrometry has been evaluated for the metabolic profiling of rat and dog bile. The selectivity of the SFC separation differed from that seen in previous reversed-phase UPLC-MS studies on bile, with the order of elution for analytes such as e.g., the bile acids showing many differences. The chromatography system showed excellent stability, reproducibility and robustness with relative standard deviation of less than 1% for retention time obtained over the course of the analysis. SFC showed excellent chromatographic performance with chromatographic peak widths in the order of 3s at the base of the peak. The use of supercritical fluid carbon dioxide as a mobile phase solvent also reduced the overall consumption of organic solvent by a factor of 3 and also reduced the overall analysis time by a factor of 30% compared to reversed-phase gradient LC. SFC-MS appear complementary to RPLC for the metabolic profiling of complex samples such as bile.

<http://dx.doi.org/10.1016/j.jchromb.2014.04.017>

### 357. Profiling Of Regioisomeric Triacylglycerols In Edible Oils By Supercritical Fluid Chromatography/Tandem Mass Spectrometry

2014 - Journal of Chromatography B

Keywords: Osaka University, Tsukishima Foods, Tokyo University of Marine Science and Technology, regioisomers, triacylglycerol, food

**Abstract**

In this study, supercritical fluid chromatography (SFC) coupled with triple quadrupole mass spectrometry was applied to the profiling of several regioisomeric triacylglycerols (TAGs). SFC conditions (column, flow rate, modifier) were optimized for the effective separation of TAGs. In the column test, a triacontyl (C30) silica gel reversed-phase column was selected to separate TAG regioisomers. Multiple reaction monitoring was used to selectively quantify each TAG. Then, the method was used to perform detailed characterization of a diverse array of TAGs in palm and canola oils. Seventy TAGs (C46:0-C60:2) of these oils were successfully analyzed as a result, and twenty isomeric TAG pairs were separated well. In particular, this method provided the fast and high resolution separation of six regioisomeric TAG pairs (PPLn/PLnP, PPL/PLP, PPO/POP, SPLn/SLnP, SPO/SOP, SSO/SOS-stearic acid (S, 18:0), oleic acid (O, 18:1), linoleic acid (L, 18:2), linolenic acid (Ln, 18:3), palmitic acid (P, 16:0)) in a short time (50min) as compared to high performance liquid chromatography. We were able to demonstrate the utility of this method for the analysis of regioisomeric TAGs in edible oils.

<http://dx.doi.org/10.1016/j.jchromb.2014.01.040>

### 358. Chiral Separation Of A Diketopiperazine Pheromone From Marine Diatoms Using Supercritical Fluid Chromatography

2014 - Journal of Chromatography B

Keywords: Friedrich Schiller University, Waters, University Gent, chiral separation, diketopiperazine, cyclodextrine, pheromone, natural products, health science

**Abstract**

The proline derived diketopiperazine has been identified in plants, insects and fungi with unknown function and was recently also reported as the first pheromone from a diatom. Nevertheless the stereochemistry and enantiomeric excess of this natural product remained inaccessible using direct analytical methods. Here we introduce a chiral separation of this metabolite using supercritical fluid chromatography/mass spectrometry. Several chromatographic methods for chiral analysis of the diketopiperazine from the diatom *Seminavis robusta* and synthetic enantiomers have been evaluated but neither gas chromatography nor high performance liquid chromatography on different chiral cyclodextrin phases were successful in separating the enantiomers. In contrast, supercritical fluid chromatography achieved baseline separation within four minutes of run time using amylose tris(3,5-dimethylphenylcarbamate) as stationary phase and 2-propanol/CO<sub>2</sub> as mobile phase. This very rapid chromatographic method in combination

with ESI mass spectrometry allowed the direct analysis of the cyclic dipeptide out of the complex sea water matrix after SPE enrichment. The method could be used to determine the enantiomeric excess of freshly released pheromone and to follow the rapid degradation observed in diatom cultures. Initially only trace amounts of c(d-Pro-d-Pro) were found besides the dominant c(l-Pro-l-Pro) in the medium. However the enantiomeric excess decreased upon pheromone degradation within few hours indicating that a preferential conversion and thus inactivation of the l-proline derived natural product takes place.

<http://dx.doi.org/10.1016/j.jchromb.2013.12.040>

### 359. Development Of A Supercritical Fluid Chromatography-Tandem Mass Spectrometry Method For The Determination Of Lacidipine In Beagle Dog Plasma And Its Application To A Bioavailability Study

2014 - Journal of Chromatography B

Keywords: Shenyang Pharmaceutical University, lacidipine, plasma, health science

#### Abstract

A simple, novel, rapid and sensitive supercritical fluid chromatography-tandem mass spectrometry (SFC-MS/MS) method was developed and validated for the determination of lacidipine in beagle dog plasma with nimodipine as internal standard. The method involved a simple liquid-liquid extraction method with tert-butyl methyl ether. The analytes were analyzed on an Acquity UPC(2) with a HSS C18 SB column (3mm×100mm, 1.8µm) set at 50°C. The mobile phase was carbon dioxide (≥99.99%) and methanol (92:8, v/v) at a flow rate of 2ml/min, the compensation solvent was methanol with 2% formic acid at a flow rate of 0.2ml/min and a total analysis time of 1.5min for each sample. The multiple reaction-monitoring mode was used for quantification of ion transitions at m/z 473.32→354.10 and 419.00→343.10 for lacidipine and internal standard, respectively. The linearity range of proposed method was 0.10-100ng/ml ( $r(2) \geq 0.9990$ ). The intra- and inter-day precision values were less than 15% and accuracy was from -0.83% to 3.27% at all quality control levels. The proposed method was successfully applied to a pharmacokinetic study of lacidipine in beagle dogs.

<http://dx.doi.org/10.1016/j.jchromb.2013.11.029>

### 360. Development And Validation Of A Supercritical Fluid Chromatography Method For The Direct Determination Of Enantiomeric Purity Of Provitamin B5 In Cosmetic Formulations With Mass Spectrometric Detection

2014 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: Orleans University, chiral separation, enantiomeric purity, dexpanthenol, cosmetics, chiralpak, adsorbex, chemical materials

#### Abstract

A rapid and efficient chiral supercritical fluid chromatography (SFC) method has been developed for the quantitative determination of panthenol enantiomers in cosmetic formulations (cream, lotion, wipe, and exfoliant). Indeed, the pharmacological effect only depends on the D form (Dexpanthenol) thus accurate measurement of its enantiomeric purity in formulated cosmetic products is of interest. The samples were prepared with liquid-liquid extraction followed by solid-phase extraction on Adsorbex amino cartridges. After testing several enantioselective columns in an attempt at reversing the elution order to have the minor enantiomer eluted first, the best separation of enantiomers and internal standard (N-acetyl-L-alanine) was achieved on a 3 µm-amylose-type immobilized polysaccharide chiral stationary phase (Chiralpak IA) in less than 6 min with a simple mobile phase comprising carbon dioxide and 11% methanol pumped at 2.3 mL/min, 25°C and 150 bar backpressure. Supercritical fluid chromatography coupled to both an optical diode-array detector and a user-friendly single-quadrupole mass spectrometer (Waters QDa) equipped with electrospray ionization source has been used. The on-line coupling ensures the technique to be more informative and improves detection sensitivity, as underivatized panthenol has a poor UV absorption. The limit of quantification (LOQ) achieved with single-ion recording was 0.5 µg/mL. The method was validated in terms of linearity, precision and accuracy and satisfactory results were obtained.

<http://dx.doi.org/10.1016/j.jpba.2014.09.036>



### 361. Preclinical Pharmacokinetic Evaluation Of A New Formulation Of A Bifendate Solid Dispersion Using A Supercritical Fluid Chromatography - Tandem Mass Spectrometry Method

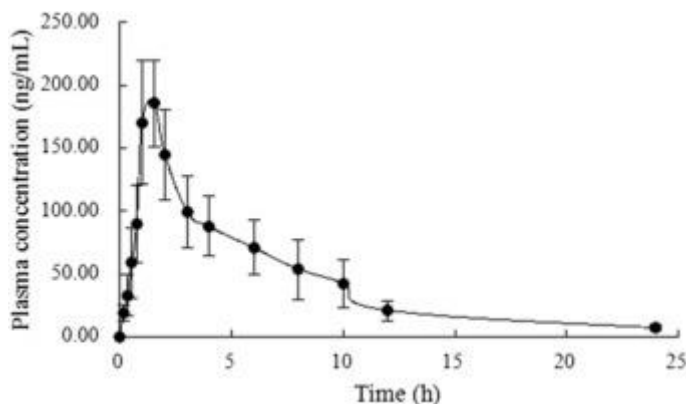
2014 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: Shenyang Pharmaceutical University, bifendate, pharmacokinetics, beagle dog plasma, health science

#### Abstract

In order to evaluate the pharmacokinetic characteristics of a new formulation of a bifendate solid dispersion in beagle dogs, a novel, sensitive and rapid supercritical fluid chromatography-tandem mass spectrometry (SFC-MS/MS) method was established and validated. Plasma samples were subjected to liquid-liquid extraction with ethyl acetate. Separation of bifendate and diazepam (internal standard, IS) was performed on an HSS C18 SB column (3×100mm, 1.8µm) with a mobile phase consisting of CO<sub>2</sub> (≥99.99%) - methanol (95:5, v/v) at a flow rate of 2mL/min and the compensation solvent was methanol with 2% formic acid at a flow rate of 0.2mL/min. A tandem triple quadrupole mass spectrometer was operated in multiple reaction monitoring (MRM) mode with an electrospray ionization (ESI) source. Quantification of the ion transitions was at m/z 419.2→387.0 and 284.5→193.2 for bifendate and IS, respectively. The method was sensitive with a lower limit of quantification (LLOQ) of 0.5ng/mL and linear over the concentration range 0.5-250ng/mL. All the validation data, such as precision, accuracy, extraction recovery and matrix effect, were all within acceptable criteria. The method has been successfully applied to a pharmacokinetic study of bifendate in beagle dogs after oral administration of a bifendate solid dispersion.

