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Screening of pharmaceuticals in water by full scan Mass Spectrometry

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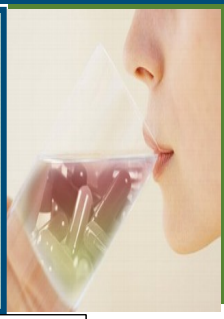
Introduction

Water for human consumption has to be free from organic contaminants like pharmaceuticals used for humans and for animal treatment as well as it needs to be free from pesticides and industrial waste. The analysis of known and unknown contaminants in water samples is complicated by the unavoidable presence of Natural Organic Matter (NOM) and inorganic constituents. High resolution analytical tools are a prerequisite for a successful screening of low concentrations (µg/L) contaminants in complex water samples. A rapid versatile and selective multi-method is presented to establish the influence of dissolved NOM content on the method characteristics. Water samples containing different concentrations of NOM were fortified with a set of 11 pharmaceuticals. The samples were analyzed using a full scan MS technique. Next to targeted screening the peaks (accurate masses) in the processed data files were identified by using RIKILT procedure for identification of unknowns [1].



Method

Eleven pharmaceuticals were screened by using one single full scan MS method. Water samples containing different amount of natural organic matter (NOM) were considered.

Compounds were: Flubendazole, Erythromycin, Dicloxacillin, ciprofloxacin, sulfamethoxazole, oxytetracycline, carazolol, diclofenac, meclofenamic acid, carbamazepine, clofibric acid.

Aliquots of fortified samples and blanks were passed through a Minisart RC4 0.20 µm filter.

All Aliquots were directly screened for residues (without clean-up and pre-concentration step) using LC-Orbitrap™ MS at 50,000 (FWHM) Resolution

The method characteristics were established over a concentration range of 0.1µg/L to 500µg/L.

A drinking water treatment plant system was considered, for our experiment. Consisted in:

Pre-treatment : $influent_1$ and $effluent_1$
Second treatment : $influent_2$ = $effluent_1$ and $effluent_2$.

Sample Type	NOM – (DOC mg/L)
$Influent_1$	≈ 8
$Influent_2$ = $Effluent_1$	5 ≈ 6
$Effluent_2$	≈ 3

Results

The limit of detection varies between 0.1µg/L to 100µg/L. The linear range varied with the analyte due to the different types of water samples. Accordingly linearity was acceptable with correlation coefficients greater than 0.99. Figure 1 shows linearity of sulfamethoxazole in water samples with 8mg/L of NOM.

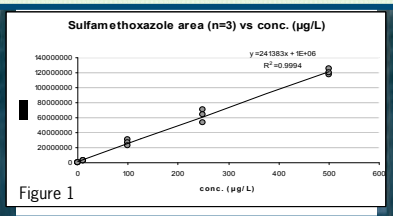


Figure 1

For the quantification performance, recoveries between 60 and 120% were found acceptable. Figure 2 shows the recoveries for carbamazepine.

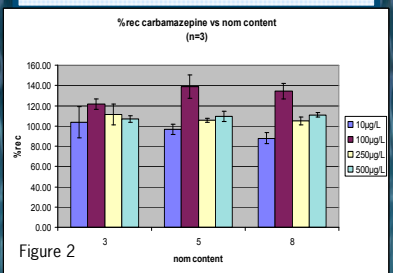


Figure 2

It was demonstrated that sensitivity could be affected by matrix constituents in both directions of signal reduction or enhancement for some compounds due to ion suppression or enhancement phenomenon (Fig. 3)

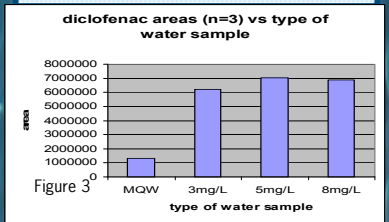


Figure 3

RSD (%) within samples for sulfamethoxazole were more than 20% for the lowest concentration levels and these values improve when concentrations are increased. (Fig. 4)

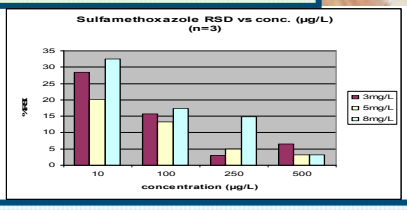


Figure 4

Accurate mass measurements were performed at 50,000(FWHM) resolution and the compounds identified with errors below <2ppm, despite the NOM presence. Influent water samples were considered as more complex matrix, since the dissolved NOM content is still not treated. (examples - following table)

compound	[M+H]+ (m/z)	Average Accurate Mass		Av. Δppm	
		Inf-1	Inf-2	Inf-1	Inf-2
sulfamethoxazole	254.059383	254.05946	254.05936	0.3	-0.1
carbamazepine	237.102233	237.10205	237.10257	-0.8	1.4

Water composition/Identification of unknowns

An unknown compound provisional identification was made and the results evaluated against RIKILT's database. For one chromatogram (15 min) more than 100 elemental compositions of detected peaks were obtained. Applying selection criteria like retention time, accurate mass deviations reduce this amount. Examples of proposed elemental compositions of unknowns are:

- Proposed identity as removed with the pre-treatment: $C_{12}H_{23}N_2O_2$ (Crotetamide) – ppm error of -0.8
- Porposed identity for new compounds after pre-treatment: $C_{14}H_{21}O_4$ (U-73975) – ppm error of 1.3
- Proposed identity as removed from second treatment: $C_{11}H_{14}N_5O$ (Cgp 53391) – ppm error of 1.3
- Proposed identity for new compounds after second treatment: $C_{14}H_{23}O$ (4-t-octylphenol) ppm error of -0.1

Evaluation of the isotopic pattern is important for an adequate identification of non-targeted and unknown compounds.

Conclusions

- The use of high resolution MS measurement techniques is feasible for resolving matrix interferences.
- All compounds were properly identified for targeted analysis. Most compounds were linear apart from a few for which some more work would be required to get acceptable linearity and sensitivity.
- Despite of the interaction among the compounds studied and the dissolved NOM present, the screening multi-method was suitable for the identification of the list of compounds selected and also for the provisional identification of unknowns.
- In the matrix (samples) the mass accuracy was good (<2 ppm)

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Reference
[1] R.J.B. Peters, J.C.W. Rijk, T.F.H. Bovee, A.W.J.M. Nijrolder, A. Lommen, M.W.F. Nielen Analytica Chimica Acta 2010, 664, 77- 88.