Delivering the Right Results

Analysis of Pharmaceuticals in Municipal Drinking Water by Gas Chromatography–Time-of-Flight Mass Spectrometry (GC-TOFMS)

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INTRODUCTION

An increasing amount of pharmaceutical products are winding up in the nation's drinking water supply. Both municipal and well water samples have displayed the presence of pharmaceuticals ranging from over the counter (OTC) pain medications to products prescribed for various medical conditions including high cholesterol, hypertension, depression, and sleep disorders. Drugs that are not fully absorbed by the body are excreted and thus end up going down the drain and into wastewater treatment facilities. The problem is that many wastewater treatment facilities are not equipped to remove all drug residues prior to replenishing the drinking water supply.

Since water supplies potentially contain many different drug residues, a GC-MS with a detector offering high sensitivity while acquiring full mass range spectra is necessary for this non-target type of analysis. This work will show proof of concept for a Gas Chromatography–Time-of-Flight Mass Spectrometry (GC-TOFMS) method to analyze water samples for various pharmaceutical products.

SAMPLE PREPARATION

For this initial study, a sample of tap water spiked with pharmaceutical products was analyzed by GC-TOFMS on the LECO Pegasus® HT to show that these analytes could be successfully detected. Two OTC medications (Ibuprofen and Acetaminophen), a prescribed antidepressant (Sertraline), a prescribed sleep aid (Zolpidem), and a prescribed cholesterol lowering medication (Lovastatin) were spiked into the water sample.

Each pill was ground using a mortar and pestle and added to 20 mL of tap water. The spiked water was placed in an ultrasonic bath for 15 minutes to aid in extracting the active ingredients. After sonication, the non-soluble portion was removed using a 0.45 µm Nylon filter disk.

EXPERIMENTAL CONDITIONS

Sample Introduction

Gerstel MPS2 Autosampler equipped with SPME Option

Fiber:	50/30 DVB-Carboxen-PDMS Stableflex
Extraction:	30 minute immersion, ambient
Desorption:	270°C for 1.5 min

GC: Agilent 6890 Gas Chromatograph

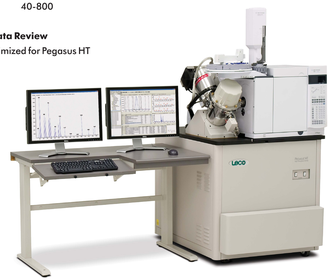
Inlet:	Split 20:1 @ 270°C
Carrier Gas:	He at 1.5 mL/min
Column:	Rtx-5 10 m x 0.18 mm x 0.18 µm
GC Oven:	40°C, hold 1.5 min, 20°C/min to 300°C, hold 10 min
MS Transfer Line:	300°C

MS: LECO Pegasus HT

Ionization:	EI at -70 eV
Ion Source Temperature:	250°C
Spectral Acquisition Rate:	10 spectra/s
Acquired Mass Range:	40-800

Instrument Control and Data Review

ChromaTOF® software optimized for Pegasus HT



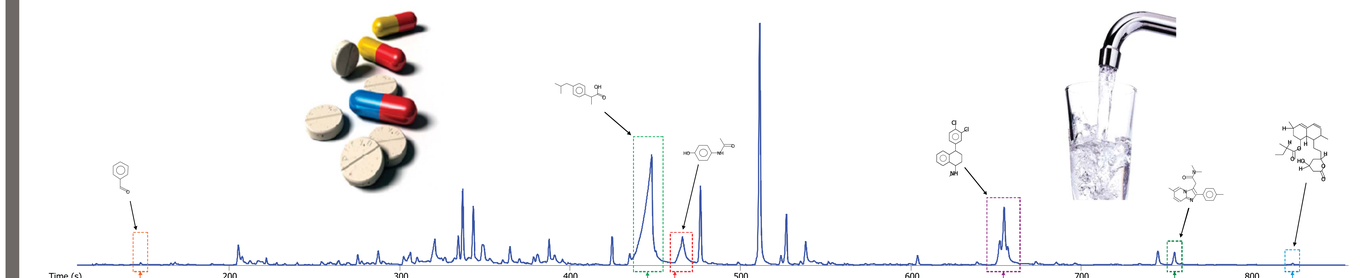


Figure 1. Analytical Ion Chromatogram (AIC) for municipal water sample spiked with OTC and prescription medications.

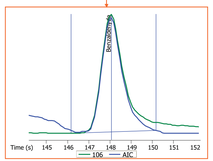


Figure 2. Expanded view of the benzaldehyde peak which was identified using the Automated Peak Find algorithm of the ChromaTOF software. Benzaldehyde is a compound used in the synthesis of many pharmaceutical products.

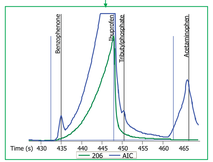


Figure 3. Expanded view of the Ibuprofen peak which was identified using the Automated Peak Find algorithm of the ChromaTOF software. Ibuprofen is a widely used OTC anti-inflammatory agent. It is apparent that this analyte does not chromatograph well under the experimental conditions used in this study.

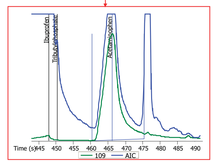


Figure 4. Expanded view of the Acetaminophen peak which was identified using the Automated Peak Find algorithm of the ChromaTOF software. Acetaminophen is a widely used OTC pain medication.