<http://dx.doi.org/10.1016/j.jpba.2014.05.030>



### 362. Robust Method Optimization Strategy—A Useful Tool For Method Transfer: The Case Of SFC

2014 - Journal of Pharmaceutical and Biomedical Analysis

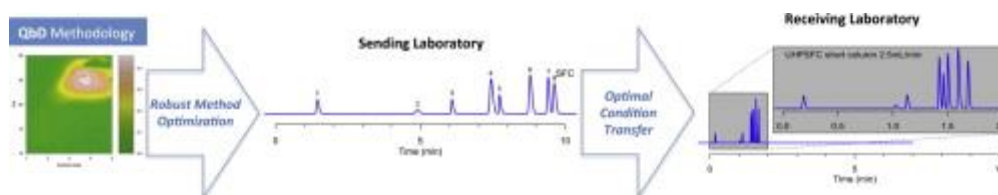
Keywords: University of Liege, QBD, design space, method optimization, inter-laboratory method transfer, separation science

#### Abstract

The concept of Quality by Design (QbD) is now well established in pharmaceutical industry and should be applied to the development of any analytical methods. In this context, the key concept of Design Space (DS) was introduced in the field of analytical method optimization. In chromatographic words, the DS is the space of chromatographic conditions that will ensure the quality of peaks separation, thus DS is a zone of robustness. In the present study, the interest of robust method optimization strategy was investigated in the context of direct method transfer from sending to receiving laboratory. The benefit of this approach is to speed up the method life cycle by performing only one quantitative validation step in the final environment of method use. A Supercritical Fluid Chromatography (SFC) method previously developed was used as a case study in this work. Moreover, the interest of geometric transfer was investigated simultaneously in order to stress a little bit more the transfer exercise and, by the way, emphasize the additional



benefit of DS strategy in this particular context. Three successful transfers were performed on two column geometries. In order to compare original and transferred methods, the observed relative retention times (RT) were modelled as a function of the predicted relative RT and of the method type (original or transferred). The observed relative RT of the original and transferred methods are not statistically different and thus the method transfer is successfully achieved thanks to the robust optimization strategy. Furthermore, the analytical method was improved considering analysis time (reduced five times) and peak capacity (increased three times). To conclude, the advantage of using a DS strategy implemented for the optimization and transfer of SFC method was successfully demonstrated in this work. <http://dx.doi.org/10.1016/j.jpba.2013.09.030>



### 363. Determination Of Coumarins In The Roots Of *Angelica Dahurica* By Supercritical Fluid Chromatography

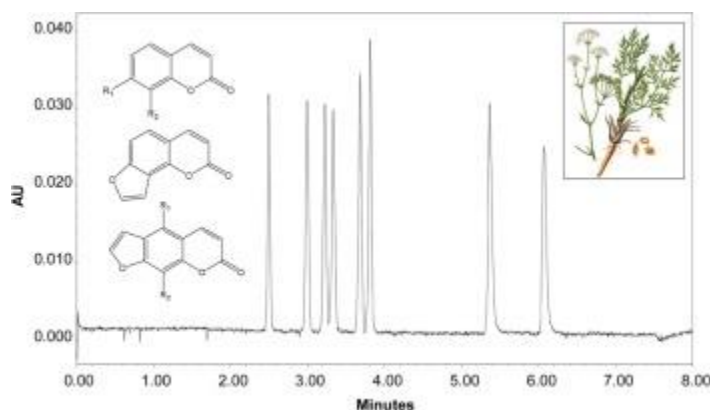
2014 - Journal of Pharmaceutical and Biomedical Analysis

Keywords: University of Innsbruck, ABPR, automated backpressure regulator, DGC, dense gas chromatography, HPGC, high pressure gas chromatography, SFC, supercritical fluid chromatography, SFE, supercritical fluid extraction, TCM, traditional Chinese medicine, TRPV1, transient receptor potential vanilloid type 1

#### Abstract

The fact that supercritical fluid chromatography (SFC) offers many desirable features is known for a long time. Yet, the number of applications on natural products is still limited, because robust and user-friendly instrumentation became available just a few years ago. As coumarins hardly have been studied by this technique we developed the first SFC assay for their determination in crude plant material. After method optimization eight standard compounds, including simple coumarins, linear and angular furanocoumarins, could be baseline separated in 6 min using an Acquity UPC<sup>2</sup> CSH Fluoro-Phenyl 1.7 μm column with supercritical CO<sub>2</sub>, methanol and diethylamine as mobile phase. Method validation confirmed that the assay is linear ( $R^2 \geq 0.9995$ ), precise (intra-day variation  $\leq 5.8\%$ ; inter-day variation  $\leq 4.4\%$ ) and accurate (recovery rates from 96.5 to 104.2%). Detection limits determined at 300 nm were below 2 ng on-column, and the method showed to be well suited for the analysis of coumarins in *Angelica dahurica* roots. It was observed that qualitative as well as quantitative composition vary significantly. In all samples Imperatorin (0.09–0.28%) was the major coumarin, followed either by Isoimperatorin or Oxypeucedanin; the total coumarin content ranged from 0.16 to 0.77%. The results were in good agreement to published data, so that because of its speed and green nature SFC is definitely an interesting alternative for the analysis of this important class of natural products.

<http://dx.doi.org/10.1016/j.jpba.2016.07.014>



### 364. Chromatographic Resolution Of Closely Related Species: Drug Metabolites And Analogs

2014 - Journal of Separation Science

Keywords: Merck, method development, high throughput analysis, drugs, metabolites, carbamazepine, methylated xanthine, steroid hormone, nicotine, morphine, GreenSep Ethyl, Luna HILIC, ChiralPak, pharmaceutical

#### Abstract

In this study, we investigate the separation of a variety of mixtures of drugs, metabolites, and related analogs including representatives of the carbamazepine, methylated xanthine, steroid hormone, nicotine, and morphine families using several automated chromatographic method development screening systems including ultra high performance liquid chromatography, core-shell HPLC, achiral supercritical fluid chromatography (SFC), and chiral SFC. Of the 138 column and mobile phase combinations examined for each mixture, a few chromatographic conditions afford the best overall performance, with a single achiral SFC method (4.6 × 250 mm, 3.0 μm GreenSep Ethyl Pyridine, 25 mM isobutylamine in methanol/CO<sub>2</sub>) affording good separation for all samples. Four of these mixtures were also resolved by achiral SFC on the Luna HILIC and chiral SFC Chiralpak IB columns using methanol or ethanol with 25 mM isobutylamine as polar modifiers. Modifications of standard chromatography screening conditions afforded fast separation methods (from 1 to 5 min) for baseline resolution of all components of each of these challenging sets of closely related compounds.

<http://dx.doi.org/10.1002/jssc.201400038>

### 365. Development Of An Automated Dual-Mode Supercritical Fluid Chromatography And Reversed-Phase Liquid Chromatography Mass - Directed Purification System For Small-Molecule Drug Discovery

2014 - Journal of Separation Science

Keywords: Theravance, chiral separation, achiral separation, pharmaceutical

#### Abstract

We report the development of a dual-mode mass-directed supercritical fluid chromatography and reversed-phase liquid chromatography purification system. The addition of a third pump allows for flexible mobile phase control between the two techniques, and enables operation of either chromatography mode within minutes by activation of a set of switching valves on a single system. Software control, fluidic pathways, interface to the mass spectrometer, and fraction collection have been modified for compatibility between both separation methods. The conditioning solvent and tuning parameters for the mass spectrometer were adjusted to achieve an ideal signal trace in either mode with good linearity ( $r^2 > 0.970$ ) over a range of concentrations and minimal noise for accurate peak detection and isolation. The registration success rate is 90% and overall sample recovery for either technique is 80–90%. Combining two orthogonal separation and purification modes in one single system has improved the purification throughput of complex mixtures and has been a valuable, cost-saving tool in our laboratory.

