**Applications of the all-ions approach for non-target screening of water contaminants by high resolution tandem mass spectrometry**

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Over the last decades, the occurrence and fate of trace organic contaminants in water became a major environmental as well as public health concern. With the constant progress in analytical chemistry allowing faster and more sensitive detection, the quantification of selected contaminants such as pesticides and pharmaceuticals is now performed routinely in many laboratories. However, screening for unknown contaminants and transformation products, processing of large datasets from high resolution mass spectrometry remains still challenging and a time-consuming task. While high resolution mass spectrometry allows the efficient detection of unknown contaminants and the suggestion of a suitable chemical formula, tandem mass spectrometry is still necessary to confirm the compound identity. Therefore, this study introduces the application of all-ions MS/MS for compound identification in screening of water contaminants.

The traditional approach of high resolution tandem mass spectrometry involves the sequential isolation of selected precursor ions in order to identify their respective product ions (m/z and relative abundance). Since a complex sample composition, such as in wastewater effluents, frequently leads to numerous co-eluting compounds, the acquisition of MS/MS spectra for a large number of precursor ions usually requires multiple injections and extended instrument/personnel time. The work presented in this study relies on the all-ions approach, the acquisition of MS/MS spectra at varied collision energies (CE = 0, 20 and 40 eV) without isolating precursor ions. Thus, product ions from each co-eluting precursor can be acquired within one run. While MS/MS spectra are no longer specific to one precursor ion, they can hardly be interpreted directly but require automated data processing based on deconvolution with information from a compound library. Initially, the “Find by Formula” algorithm gathers the chemical formulae of the compounds from the library and calculates the m/z corresponding to their molecular ion (different adducts or neutral loss can be considered). In a second phase, the algorithm looks for a potential match within the data set acquired on the low energy channel (CE = 0 eV). In a third phase, the algorithm reviews MS/MS information. For each compound with a positive match at 0 eV, the algorithm considers its product ions from the library and extracts the corresponding chromatograms on the 20 eV and 40 eV channels. In a last phase, the algorithm assesses the co-elution of the molecular ion on the 0 eV channel with the product ions on the 20 and 40 eV channels. Finally, the analyst is provided with a summary table containing the list of compounds identified with the mass error (in ppm) and the number of product ions found.

The all-ions approach was successfully applied for screening contaminants in wastewater effluent. Pharmaceuticals were among the main compounds identified and included for instance the anticonvulsants temazepam and lamotrigine; the antihypertensives valsartan and irbesartan; the beta-blocker metoprolol and the antibiotic sulfamethoxazole. Moreover, the all-ions approach also identified some metabolites of pharmaceuticals, such as desvenlafaxine (metabolite of the antidepressant venlafaxine). The minimum number of product ions required for confirmation of the compound identity depends on the analyst but a minimum of three is advised in order to limit false positives. While all-ions MS/MS was proven efficient for fast screening of compounds for which at least one library spectrum at high resolution is available, another advantage of this approach is its applicability for the detection of compounds from the same family characterized by common fragments. For instance, the product ion of valsartan revealed the occurrence of several precursors sharing the same product ion throughout the chromatogram, which allowed identifying additional compounds from the “sartan” group or their metabolites. Nevertheless, the all-ions MS/MS approach shows its limitations for the identification of “true unknowns” due to the difficulty to unequivocally link product ions to a specific precursor ion.