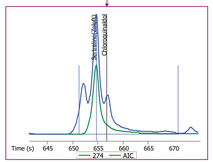


Figure 5. Expanded view of the Sertraline peak which was identified using the Automated Peak Find algorithm of the ChromaTOF software. Sertraline is the active ingredient used in many prescription anti-depressants.

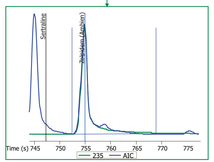


Figure 6. Expanded view of the Zolpidem peak which was identified using the Automated Peak Find algorithm of the ChromaTOF software. Zolpidem is the active ingredient used in many prescriptions to treat insomnia.

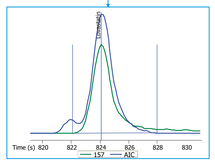


Figure 7. Expanded view of the Lovastatin peak which was identified using the Automated Peak Find algorithm of the ChromaTOF software. Lovastatin is an active ingredient in medications prescribed to lower cholesterol levels.

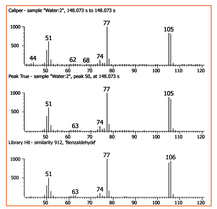


Figure 8. Caliper (raw), Peak True (deconvoluted), and library hit spectra for benzaldehyde.

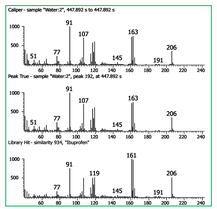


Figure 9. Caliper (raw), Peak True (deconvoluted), and library hit spectra for Ibuprofen.

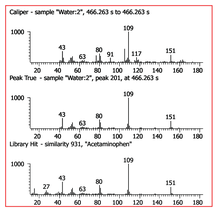


Figure 10. Caliper (raw), Peak True (deconvoluted), and library hit spectra for Acetaminophen.

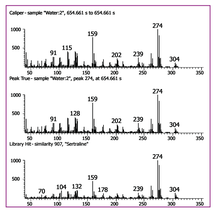


Figure 11. Caliper (raw), Peak True (deconvoluted), and library hit spectra for Sertraline.

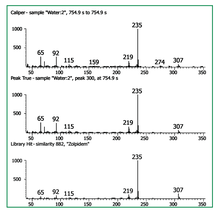


Figure 12. Caliper (raw), Peak True (deconvoluted), and library hit spectra for Zolpidem.

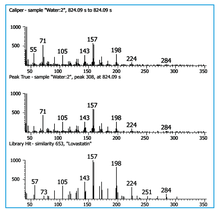


Figure 13. Caliper (raw), Peak True (deconvoluted), and library hit spectra for Lovastatin.

MASS SPECTRAL DECONVOLUTION

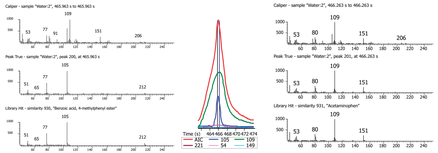


Figure 14. Example of spectral deconvolution for the identification of two unresolved components in the spiked water sample.

Observations

Figure 14 shows an example of spectral deconvolution observed in the analysis of the spiked water sample. The TIC (red) appears to show the presence of a single chromatographic peak. However, by plotting the extracted unique ions (m/z 105 and 109) which have been determined by the Deconvolution algorithm of the ChromaTOF software, it is clear that there are in fact two analytes present. The stacked spectra on either side of the chromatogram represent the two overlapping analytes. The Caliper (raw) spectra show all ions present at the peak apex. Note the presence of m/z 105 and 109 in the Caliper spectra for each analyte. As a result of the overlap between the two compounds, ions from both analytes are present in each Caliper spectrum. Following deconvolution, the Peak True spectrum is generated which contains only ions specific to that compound. The deconvoluted spectra no longer contain ions from coeluting analytes. The Peak True spectra were automatically compared against library spectra in order to identify the compounds as Benzoic acid, 4-methylphenyl ester, and Acetaminophen with similarity rankings of 930 and 931, respectively.

RESULTS AND DISCUSSION

The results of this preliminary study have shown the ability of the Pegasus HT GC-TOFMS to successfully identify all of the active pharmaceutical ingredients that were spiked into the water sample in addition to many other analytes present in the tablet matrices. All of these analytes were identified using the Automated Peak Find algorithm of the ChromaTOF software. The non-skewed spectra generated by the TOFMS allow for better success from the Mass Spectral Deconvolution algorithms which provide "clean" spectra for library comparison. Figure 1 shows the Analytical Ion Chromatogram (AIC) from the analysis of the spiked water sample. Figures 2 through 7 show expanded regions of the chromatogram in which analytes of interest have been identified, and Figures 8 through 13 show the Caliper (raw), Peak True (deconvoluted), and Library Hit spectra for each analyte. Figure 14 shows an example of the Mass Spectral Deconvolution capabilities of the ChromaTOF software.

CONCLUSIONS

The Pegasus HT GC-TOFMS was successfully used to identify pharmaceutical products in water. The Mass Spectral Deconvolution capabilities of the ChromaTOF software with Automated Peak Find is a very valuable time saving tool; especially when analyzing for non-target analytes within complex matrices. In addition to significant time savings, the algorithms used can aid in identifying components that may normally go undetected. The ability of the TOFMS to provide superior sensitivity while acquiring across the full mass range make it a very powerful tool for detecting and characterizing new and emerging contaminants which are finding their way into the nation's drinking water supply.

ChromaTOF®