<http://dx.doi.org/10.1002/jssc.201301366>

### 366. Supercritical Fluid Extraction And Convergence Chromatographic Determination Of Parthenolide In *Tanacetum Parthenium* L.: Experimental Design, Modeling And Optimization

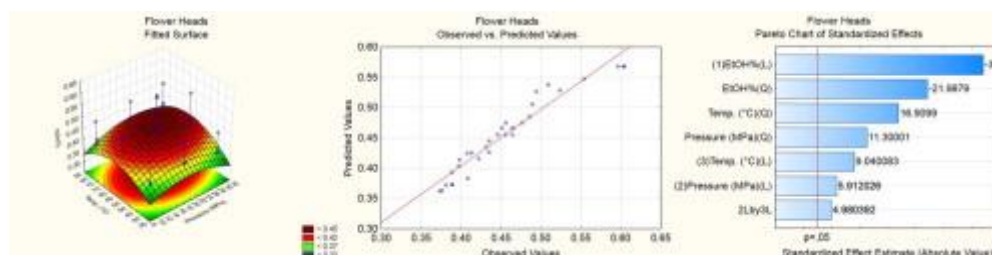
2014 - The Journal of Supercritical Fluids

Keywords: Semmelweis University, medicinal plant, sesquiterpene-γ-lactones, flavonoids, volatile oil, parthenolide, natural products, health science

#### Abstract

Feverfew (*Tanacetum parthenium* L., Asteraceae) is a perennial medicinal plant which has been used to alleviate the symptoms of migraines, headaches and rheumatoid arthritis. The herb contains various potentially active constituents such as sesquiterpene-γ-lactones, flavonoids and volatile oil. The main sesquiterpene-lactone in feverfew is parthenolide which is considered to be responsible for the therapeutical effects. Supercritical CO<sub>2</sub> extraction was carried out at different

pressures (10–30 MPa), temperatures (40–80 °C) and co-solvent contents (0–10% ethanol) in order to study the extraction yield and the parthenolide recovery of the extracts. Leaves collected before and during flowering and flower heads were investigated. A factorial experiment using a full  $3^3$  design was followed during the experiments and response surface methodology was implemented to analyze the influence of the variables and optimize the extraction. The critical values of parthenolide content were found to be 7% EtOH, 22 MPa and 64 °C in case of all three samples. It was determined, that the optimal conditions of the extraction, where the maximum parthenolide content and extract yield can be reached, do not coincide. The highest yield of parthenolide was obtained in the flower heads (0.604 wt.%).  
<http://dx.doi.org/10.1016/j.supflu.2014.07.029>



### 367. Determination Of Niacin And Its Metabolites Using Supercritical Fluid Chromatography Coupled To Tandem Mass Spectrometry

2014 - Mass Spectrometry, Journal of the Mass Spectrometry Society of Japan

Keywords: Osaka University, water soluble vitamin, vitamin B, hydrophilic metabolites, biofluid, pharmaceutical

#### Abstract

Niacin, a water-soluble vitamin belonging to the vitamin B group, has been known to cause various problems in the human body when deficient. The vitamin is derived from the diet and afterwards, niacin and its metabolites are secreted in blood or urine. It can be analyzed using liquid chromatography (LC) coupled to mass spectrometry, but niacin and its metabolites are very polar compounds. Recently, supercritical fluid chromatography (SFC) is gaining attention for polar compound analysis. To our best knowledge, the report on the analysis of endogenous-very hydrophilic metabolites in biofluids by SFC has not been found. In this study, we investigated whether the separation of hydrophilic metabolites in biofluids is achievable by SFC. In addition, we also examined the applicability of SFC coupled to MS in extrapolating unknown metabolites by means of spectra information. As a result, an analysis method to quantify the target compounds using SFC/MS/MS was constructed for niacin and its metabolites. Additional putative metabolites from niacin were also identified using the MS fragmentation spectra in plasma and urine. Consequently, the method using SFC/MS/MS allowed for the analysis of polar compounds with low log P ranging from  $-3.7$  to  $0.29$ . This study is the first report of the separation of niacin and its seven metabolites in human urine and these results showed that SFC-MS/MS can be an alternative technique for hydrophilic metabolite analysis.

<http://dx.doi.org/10.5702/massspectrometry.A0029>

### 368. Review Article: Support Of Academic Synthetic Chemistry Using Separation Technologies From The Pharmaceutical Industry

2014 - Organic and Biomolecular Chemistry

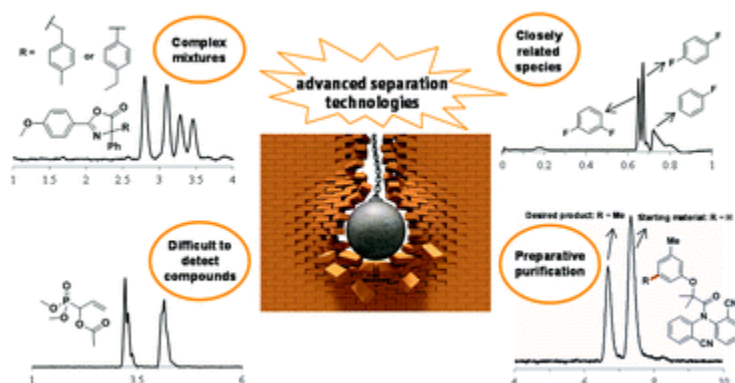
Keywords: Merck, University of Pennsylvania, Harvard University, University of Missouri, Scripps Research Institute, achiral screening, chiral screening, chiral loading and purification, pharmaceutical

#### Abstract

The use of state-of-the-art separation tools from the pharmaceutical industry for addressing intractable separation problems from academic synthetic chemistry is evaluated, showing fast and useful results for the resolution of complex mixtures, separation of closely related components, visualization of difficult to detect compounds and purification of synthetic intermediates. Some

recommendations for potential near term deployment of separation tools within academia and the evolution of next generation separation technologies are discussed.

<http://dx.doi.org/10.1039/C3OB42195C>



### 369. Ultra-Fast Separation Of Estrogen Steroids Using Subcritical Fluid Chromatography On Sub-2-Micron Particles

2014 - Talanta

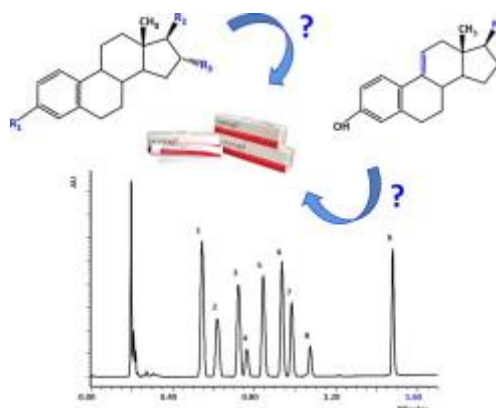
Keywords: Charles University, Steroids, estrogens, health science

#### Abstract

Estrogen steroids, represented by estradiol and its related substances, include both structurally very close and simultaneously different analogs. Their separation still remains an analytical challenge. Subcritical fluid chromatography (SbFC) on sub-2-micron particles was found to be an appropriate tool to obtain fast and efficient separation of nine target analytes. Among the four tested stationary phases charged hybrid modified with PFP (pentafluorophenyl) moiety was found to be the most convenient providing the fastest separation within 1.6 min using quick gradient elution with carbon dioxide and methanol as an organic modifier. However, complete separation was obtained also on other tested phases including bare hybrid stationary phase, hybrid stationary phase modified with 2-EP (2-ethylpyridine) and also C18, which is less typical in SbFC. The baseline separation on the latter columns was achieved by means of a temperature increase, a change in organic modifier type and gradient time increase respectively.

Quantitative performance was evaluated at optimized conditions and method validation was accomplished. Excellent repeatability of both retention times (RSD<0.15%) and peak areas (RSD<1%) was observed. The method was linear in the range of 1.0–1000.0 µg/ml for all steroids with the lowest calibration point being an LOQ, except for  $\Delta$ -derivatives, that provided better sensitivity and thus LOQ of 0.5 µg/ml. The sensitivity was sufficient for the analysis of real samples although it was still five times lower compared to UHPLC-UV experiments.

<http://dx.doi.org/10.1016/j.talanta.2013.12.056>



### 370. Simultaneous Determination Of 17 Disperse Dyes In Textile By Ultra-High Performance Supercritical Fluid Chromatography Combined With Tandem Mass Spectrometry

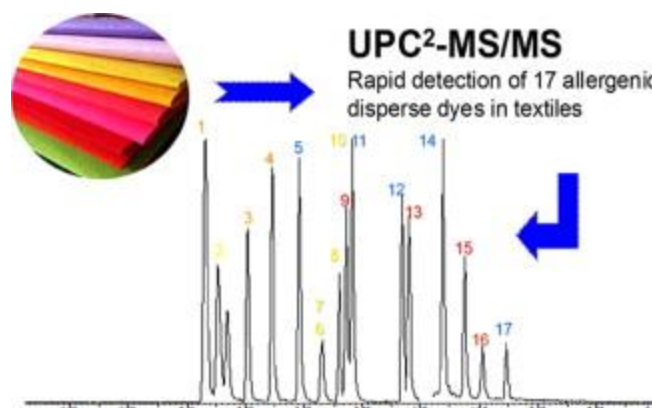
2014 - Talanta

Keywords: Beijing University of Chemical Technology, dyes, textiles, BEH, BEH 2-ethyl-pyridine, HSS C18 SB and CSH fluorophenyl, chemical materials

#### Abstract

A simple, highly sensitive and fast procedure for the control of 17 allergenic and prohibited disperse dyes in textile products was optimized. The method was based on ultrasound assisted extraction of textile samples with 10 mL of methanol under controlled conditions (30 min, 70°C). The extracts were analyzed by the ultra-high performance supercritical fluid chromatography (UHPSFC) system coupled with triple quadrupole tandem mass spectrometry (MS/MS). Four stationary phases (BEH, BEH 2-ethyl-pyridine, HSS C18 SB and CSH fluorophenyl) were screened as well as analytical conditions (modifier percentage, backpressure and column temperature) were investigated to improve the separation. All 17 disperse dyes were simultaneously separated and determined by UHPSFC-MS/MS in 5 min. The dyes were monitored via the ESI(+) ionization method and quantified by 3-channel multiple reaction monitoring (MRM). The calibrations were performed and good linear relationship ( $R \geq 0.99$ ) was observed within the concentration range of 2-50  $\mu\text{g mL}^{-1}$ . Satisfactory recoveries (70.55-103.03%) of all the disperse dyes spiked with standards at different levels were demonstrated. This is the first report on the simultaneous analysis of disperse dyes using UHPSFC-MS/MS.

