ANALYSIS FOR EXTRACTABLE AND LEACHABLE COMPOUNDS FROM POLYMERIC MATERIALS

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INTRODUCTION

Extractable and leachable compounds, which are potentially harmful to human health, are of great concern to manufacturing industries, particularly manufacturers of food contact materials and of materials intended for use in the pharmaceutical industry or in medical devices. Recent changes in regulatory requirements[1] have resulted in an increased need for the accurate analysis of these compounds.

This study focused on a group of 24 polymer additives (e.g. Irganox® 1010, Ethanox® 330, et.al.) that would be of interest in analyses for extractables and leachables. The method was developed for MRM analysis and analyses were performed for extractable and leachable compounds using two different tandem quadrupole systems. An electrospray based ion source was compared against UniSpray™, an ion source based on surface enhanced ionization to determine the best ionization scheme for compounds in this area.
To test the applicability of the method, samples of polymeric materials were extracted with isopropanol and analyzed.

METHODS

UPLC Method Conditions

UPLC system:	ACQUITY UPLC I-Class
Column:	UPLC BEH C_{18}, 2.1 x 50 mm, 1.7 µm
Column temp.:	40 °C
Injection volume:	3 µL
Flow rate:	0.5 mL/min
Mobile phase A:	Water - 20 µM Ammonium Formate
Mobile phase B:	Methanol - 20 µM Ammonium Formate

Gradient Conditions

0 min 10% B	4 min 99%B
0.5 min 10%B	6.5 min 99% B
1 min 60% B (Curve 3)	6.6 - 8.3 min 10%B

Standards: Waters Extractables & Leachables Screening Standard [Part No. 186008063] (mix of 18 compounds). Additional compounds were obtained from AccuStandard (New Haven, CT, USA).

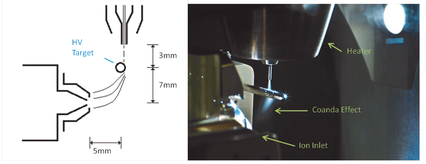
MS Conditions

MS systems:	Xevo® TQ-S and Xevo® TQ-XS
Ionization mode:	ESI Positive and Negative
Capillary voltage:	2.5 kV
Desolvation temp:	600 °C
Source temp.:	150 °C
Cone gas flow:	150 L/hr
Desolvation gas:	1000 L/hr
Source:	ESI and UniSpray on Xevo TQ-XS
Software:	MassLynx

Sample Preparation

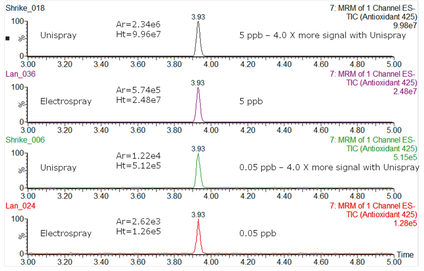
Samples of polymeric material were extracted with isopropanol at 37 °C for one hour.

UNISPRAY



UniSpray is a novel ionization technique that works by having a collimated, high velocity spray from a grounded pneumatic nebulizer aimed at a 1.6mm polished, stainless steel rod target typically held at 1-3kV. Signal is optimized when the impact point on the target is off-center. Under these conditions, the downstream gas flow from the nebulizer follows the curvature of the target and is directed towards the inlet orifice (Coanda Effect) leading to enhanced desolvation.

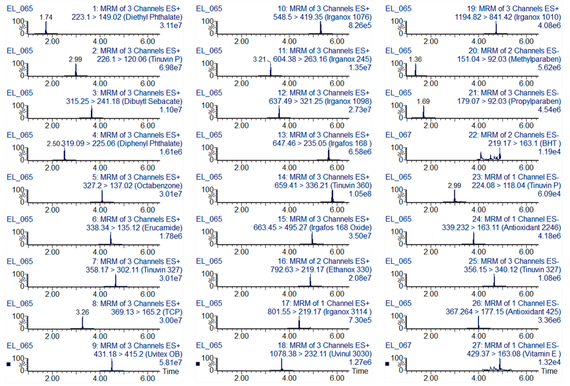
Xevo TQ-XS – Negative Ion - ESI vs. Unispray