<http://dx.doi.org/10.1016/j.talanta.2014.03.055>



### 371. Synthesis Of Dopamine D<sub>2</sub>/D<sub>3</sub> Receptor Agonist (+)-PHNO Via Super Critical Fluid Chromatography: Preliminary PET Imaging Study With [3-<sup>11</sup>C]-(+)-PHNO

2014 - Tetrahedron Letters

Keywords: Massachusetts General Hospital, Harvard Medical School, Waters, PHNO, Carbon-11, dopamine D<sub>3</sub> agonist, [<sup>11</sup>C]methyl iodide, brown fat, health science,

#### Abstract

Carbon-11 labeled (+)-4-[1-<sup>11</sup>C]propyl-3,4,4a,5,6,10b-hexahydro-2H-naphtho[1,2-b][1,4]oxazin-9-ol ([1-<sup>11</sup>C]-(+)-PHNO) is a dopamine D<sub>3</sub>-preferring agonist radiopharmaceutical used for medical imaging by positron emission tomography (PET). We report the synthesis of (+)-PHNO using supercritical fluid chromatography for enantiomeric resolution of its norpropyl derivative, HNO, followed by propylation. (+)-HNO was used to prepare the radiolabeling precursor, (+)-trans-4-acetyl-9-triisopropylsilyloxy-2,3,4a,5,6,10b-hexahydro-4H-naphth[1,2b][1,4]oxazine, in 12 steps. Modifications to the labeling procedure were made to ensure consistent preparation of [3-<sup>11</sup>C]-(+)-PHNO via [<sup>11</sup>C]CH<sub>3</sub>I. A preliminary PET imaging study was carried out with this tracer in an attempt to image dopamine receptors in brown adipose tissue (brown fat) in vivo.

<http://dx.doi.org/10.1016/j.tetlet.2013.11.113>

### 372. The Use Of Columns Packed With Sub-2- $\mu\text{m}$ Particles In Supercritical Fluid Chromatography

2014 - TrAC Trends in Analytical Chemistry

Keywords: University of Geneva, isopycnic plot, kinetic plot, orthogonal selectivity, separation science Sub-2  $\mu\text{m}$  particle, Supercritical fluid chromatography (SFC), UHPSFC-MS, Ultra-high-performance supercritical fluid chromatography (UHPSFC), Ultra-high-performance liquid chromatography (UHPLC), van Deemter representation

#### **Abstract**

The development of greener analytical techniques is a topic of great interest and in this context, supercritical fluid chromatography (SFC) is making an interesting comeback. The present review focuses on the latest developments of this technique. Improvements brought to the chromatographic systems and requirements to achieve full compatibility with columns packed with sub-2  $\mu\text{m}$  particles (UHPSFC) are discussed. A thorough kinetic evaluation made using van Deemter representations, isopycnic and kinetic plots shows that performance achieved with state-of-the-art UHPSFC hardware and columns is comparable to that obtained in UHPLC. Orthogonal selectivity compared to reversed phase LC (RPLC) and extended selectivity modulation possibilities achievable in supercritical conditions using different stationary phase chemistries are presented. Finally, current applications of UHPSFC and its different hyphenation possibilities including mass spectrometry (MS) are also reviewed, in the hope of helping chromatography users to have a new look on the possibilities offered by this technique.

<http://dx.doi.org/10.1016/j.trac.2014.06.023>



## 2013 Publications

### 373. Chromatographic Resolution Of Closely Related Species In Pharmaceutical Chemistry: Dehalogenation Impurities And Mixtures Of Halogen Isomers

December 2013 - Analytical Chemistry

Keywords: Merck, halogen isomers, dehalogenated isosteres, Hypersil Gold PFP, Chiralcel, Chiralpak, Zorbax, pharmaceutical

#### Abstract

In recent years, the use of halogen-containing molecules has proliferated in the pharmaceutical industry, where the incorporation of halogens, especially fluorine, has become vitally important for blocking metabolism and enhancing the biological activity of pharmaceuticals. The chromatographic separation of halogen-containing pharmaceuticals from associated isomers or dehalogenation impurities can sometimes be quite difficult. In an attempt to identify the best current tools available for addressing this important problem, a survey of the suitability of four chromatographic method development platforms (ultra high-performance liquid chromatography (UHPLC), core shell HPLC, achiral supercritical fluid chromatography (SFC) and chiral SFC) for separating closely related mixtures of halogen-containing pharmaceuticals and their dehalogenated isosteres is described. Of the 132 column and mobile phase combinations examined for each mixture, a small subset of conditions were found to afford the best overall performance, with a single UHPLC method (2.1 × 50 mm, 1.9 μm Hypersil Gold PFP, acetonitrile/methanol based aqueous eluents containing either phosphoric or perchloric acid with 150 mM sodium perchlorate) affording excellent separation for all samples. Similarly, a survey of several families of closely related halogen-containing small molecules representing the diversity of impurities that can sometimes be found in purchased starting materials for synthesis revealed chiral SFC (Chiralcel OJ-3 and Chiralpak IB, isopropanol or ethanol with 25 mM isobutylamine/carbon dioxide) as well as the UHPLC (2.1 × 50 mm, 1.8 μm ZORBAX RRHD Eclipse Plus C18 and the Gold PFP, acetonitrile/methanol based aqueous eluents containing phosphoric acid) as preferred methods.

<http://dx.doi.org/10.1021/ac403376h>

### 374. Development Of Supercritical Fluid (Carbon Dioxide) Based Ultra Performance Convergence Chromatographic Stability Indicating Assay Method For The Determination Of Clofarabine In Injection

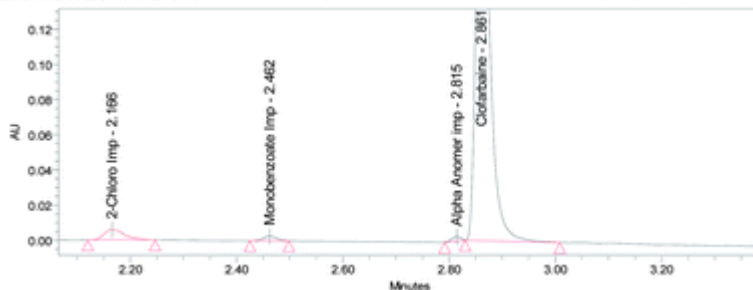
2013 - Analytical Methods

Keywords: Mylan Labs, clofarabine, stability indicating method, BEH 2-EP, pharmaceutical

#### Abstract

The present study reports the development and validation of a stability indicating assay method for clofarabine in injection on a UPC<sup>2</sup>™ (ultra performance convergence chromatography) instrument, which utilizes the unrealized potential of supercritical fluid chromatography. The use of UPC<sup>2</sup>™ provides a single viable technique that is a sustainable, reduced cost, and green technology that lowers the use of organic solvents. Based on this advantage, we explored a simple and robust method in order to increase sample throughput and productivity to quantify clofarabine in the presence of its potential impurities and other degradants. The separation was achieved on a BEH-2-ethyl pyridine (BEH 2EP) column (100 mm × 3.0 mm I.D. with an average pore diameter of 1.7 μm) by using methanol as a co-solvent and carbon dioxide as a mobile phase in the ratio of 30 : 70. The detection is carried out at a wavelength of 254 nm. We are able to achieve the separation of clofarabine from its potential impurities and other degradants in less than 6 minutes with a low amount of solvent consumption. The new method is validated in accordance with the ICH-guidelines and exhibited good intra- and inter-day precision, accuracy and linearity ( $r^2 \geq 0.999$ ) over a range of 50% to 150% of target concentration.

<http://dx.doi.org/10.1039/C3AY41561A>



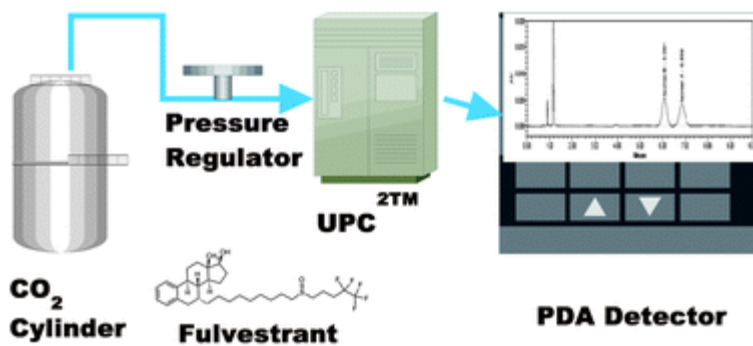
### 375. Supercritical Fluid (Carbon Dioxide) Based Ultra Performance Convergence Chromatography For The Separation And Determination Of Fulvestrant Diastereomers

2013 - Analytical Methods

Keywords: Mylan Labs, fulvestrant diastereomers, stability indicating method, BEH 2-EP, pharmaceutical

#### Abstract

UltraPerformance convergence chromatography (UPC<sup>2</sup>™) is a new category of separation science which utilizes the unrealized potential of the supercritical chromatography phenomenon. UPC<sup>2</sup>™ is a stand-alone, viable technique that is cost effective, sustainable, and uses green technology that lowers the use of organic solvents. Based on this advantage, we explored a simple and robust supercritical liquid-based UPC<sup>2</sup> method in order to increase sample throughput and productivity to quantify the diastereomers of fulvestrant. The two isomers of fulvestrant were well separated on a chiral column (150 mm × 4.6 mm, I.D.) by applying a mixture of methanol and acetonitrile (9.5 : 0.5) as the co-solvent of the mobile phase of carbon dioxide (75%). The detection was carried out at 280 nm. We were able to achieve a three-fold reduction in retention with an isocratic mode as compared to the United States Pharmacopoeias (USP) normal phase method. This new method was validated in accordance with the ICH guidelines; it exhibited good intra- and inter-day accuracy, precision, and the results were linear over a range of 25% to 150% of the target concentration. The method could be successfully applied for the determination of the diastereomeric ratio of fulvestrant as an API and in fulvestrant injectable finished products. <http://dx.doi.org/10.1039/C3AY40802G>



### 376. Organocatalytic Enantioselective Cycloaddition Reactions Of Dienamines With Quinones

2013 - Chemistry, A European Journal

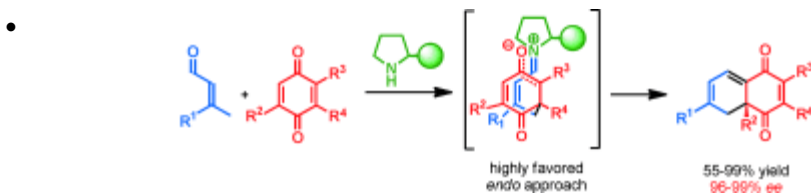
Keywords: Aarhus University, organocatalysis, quinones, separation science

#### Abstract

Matching catalyst and substrate: Organocatalytic cycloaddition between dienamines and 1,4-benzo- or 1,4-naphthoquinones affords biologically interesting dihydronaphtho- and dihydroanthraquinone core structures. The enantioselectivity of this new reaction is ensured by a

steric shielding catalyst and carefully selecting substrates that greatly favor the *endo* approach (see scheme) due to electrostatic interactions in the zwitterionic intermediate.

<http://dx.doi.org/10.1002/chem.201303526>



### 377. Breaking Symmetry With Symmetry: Bifacial Selectivity In The Asymmetric Cycloaddition Of Anthracene Derivatives

2013 - Chemistry, A European Journal

Keywords: Aarhus University, anthracene, separation science

#### Abstract

A new catalytic strategy for the activation of anthracene derivatives has been developed. From symmetrical starting materials, enantioselective cycloaddition reactions can be achieved by employing a  $C_2$ -symmetric aminocatalyst. This selectivity is due to the gain or loss of conjugation between the enamine and the anthracene in the two transition-state structures. This methodology is demonstrated in 14 examples with 70–96 % yield and 76–95 % ee.

<http://dx.doi.org/10.1002/chem.201300142>

### 378. Chromatographic Separation And Assignment Of Absolute Configuration Of Hydroxywarfarin Isomers

2013 - Chirality

Keywords: Merck, hydroxywarfarin isomers, chiral SFC, human liver microsomes, pharmaceuticals

#### Abstract

The absolute configuration of several hydroxywarfarin isomers was assigned using a comparison of elution order on chiral stationary phases, optical rotation, and circular dichroism (CD) spectra, with confirmation of assignments made by comparison between experimental and calculated CD spectra and selective synthesis of hydroxywarfarin isomers from enantiopure warfarin using human liver microsomes.

<http://dx.doi.org/10.1002/chir.22274>

### 379. Improved Chiral SFC Screening For Analytical Method Development

2013 - Chirality

Keywords: Merck, chiral sfc, method development, Chiralpak, Chiralcel, Phenomenex, pharmaceutical

#### Abstract

In this study we describe the evaluation of a recently developed supercritical fluid chromatography (SFC) instrument for automated chiral SFC method development. The greatly improved gradient dwell volume and liquid flow control of the new instrument in combination with the use of shorter columns containing smaller stationary phase particles affords chiral SFC method development that is faster and more universal than previous systems.

<http://dx.doi.org/10.1002/chir.22218>

### 380. Application Of 'Omics Technologies To Biomarker Discovery In Inflammatory Lung Diseases

2013 - European Respiratory Journal

Keywords: Karolinska Institute, omics, biomarker discovery, lung disease, health science

#### Abstract

Inflammatory lung diseases are highly complex in respect of pathogenesis and relationships between inflammation, clinical disease and response to treatment. Sophisticated large-scale analytical methods to quantify gene expression (transcriptomics), proteins (proteomics), lipids (lipidomics) and metabolites (metabolomics) in the lungs, blood and urine are now available to identify biomarkers that define disease in terms of combined clinical, physiological and pathological abnormalities. The aspiration is that these approaches will improve diagnosis, *i.e.* define pathological phenotypes, and facilitate the monitoring of disease and therapy, and also, unravel underlying molecular pathways. Biomarker studies can either select predefined biomarker(s) measured by specific methods or apply an “unbiased” approach involving detection platforms that are indiscriminate in focus. This article reviews the technologies presently available to study biomarkers of lung disease within the ‘omics field. The contributions of the individual ‘omics analytical platforms to the field of respiratory diseases are summarised, with the goal of providing background on their respective abilities to contribute to systems medicine-based studies of lung disease.

<http://dx.doi.org/10.1183/09031936.00078812>

### 381. Asymmetric Organocatalytic Thio-Diels–Alder Reactions Via Trienamine Catalysis

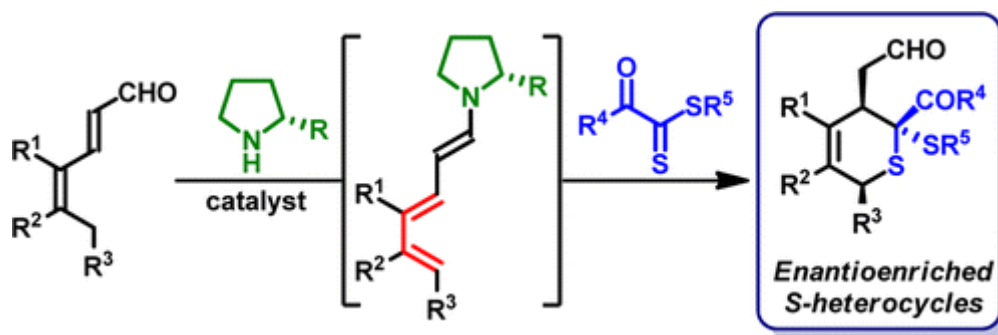
2013 - Journal of the American Chemical Society

Keywords: Aarhus University, enantioselective synthesis, diastereoselective synthesis, separation science

#### Abstract

We report a new process to access highly enantioenriched sulfur-based heterocycles by an asymmetric catalytic thio-Diels–Alder reaction. Thiocarbonyls are challenging heterodienophiles in enantioselective Diels–Alder reactions, due to their inherent high reactivity and their poor ability to coordinate to chiral catalysts. We successfully circumvented these problems by employing a different strategy, which explores the use of *in situ* generated catalyst-bound dienes. Synthetically useful dihydrothiopyrans as well as other bi- and tricyclic sulfur-containing heterocycles are formed in high yields and high to excellent selectivities. DFT calculations were performed to examine the mechanism of the developed reaction. Furthermore, a series of synthetic transformations of the optically active sulfur-based heterocycles are presented.

<http://dx.doi.org/10.1021/ja4007244>



### 382. Characterization Of Five Chemistries And Three Particle Sizes Of Stationary Phases Used In Supercritical Fluid Chromatography

2013 - Journal of Chromatography A

Keywords: University of Orleans, linear solvation energy parameters, BEH, XSelect, HSS, separation science

#### Abstract

Sub-2-microns particles employed as supporting phases are known to favor column efficiency. Recently a set of columns based on sub-2-microns particles for use with supercritical fluid mobile phases have been introduced by Waters. Five different stationary phase chemistries are available: BEH silica, BEHEthyl-pyridine, X Select CSH Fluorophenyl, HSS C18 SB and BEH Shield RP18. This

paper describes the characterization of 15 stationary phases, the five different chemistries, and three particle sizes, 1.7 (or 1.8), 3.5 and 5 microns, with the same carbon dioxide–methanol mobile phase and a set of more than a hundred compounds. The interactions established in the 15 different chromatographic systems used in supercritical fluid chromatography (SFC) are assessed with linear solvation energy relationships (LSERs). The results show the good complementarity of the five column chemistries, and their comparative location inside a classification map containing today around 70 different commercial phases. Among the five different chemistries, the HSS C18 SB phase displays a rather unusual behavior in regards of classical C18 phases, as it displays significant hydrogen–bonding interactions. Besides, it appears, as expected, that the BEH Ethyl–pyridine phase has weak interactions with basic compounds. The effect of particle size was studied because smaller particles induce increased inlet and internal pressure. For compressible fluids, this pressure change modifies the fluid density, i.e. the apparent void volume and the eluting strength. These changes could modify the retention and the selectivity of compounds in the case of method trans-fer, by using different particle sizes, from 5 down to 1.7  $\mu\text{m}$ . A hierarchical cluster analysis shows that stationary phase clusters were based on the phase chemistry rather than on the particle size, meaning that method transfer from 5 to 1.7 microns can be achieved in the subcritical domain i.e. by using a weakly compressible fluid.  
<http://dx.doi.org/10.1016/j.chroma.2013.10.037>

### 383. Accurate On-Line Mass Flow Measurements In Supercritical Fluid Chromatography

2013 - Journal of Chromatography A

Keywords: University of Tennessee, Waters, separation science

#### Abstract

This work demonstrates the possible advantages and the challenges of accurate on-line measurements of the CO<sub>2</sub> mass flow rate during supercritical fluid chromatography (SFC) operations. Only the mass flow rate is constant along the column in SFC. The volume flow rate is not. The critical importance of accurate measurements of mass flow rates for the achievement of reproducible data and the serious difficulties encountered in supercritical fluid chromatography for its assessment were discussed earlier based on the physical properties of carbon dioxide. In this report, we experimentally demonstrate the problems encountered when performing mass flow rate measurements and the gain that can possibly be achieved by acquiring reproducible data using a Coriolis flow meter. The results obtained show how the use of a highly accurate mass flow meter permits, besides the determination of accurate values of the mass flow rate, a systematic, constant diagnosis of the correct operation of the instrument and the monitoring of the condition of the carbon dioxide pump.