MRM TRANSITIONS

Compound	Use	Mode	RT	Prec	Prod	CV	CE	Prod 2	CE 2	Prod 3	CE 3
Dibutyl Sebacate	Plasticizer	ES +	3.64	315.25	241.18	42	9	185.12	13	139.11	19
Diethyl Phthalate	Plasticizer	ES +	1.74	223.10	149.02	15	16	121.03	28	177.06	7
Diphenyl Phthalate	Plasticizer	ES +	2.51	319.09	225.06	20	10	77.04	30	197.06	30
Erucamide	Slip agent	ES +	4.44	338.34	135.12	100	17	303.31	14	321.32	14
Ethanox 330	Antioxidant	ES +	4.87	792.63	219.17	30	32	203.18	70		
Irgafos 168	Processing stabilizer	ES +	5.64	647.46	235.05	100	50	291.12	43	441.29	36
Irgafos 168 Oxide	Degradant	ES +	4.95	663.45	495.27	100	35	607.39	20	551.33	37
Irganox 1010	Antioxidant	ES +	4.72	1194.82	841.42	80	32	785.35	32	897.48	32
Irganox 1076	Antioxidant	ES +	5.31	548.50	419.35	50	14	107.05	20	149.06	17
Irganox 1098	Antioxidant	ES +	3.57	637.49	321.25	40	42	100.11	64	581.43	22
Irganox 245	Antioxidant	ES +	3.21	604.38	263.16	40	22	207.10	22	177.13	48
Irganox 3114	Antioxidant	ES +	4.42	801.55	219.17	40	33				
Octabenzone	UV stabilizer	ES +	4.09	327.20	137.02	45	28	215.07	19	105.03	28
TCP	Plasticizer	ES +	3.26	369.13	165.20	30	50	91.00	50	107.00	30
Tinuvin 327	UV stabilizer	ES +	4.65	358.17	302.11	30	24	57.07	24	41.01	56
Tinuvin 360	UV stabilizer	ES +	5.81	659.41	336.21	80	28	224.08	34	58.00	60
Tinuvin P	UV stabilizer	ES +	3.00	226.10	120.06	40	18	107.05	18	79.05	25
Uvinul 3030	UV stabilizer	ES +	3.67	1078.38	232.11	30	30	350.10	30	581.21	30
Uvitex OB	Brightening agent	ES +	4.50	431.18	415.20	30	40	400.10	60	105.10	70
Antioxidant 2246	Antioxidant	ES -	3.79	339.23	163.11	35	30				
Antioxidant 425	Antioxidant	ES -	4.00	367.26	177.15	35	30				
BHT	Antioxidant	ES -	4.42	219.17	163.10	30	28	203.11	26		
Cyasorb 2908	UV stabilizer	ES -	5.05	473.40	204.30	30	50	429.30	50		
Ethanox 330	Antioxidant	ES -	4.88	773.59	205.18	96	70	717.47	48	701.47	66
Irganox 1010	Antioxidant	ES -	4.72	1175.78	521.28	100	55	739.44	50	957.61	40
Irganox 1098	Antioxidant	ES -	3.58	635.48	417.30	40	40	199.12	50	57.96	62
Irganox 245	Antioxidant	ES -	3.23	585.34	367.21	80	26	409.22	26	235.13	28
Methylparaben	Preservative	ES -	1.36	151.04	92.03	45	19	136.02	14		
Propylparaben	Preservative	ES -	1.70	179.07	92.03	45	21	137.02	15	93.03	21
Tinuvin 327	UV stabilizer	ES -	4.65	356.15	340.12	30	34	305.15	30	152.00	48
Tinuvin 360	UV stabilizer	ES -	5.81	657.39	322.10	100	42	250.10	75	251.10	60
Tinuvin P	UV stabilizer	ES -	3.00	224.08	118.04	45	28	163.08	28		
Vitamin E	Plasticizer	ES-	4.78	429.37	163.08	60	28				

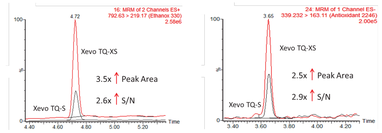
Example MRM Chromatograms for 1.5 ng/mL Standard



BHT and **Vitamin E** chromatograms are from a 5 ng/mL Standard

XEVO TQ-XS

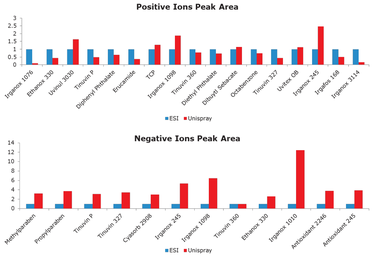
Using the new Xevo TQ-XS tandem quadrupole instrument, the observed signal to noise and peak areas were higher compared to the Xevo TQ-S for the compounds of interest. Most compounds showed an increase of 2-3x in both S/N and peak area with the greatest gain in peak area seen with the fragile diethyl phthalate ion.



Example traces detected with the Xevo TQ-S and Xevo TQ-XS tandem mass spectrometers for ethanox 330 (left) and antioxidant 2246 (right). Both compounds were detected with higher signal with the Xevo TQ-XS.

IONIZATION COMPARISON

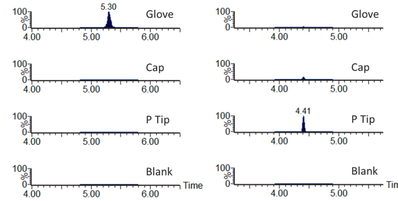
UniSpray combines the benefits of electrospray and atmospheric pressure chemical ionization to increase compound detection. Due to the diversity of the compounds of interest, both electrospray and UniSpray were investigated to determine which ionization provides the best coverage for the compounds tested. The results were mixed for compounds detected as positive ions. UniSpray showed greater peak areas for only a few compounds. In contrast, compounds detected as negative ions show an almost universal increase in the detected peak area with UniSpray ionization.



Bar graphs comparing the normalized peak areas for the compounds of interest with electrospray and UniSpray ionization.

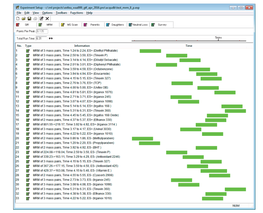
SAMPLE ANALYSIS

To test the applicability of the developed method to unknown samples, heated isopropanol extractions were performed with a nitrile glove, vial screw caps and a plastic pipette tip. Only a few of the tested compounds were detected in the extracts with two of them highlighted below.



MRM chromatograms for Irganox 1010 and Irganox 3114 acquired from samples of extracts of a nitrile glove, a vial screw cap and a plastic pipette tip.

MRM Method for the analysis of extractable and leachable compounds.



CONCLUSIONS

- **A highly sensitive and selective method for low level quantitation of extractable and leachable compounds on a tandem quadrupole mass spectrometer was developed.**
- **The method was tested on two different tandem quadrupoles with the Xevo TQ-XS showed increased sensitivity compared to the Xevo TQ-S.**
- **The novel ionization technique, UniSpray, was tested with these compounds and an increase in peak area was observed for negative ions.**

REFERENCES

[1] Summarized in "Non-Targeted Screening Analysis of Packaging Extracts Using the UNIFI Scientific Information System", Baiba Cabovska, Waters, Application Note: 720005326EN.

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