<http://dx.doi.org/10.1016/j.chroma.2013.10.041>

### 384. Maximizing Kinetic Performance In Supercritical Fluid Chromatography Using State-Of-The-Art Instruments

2013 - Journal of Chromatography A

Keywords: University of Geneva, Genentech, extra-column band broadening, kinetic performance, separation science

#### Abstract

Recently, there has been a renewed interest in supercritical fluid chromatography (SFC), due to the introduction of state-of-the-art instruments and dedicated columns packed with small particles. However, the achievable kinetic performance and practical possibilities of such modern SFC instruments and columns has not been described in details until now. The goal of the present contribution was to provide some information about the optimal column dimensions (i.e. length, diameter and particle size) suitable for such state-of-the-art systems, with respect to extra-column band broadening and system upper pressure limit. In addition, the reliability of the kinetic plot methodology, successfully applied in RPLC, was also evaluated under SFC conditions. Taking into account the system variance, measured at  $\sim 85\mu\text{L}^2$ , on modern SFC instruments, a column of 3mm I.D. was ideally suited for the current technology, as the loss in efficiency remained reasonable (i.e. less than 10% decrease for  $k>6$ ). Conversely, these systems struggle with 2.1mm I.D. columns (55% loss in  $N$  for  $k=5$ ). Regarding particle size, columns packed with  $5\mu\text{m}$  particles

provided unexpectedly high minimum reduced plate height values ( $h_{min}=3.0-3.4$ ), while the 3.5 and 1.7 $\mu\text{m}$  packing provided lower reduced plate heights  $h_{min}=2.2-2.4$  and  $h_{min}=2.7-3.2$ , respectively. Considering the system upper pressure limit, it appears that columns packed with 1.7 $\mu\text{m}$  particles give the lowest analysis time for efficiencies up to 40,000-60,000 plates, if the mobile phase composition is in the range of 2-19% MeOH. The 3.5 $\mu\text{m}$  particles were attractive for higher efficiencies, particularly when the modifier percentage was above 20%, while 5 $\mu\text{m}$  was never kinetically relevant with modern SFC instruments, due to an obvious limitation in terms of upper flow rate value. The present work also confirms that the kinetic plot methodology could be successfully applied to SFC, without the need for isopycnic measurements, as the difference in plate count between predicted and experimental values obtained by coupling several columns in series (up to 400mm) was on average equal to 3-6% and with a maximum of 13%.  
<http://dx.doi.org/10.1016/j.chroma.2013.09.039>

### 385. Supercritical Fluid Chromatography In Food Analysis

2013 - Journal of Chromatography A

Keywords: University of Valladolid, lipid, carotenoids, fat soluble vitamins, food

#### Abstract

In the last years, supercritical fluid chromatography (SFC) has increased its acceptance between scientists. The unique selectivity, short analysis times, low consumption of organic solvents as well as the improvements in instrumentation have contributed to expand its use. These characteristics make SFC a powerful tool when food analysis requires individualized evaluation of several compounds in very complex samples. In this work, the advantages and main applications of SFC in food analysis are reviewed, focusing special attention onto analytical and preparative separations.  
<http://dx.doi.org/10.1016/j.chroma.2013.07.022>

### 386. Determination Of Adsorption Isotherms In Supercritical Fluid Chromatography

2013 - Journal of Chromatography A

Keywords: Karlstad University, adsorption isotherms, perturbation peak method, retention time method, inverse method, separation science

#### Abstract

In this study we will demonstrate the potential of modern integrated commercial analytical SFC-systems for rapid and reliable acquisition of thermodynamic data. This will be done by transferring the following adsorption isotherm determination methods from liquid chromatography (LC) to supercritical fluid chromatography (SFC): Elution by Characteristic Points (ECP), the Retention Time Method (RTM), the Inverse Method (IM) and the Perturbation Peak (PP) method. In order to transfer these methods to SFC in a reliable, reproducible way we will demonstrate that careful system verification using external sensors of mass flow, temperature and pressure are needed first. The adsorption isotherm data generated by the different methods were analyzed and compared and the adsorption isotherms ability to predict new experimental elution profiles was verified by comparing experiments with simulations. It was found that adsorption isotherm data determined based on elution profiles, i.e., ECP, IM and RTM, were able to accurately predict overloaded experimental elution profiles while the more tedious and time-consuming PP method, based on small injections on concentration plateaus, failed in doing so.  
<http://dx.doi.org/10.1016/j.chroma.2013.09.007>

### 387. Strong Cation Exchange Chiral Stationary Phase – A Comparative Study In High-Performance Liquid Chromatography And Subcritical Fluid Chromatography

2013 - Journal of Chromatography A

Keywords: University of Vienna, Waters, Institute of Chemical Technology, enantiomer separation, chiral cation exchange, transition buffer salts, separation science

#### Abstract

The performance of a strong cation exchange-type (SCX) chiral stationary phase (CSP) was evaluated with subcritical fluid chromatography (subFC) and high performance liquid



chromatography (HPLC). The chromatographic conditions in subFC were optimized by changing the amount of polar organic modifier, concentration of a basic additive in the modifier, system pressure and temperature. In this way the concentration of in situ formed transient ionic species could be varied. The gradual change of the concentration of the transient buffer, i.e. gradient elution conditions in subFC, was found beneficial for separation of a mixture of racemic compounds. The strength and amount of the in situ formed buffer was estimated on the basis of comparative experiments in subSFC and HPLC.

<http://dx.doi.org/10.1016/j.chroma.2013.08.037>

### 388. In-Depth Characterization Of Six Cellulose Tris-(3,5-Dimethylphenylcarbamate) Chiral Stationary Phases In Supercritical Fluid Chromatography

2013 - Journal of Chromatography A

Keywords: University of Orleans, Bristol Myers Squibb, chemometrics, chiral recognition, quantitative structure retention relationships, solvation parameter model, separation science

#### Abstract

Since the expiration of the patent protection of Chiralcel OD, similar chiral stationary phases (CSPs), all based on the same chiral selector, have been introduced on the market with the promise to reproduce or improve the performance of the original cellulose tris-(3,5-dimethylphenylcarbamate) CSP. We report here-in an in-depth evaluation of four generic versions of Chiralcel OD (CelluCoat, RegisCell, Lux Cellulose-1, Reprosil-OM) and the immobilized version (Chiralpak IB) in comparison to the original Chiralcel OD in terms of retention and enantioselectivity, with the help of chemometrics. First of all, the CSPs are compared based on the retentions of 230 achiral compounds. Agglomerative hierarchical clustering and quantitative structure-retention relationships based on a modified version of the solvation parameter model are used to assess the differences in non-enantioselective interactions contributing to retention. Secondly, the CSPs are compared based on the separation factors measured for 130 racemates. Discriminant analysis is then used to unravel the structural features contributing to the successful enantioselective separations. Chiralcel OD is shown to be the most versatile of the six tested CSPs, and involves a unique and unequalled mechanism to achieve enantioseparation.

<http://dx.doi.org/10.1016/j.chroma.2013.06.040>

### 389. Chromatographic Resolution Of Closely Related Species: Separation Of Warfarin And Hydroxylated Isomers

2013 - Journal of Chromatography A

Keywords: Merck, chiral screening, method development, pharmaceutical

#### Abstract

Recent developments in the field of organic synthesis are leading to increasingly complex mixtures of closely related species (positional isomers, regioisomers, diastereomers, etc.) that often prove challenging for chromatographic analysis and separation. In this study we investigate the separation of a representative mixture of warfarin and 5 different monohydroxylation isomers to assess whether conventional techniques are suitable for addressing this separation challenge, or whether 'next generation' separation tools such as multidimensional chromatography may be required. In this example, modifications of results obtained from conventional achiral and chiral chromatography method development screening platforms afford rapid separation of all components for both achiral and chiral analysis, with supercritical fluid chromatography showing the best performance in both cases (1.8min for separation of six components by achiral SFC and 8.0min for separation of twelve components by chiral SFC). While other more complex mixtures may require additional tools, these results suggest that new applications of existing separation platforms may be useful for creating the chromatographic methods required to support this new area of synthetic chemistry.

<http://dx.doi.org/10.1016/j.chroma.2013.07.092>

### 390. The Evaluation Of 25 Chiral Stationary Phases And The Utilization Of Sub-2.0 Mm Coated Polysaccharide Chiral Stationary Phases Via Supercritical Fluid Chromatography

2013 - Journal of Chromatography A

Keywords: Genentech, chiral screening, polysaccharide chiral stationary phases, separation science

#### Abstract

A rapid screening method to identify the best conditions for chiral separations is described. We analyzed a representative set of 80 racemic compounds against 25 different chiral stationary phases with three different mobile phases to identify the combination of columns and mobile phases that will separate the most compounds on the initial screen. While the OD separated the largest number of compounds, we found the best combination of six columns to be the AD, AS, AY, CC4, ID and Whelk-O1. The second team included the CCC, Cellulose-1, Cellulose-3 or OJ, IA, IE and IF. All 80 compounds were separated with a resolution range of 0.65–15.36. Screening the covalently bonded phases provided separation for 79 of the 80 compounds. We also found ethanol (0.1% NH<sub>4</sub>OH) separated more compounds than methanol (0.1% NH<sub>4</sub>OH) or isopropanol (0.1% NH<sub>4</sub>OH). As part of this study, we also compared the effectiveness of stationary phases that have the same chiral selector. Finally, we demonstrated the effectiveness of using a fast, 1.5-min screening method that utilizes a 1.7 μm coated polysaccharide chiral stationary phase.  
<http://dx.doi.org/10.1016/j.chroma.2013.07.046>

### 391. Simultaneous And Rapid Analysis Of Bile Acids Including Conjugates By Supercritical Fluid Chromatography Coupled To Tandem Mass Spectrometry

2013 - Journal of Chromatography A

Keywords: Waters, Osaka University, metabolic profiling, health science

#### Abstract

A number of analysis methods for bile acids using LC-MS and GC-MS have been reported. However, there is no reported method for the simultaneous analysis of bile acids using supercritical fluid chromatography (SFC). In this study, we have successfully developed a rapid method using SFC coupled to electrospray ionization tandem mass spectrometry (ESI-MS/MS) for comprehensive bile acid profiling. 25 bile acids including glycine and taurine conjugates were analyzed simultaneously within 13min. The method was applied to rat serum samples, 24 of the bile acids were quantified without any solid-phase extraction and complicated sample preparation. This study not only reports simultaneous analysis of bile acids including conjugates but also indicates the method is applicable to a biological sample. This is the first report on the simultaneous analysis of bile acids using SFC/MS. The developed method will be an alternative to existing analysis methodology for studies on the bile acid metabolism in the medical and pharmaceutical fields.  
<http://dx.doi.org/10.1016/j.chroma.2013.05.043>

### 392. Strong Cation Exchange-Type Chiral Stationary Phase For Enantioseparation Of Chiral Amines In Subcritical Fluid Chromatography

2013 - Journal of Chromatography A

Keywords: University of Vienna, Waters, beta blockers, transient buffer species, separation science

#### Abstract

A new strong cation exchange type chiral stationary phase (SCX CSP) based on a syringic acid amide derivative of trans-(R, R)-2-aminocyclohexanesulfonic acid was applied to subcritical fluid chromatography (SFC) for separation of various chiral basic drugs and their analogues. Mobile phase systems consisting of aliphatic alcohols as polar modifiers and a broad range of amines with different substitution patterns and lipophilicity were employed to evaluate the impact on the SFC retention and selectivity characteristics. The observed results point to the existence of carbonic and carbamic acid salts formed as a consequence of reactions occurring between carbon dioxide, the alcoholic modifiers and the amine species present in the sub/supercritical fluid medium, respectively. Evidence is provided that these species are essential for affecting ion exchange

between the strongly acidic chiral selector units and the basic analytes, following the well-established stoichiometric displacement mechanisms. Specific trends were observed when different types of amines were used as basic additives. While ammonia gave rise to the formation of the most strongly eluting carbonic and carbamic salt species, simple tertiary amines consistently provided superior levels of enantioselectivity. Furthermore, trends in the chiral SFC separation characteristics were investigated by the systematic variation of the modifier content and temperature. Different effects of additives are interpreted in terms of changes in the relative concentration of the transient ionic species contributing to analyte elution, with ammonia-derived carbamic salts being depleted at elevated temperatures by decomposition. Additionally, in an effort to optimize SFC enantiomer separation conditions for selected analytes, the impact of the type of the organic modifier, temperature, flow rate and active back pressure were also investigated.

<http://dx.doi.org/10.1016/j.chroma.2013.03.018>

### 393. Coupling Ultra High-Pressure Liquid Chromatography With Mass Spectrometry: Constraints And Possible Applications

2013 - Journal of Chromatography A

Keywords: University of Geneva, bioanalysis, multi-residue screening, separation science

#### Abstract

The introduction of columns packed with porous sub-2 $\mu$ m particles and the extension of the upper pressure limit of HPLC instrumentation to 1300bar (ultra-high pressure liquid chromatography, UHPLC) has opened new frontiers in resolution and speed of analysis. However, certain constraints appear when coupling UHPLC technology with mass spectrometry (MS). First, the most significant limitation is related to the narrow peaks that are produced by UHPLC that require a fast duty cycle, which is only available on the latest generations of MS devices. Thus, certain analyzers are more readily compatible with UHPLC (e.g., QqQ or TOF/MS) than others (e.g., ion trap or FT-MS). Second, due to the reduction of the column volume, extra-column band broadening can become significant, leading to a reduction in the kinetic performance of the UHPLC-MS configuration. Third, as the mobile phase linear velocity is higher in UHPLC, the electrospray ionization source must also be able to provide high sensitivity at flow rates of up to 1mL/min. Despite these limitations, the UHPLC-MS/MS platform has successfully been employed over the last decade for various types of applications, including those related to bioanalysis, drug metabolism, multi-residue screening, metabolomics, biopharmaceuticals and polar compounds

<http://dx.doi.org/10.1016/j.chroma.2012.09.061>

### 394. Evaluation And Comparison Of Various Separation Techniques For The Analysis Of Closely-Related Compounds Of Pharmaceutical Interest

2013 - Journal of Chromatography A

Keywords: University of Geneva, Sanofi, diastereoisomers, Z/E isomers, separation science

#### Abstract

The aim of the present work was to compare various separation techniques for the fast analysis of closely-related compounds, including structurally-related compounds, positional isomers, diastereoisomers, Z/E isomers. Three analytical techniques were evaluated, namely ultra high performance liquid chromatography (UHPLC), ultra high performance supercritical fluid chromatography (UHPSFC), both with sub-2 $\mu$ m particles, and capillary electrophoresis (CE) using non-aqueous solvents. To fairly compare the three analytical techniques, only two starting conditions for further method development were considered. All the selected mobile phases or background electrolyte were MS-compatible. As expected, CE often provided excellent results for the analysis of basic compounds but it was difficult to find out conditions that could be widely applied. On the other hand, UHPLC and UHPSFC were more generic and the performance was better than CE for the analysis of neutral and acidic compounds. In all cases, the analysis time was systematically lower than 3min. In conclusion, UHPLC was the most versatile strategy for the analysis of closely-related compounds and should be tested in a first instance. UHPSFC and CE approaches offered some drastic changes in selectivity and should be considered a second choice to reach alternative selectivity as they also allow high throughput separations.

<http://dx.doi.org/10.1016/j.chroma.2013.01.095>

### 395. Analysis Of Food Polyphenols By Ultra High-Performance Liquid Chromatography Coupled To Mass Spectrometry: An Overview

2013 - Journal of Chromatography A

Keywords: University of Lleida, phenolic, food, feeds, plant-derived foods

#### Abstract

Phenolic compounds, which are widely distributed in plant-derived foods, recently attracted much attention due to their health benefits, so their determination in food samples is a topic of increasing interest. In the last few years, the development of chromatographic columns packed with sub-2 $\mu$ m particles and the modern high resolution mass spectrometry (MS) have opened up new possibilities for improving the analytical methods for complex sample matrices, such as ingredients, foods and biological samples. In addition, they have emerged as an ideal tool for profiling complex samples due to its speed, efficiency, sensitivity and selectivity. The present review addresses the use of the improved liquid chromatography (LC), ultra-high performance LC (UHPLC), coupled to MS or tandem MS (MS/MS) as the detector system for the determination of phenolic compounds in food samples. Additionally, the different strategies to extract, quantify the phenolic compounds and to reduce the matrix effect (%ME) are also reviewed. Finally, a briefly outline future trends of UHPLC-MS methods is commented.

<http://dx.doi.org/10.1016/j.chroma.2013.01.012>

### 396. Efficient Optimization Of Ultra-High Performance Supercritical Fluid Chromatographic Separation Of *Rosa Sericea* By Response Surface Methodology

2013 - Journal of Separation Science

Keywords: Chengdu Institute of Biology, Shanghai University of Traditional Chinese Medicine, box-behnen design, response surface methodology, natural products, tcm, health science

#### Abstract

An approach for rapid optimization of ultra-high-performance supercritical fluid chromatographic (UHPSFC) gradient by response surface methodology was developed for fast separation of complex crude extracts of the leaves of *Rosa sericea*. The optimization was performed with Box–Behnken designs and the multicriteria response variables were described using Derringer's desirability. Based on factorial design experiments, five factors were selected for Box–Behnken designs to optimize the UHPSFC conditions, which led to 46 experiments being performed within 8 h. An evaporative light-scattering detector (ELSD) was used, and quantitative analysis of main components in *R. sericea* samples was employed to evaluate the statistical significance of the parameters on UHPSFC-ELSD analytes response. The results indicated that the optimized UHPSFC-ELSD method is very sensitive with LODs and LOQs below 1.19 and 4.55  $\mu$ g/mL, respectively. The overall intra- and interday variations were less than 3.91 and 6.41%, respectively. The recovery of the method ranged from 95.66 to 104.22%, with RSD < 5.91%. This newly developed UHPSFC-ELSD method was demonstrated to be fast and sensitive in analyzing complex herbal extracts of Traditional Chinese Medicines.

<http://dx.doi.org/10.1002/jssc.201300289>

### 397. Evaluation Of Various Chromatographic Approaches For The Retention Of Hydrophilic Compounds And MS Compatibility

2013 - Journal of Separation Science

Keywords: University of Geneva, polar compounds, hydrophilic analytes, separation science

#### Abstract

The goal of this study was to compare the performance of three separation techniques for the analysis of 57 hydrophilic compounds. RPLC, hydrophilic interaction liquid chromatography (HILIC) and subcritical fluid chromatography (SFC) were tested. The comparison was based on the retention, selectivity, peak shape (asymmetry and peak width) and MS sensitivity. As expected, RPLC had some obvious limitations for such classes of compounds, and on average the %ACN required to elute these hydrophilic substances was 4, 7, and 11% ACN at pH 3, 6, and 9, respectively. However, a hybrid polar-embedded C<sub>18</sub> phase with an appropriate mobile phase could

represent a viable strategy for hydrophilic basic compounds with  $\log D$  greater than  $-2$  on average. HILIC and SFC were found to be more appropriate for analyzing a large majority of these hydrophilic analytes ( $\sim 60$  and  $70\%$  of compounds eluted during the gradient in HILIC and SFC), while maintaining good MS sensitivity. Finally, this work demonstrated the complementarity of the three analytical techniques and showed that the selection of a suitable strategy should mostly be based on physicochemical properties of the analytes ( $pK_a$ ,  $\log D$ , H-bonding capability, etc.).  
<http://dx.doi.org/10.1002/jssc.201300567>

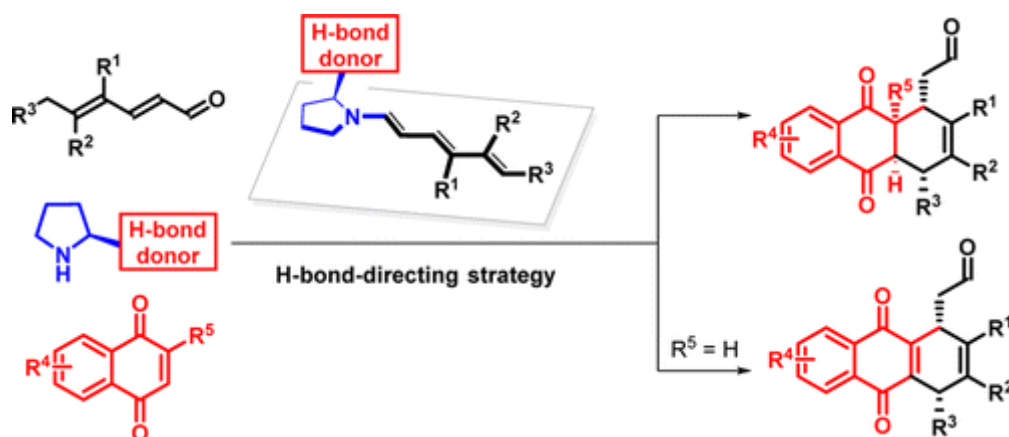
### 398. 1,4-Naphthoquinones In H-Bond-Directed Trienamine-Mediated Strategies

2013 - Organic Letters

#### Abstract

The synthesis of optically active, carboannulated dihydronaphthoquinone and naphthoquinone derivatives with up to four stereogenic centers is demonstrated by H-bond-directed, trienamine-mediated  $[4 + 2]$ -cycloadditions. The outcome of the reaction between 2,4-dienals and 1,4-naphthoquinones is controlled by the substituent in the 2-position of the 1,4-naphthoquinone. In the case of sterically demanding 2-substituted derivatives, dihydronaphthoquinones are obtained. However, when a hydrogen atom is present in the 2-position, a subsequent oxidation of the initially formed cycloadducts occurs yielding naphthoquinones.

<http://dx.doi.org/10.1021/ol401204a>



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### 399. Dienamine-Mediated Inverse-Electron-Demand Hetero-Diels–Alder Reaction By Using An Enantioselective H-Bond-Directing Strategy

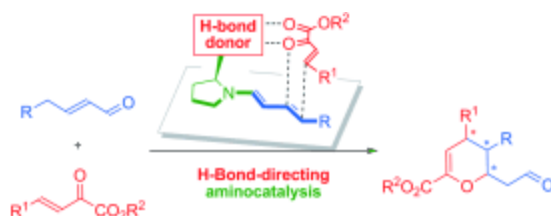
2012 - Angewandte Chemie

Keywords: Aarhus University, asymmetric synthesis, bifunctional catalysis, dienamines, dihydropyrans, organocatalysis, separation science

#### Abstract

Optically active dihydropyrans bearing three contiguous stereogenic centers can be efficiently prepared by the title reaction. High stereo- and regiocontrol can be achieved by employing a bifunctional H-bond-directing aminocatalyst.

<http://dx.doi.org/10.1002/anie.201207122>



### 400. Analysis Of Basic Compounds By Supercritical Fluid Chromatography: Attempts To Improve Peak Shape And Maintain Mass Spectrometry Compatibility

2012 - Journal of Chromatography A

Keywords: University of Geneva, basic compounds, 2-ethylpyridine ammonium hydroxide, BEH, GreenSep, Viridis, Zymor Pegasus, PrincetonSFC, pharmaceutical

#### Abstract

While neutral and acidic compounds are well separated by supercritical fluid chromatography (SFC), basic analytes are more challenging to separate and often problems occur with their peak shapes. Two different methods were explored in the present paper to reduce these problems and maintain compatibility with mass spectrometry (MS). Five different, commercially available 2-ethylpyridine (2-EP) stationary phases were tested without a mobile phase additive using 92 pharmaceutical compounds with basic properties. The kinetic performances of the 5 columns were nearly identical, but the peak shapes of the basic drugs were strongly affected by the stationary phase. The PrincetonSFC 2-EP and Zymor Pegasus 2-EP phases clearly outperformed the other stationary phases, with 77% and 69% of the compounds having Gaussian peaks (and asymmetries between 0.8 and 1.4), respectively. Comparatively, the Waters Viridis Silica 2-EP, Waters Viridis BEH 2-EP and ES industries GreenSep 2-EP phases provided only 52%, 44% and 22% of the compounds with Gaussian peaks, respectively. These differences were attributed to the significant dissimilarities in their silica matrix properties. An alternative strategy was also performed with a hybrid silica stationary phase, Viridis BEH, using 20mM ammonium hydroxide in the mobile phase, which was a mixture of CO<sub>2</sub> and MeOH. With these conditions, 81% of the peaks observed for the basic analytes were Gaussian; however, this value dropped to 17% and 10% in the absence of additive and in the presence of 20mM formic acid, respectively. Finally, the use of a hybrid bare silica stationary phase in the presence of 20mM ammonium hydroxide is quite an interesting solution as this system is compatible with both ultra high performance SFC (UHPSFC) columns packed with sub-2 μm particles and with MS detection. The overall applicability of this system was demonstrated with various mixtures of basic drugs.

<http://dx.doi.org/10.1016/j.chroma.2012.08.091>

### 401. Comparison Of Ultra-High Performance Supercritical Fluid Chromatography And Ultra-High Performance Liquid Chromatography

2012 - Journal of Chromatography A



Keywords: University of Geneva, acidic, neutral, basic, backpressure, frictional heating, separation science

**Abstract**

Currently, columns packed with sub-2  $\mu\text{m}$  particles are widely employed in liquid chromatography but are scarcely used in supercritical fluid chromatography. The goal of the present study was to compare the performance, possibilities and limitations of both ultra-high performance liquid chromatography (UHPLC) and ultra-high performance supercritical fluid chromatography (UHPSFC) using columns packed with sub-2  $\mu\text{m}$  particles. For this purpose, a kinetic evaluation was first performed, and van Deemter curves and pressure plots were constructed and compared for columns packed with hybrid silica stationary phases composed of 1.7 and 3.5  $\mu\text{m}$  particles. As expected, the kinetic performance of the UHPSFC method was significantly better than that of the UHPLC. Indeed, the  $h(\text{min})$  values were in the same range with both strategies and were between 2.2 and 2.8, but  $u(\text{opt})$  was increased by a factor of  $>4$  in UHPSFC conditions. Another obvious advantage of UHPSFC over UHPLC is related to the generated backpressure, which is significantly lower in the presence of a supercritical or subcritical fluid. However, the upper pressure limit of the UHPSFC system was only  $\sim 400$  bar vs.  $\sim 1000$  bar in the UHPLC system, which prevents the use of highly organic mobile phases at high flow rates in UHPSFC. Second, the impact of reducing the particle size (from 3.5 to 1.7  $\mu\text{m}$ ) was evaluated in both UHPLC and UHPSFC conditions. The effect of frictional heating on the selectivity was demonstrated in UHPLC and that of fluid density or decompression cooling was highlighted in UHPSFC. However, in both cases, a change in selectivity was observed for only a limited number of compounds. Third, various types of column chemistries packed with 1.7  $\mu\text{m}$  particles were evaluated in both UHPLC and UHPSFC conditions using a model mixture of acidic, neutral and basic compounds. It has been shown that more drastic changes in selectivity were obtained using UHPSFC columns compared to those obtained by changing UHPLC columns. In addition, there was a good complementarity between the two separation modes. Finally, by combining the use of small particles with supercritical fluids as a mobile phase, it was possible to achieve the analysis of pharmaceutical compounds in less than 1 min or to attain a peak capacity of more than 250 in approximately 40 min, both with a high degree of repeatability.

<http://dx.doi.org/10.1016/j.chroma.2012.10.005>

## 402. Enantioselective Formation Of Substituted 3,4-Dihydrocoumarins By A Multicatalytic One-Pot Process

2012 - Organic Letters

Keywords: dihydrocoumarins, aminocatalysis, redox reaction monitoring

**Abstract**

The formation of optically active 3,4-dihydrocoumarins is presented by merging aminocatalysis with an *N*-heterocyclic carbene-catalyzed internal redox reaction. The products are formed in good to excellent yields and in general with excellent enantioselectivities. Moreover, the developed procedure demonstrates the potential of enantioselective, multicatalytic sequences. By employing an enantiopure aminocatalyst in the enantiodifferentiating step, the challenges related to achieving high stereoinductions by deployment of optically active NHC-catalysts can be circumvented.

<http://dx.doi.org/10.1021/ol302627u>

