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Measurement of pollution levels of N-nitroso compounds of health concern in water using ultra-performance liquid chromatography–tandem mass spectrometry

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ABSTRACT

This paper reports the development of a highly sensitive analytical method combining solid-phase extraction (SPE) with ultra-high performance liquid chromatography coupled with tandem mass spectrometry (UHPLC–MS/MS), for the monitoring of ultra-trace levels of N-nitrosamines in water samples.

Under optimized analytical conditions, chromatographic separation was performed in 3 min, in isocratic mode, using an Acquity UHPLC C18 column and a mobile phase consisting of acetonitrile, water, and formic acid (60:40:0.1, v/v/v) at a flow rate of 0.4 mL min^{-1}. Electrospray ionization tandem interface was employed prior to mass spectrometric detection. Good linearity ($R^2 \geq 0.9987$) and low limits of detection (0.04–0.4 ng L^{-1}) and quantification (0.1–1.2 ng L^{-1}) were obtained. The extraction recoveries ranged from $98 \pm 1\%$ to $100 \pm 1\%$ and the relative standard deviations were less than 1.53%. The matrix effect was between 98 ± 2 and $100 \pm 1\%$.

The obtained results clearly demonstrate that the developed method is accurate and highly sensitive for the simultaneous determination of N-nitroso-n-propylamine, N-nitrosomorpholine, N-nitrosomethylethylamine and N-nitrosodimethylamine at ultra-trace levels (ng L^{-1}) in different types of water samples. Therefore, this method can be a useful analytical tool for future toxicological, water quality surveillance studies and for the investigation of drinking water quality.

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1. Introduction

The occurrence of N-nitrosamines (NAms), in water is considered as an emerging issue, due to their mutagenic and carcinogenic effects at ultra trace levels (ng L^{-1}). As a consequence, in recent years, this class of molecules has received an increased interest from environmental and analytical chemists. They are generally produced during different industrial processes such as cosmetics, metal casting, leather tanning, food (beverages and meats) or during the rubber or dyes manufacturing. Thus, these kinds of applications commonly lead to wastewater and groundwater contamination. For example, high concentrations (2 mg L^{-1}) of N-nitrosodimethylamine (NDMA) were found in Ontario, in downstream industrial water of a tyre factory (Mitch et al., 2003). More recently, another study carried out in Switzerland reported the presence of N-nitrosamines in the influents of an urban wastewater treatment plant at a concentration level ranging from 5 to 25 ng L^{-1} (Krauss et al., 2009; Sedlak et al., 2005).

Moreover, it was found that drinking water disinfection processes with chlorine, monochloramine, chlorine dioxide, and ozone generally lead to the formation of these compounds in treated water, by the reaction between disinfectant and the nitrogen containing organic matter (Andrzejewski et al., 2008; Kadmi et al., 2015a,b; Schreiber and Mitch, 2005).

Several studies reported the occurrence of NAms in treated drinking water from different sites situated in North America and Canada. Other studies confirmed their presence in drinking water (Richardson, 2009; Zhao et al., 2006) and of NDMA, NMOR in surface water (Kosaka et al., 2010; Zhao et al., 2008).

N-nitrosamines are a class of non-halogenated emerging disinfection by-products (DBPs) which have been recently identified in drinking water. NAms are alkylating agents characterized by the presence of the N-nitroso group and may be aliphatic or ring structures. Different studies reported that these molecules are significantly more toxic than the regulated DBPs (Oya et al., 2008).

In response to their suspected adverse risks on human health, different guidelines have been implemented in United States and Canada for these molecules and more particularly, for NDMA, which is one of the most detected. However, in the European Community these molecules are not yet regulated. Indeed, NAms are not listed in the Drinking Water Directive (Council Directive 98/93/EC), but a few European Union (EU) member states have regulated their presence in drinking water. Provisional standard values were proposed only in Netherlands and in Germany for NDMA and N-nitrosomorpholine (NMOR) (Kadmi et al., 2014; Planas et al., 2008). In addition, the French government proposed recently the addition of NDMA in the EU Directive for drinking water, and a guideline value of 100 ng L^{-1}, according with the guideline of the World Health Organization (WHO, 2011).

Therefore, in the light of new regulations at European level and for water quality monitoring purposes it is of great interest to develop fast, sensitive and environmentally friendly analytical methods for the monitoring of trace and ultra-trace levels of N-nitrosamines in water samples. The major challenge in the determination of these molecules is to attain the high sensitivity required for the quantification of trace levels in environmental samples.

Presently there are no standard analytical methods for the quantification of NAms in environmental samples in the range of nanogram per liter. Due to the low concentration level of these compounds in the aquatic environment and in drinking water an extraction and pre-concentration step of analytes is generally required.

N-nitrosamines are polar compounds with low molecular weights (<200 g mol^{-1}), usually water soluble and have low octanol/water (K_{ow}) partition coefficients. Consequently, they are difficult to extract with organic solvents or to remove by adsorption.

Several selective analytical techniques have been reported for the quantification of NAms. The analytical strategies currently used mainly consists of two steps, i.e., analysis by gas chromatography (GC) or liquid chromatography (LC) and an extraction/concentration procedure for the concentration of analytes. The NAms have been determined in water samples by using GC coupled with different types of detectors, such as gas chromatography coupled with mass spectrometry (GC/MS) (Huang et al., 2013; Reyes-Contreras et al., 2012; Ventanas and Ruiz, 2006) and gas chromatography–tandem mass spectrometry (GC/MS/MS) (Llop et al., 2012; McDonald et al., 2012). However, these methods are limited to the analysis of volatile and thermally stable compounds. Other studies focused on the determination and quantification of NAms by liquid chromatography using a fluorescence detector (Cha et al., 2006) and high pressure liquid chromatography–tandem mass spectrometry (HPLC/MS/MS) (Cheng et al., 2011; Zhao et al., 2006).

The aim of the present work was to develop a rapid and robust analytical SPE–UHPLC–MS/MS protocol for the simultaneous quantification of N-nitrosamines in water samples. The developed analytical procedure has been selected in order to attain the selectivity, sensitivity and sample throughput which is needed for the quantification of these molecules in water samples. Based on occurrence and toxicity data, the N-nitrosamines selected for this work were: N-nitroso-n-propylamine (NDPA), N-nitrosomorpholine (NMOR), N-nitrosomethylethylamine (NMEA) and N-nitrosodimethylamine (NDMA).

The study of the performance of the developed method was carried out in terms of method detection limits (MDL), method of quantification limits (MQL), linearity, extraction recovery and matrix effect.

The developed analytical method was then applied to real water samples (surface water and treated water samples from public water system) collected from different locations in Brittany region (France) in order to measure the pollution levels. Since these molecules are usually not considered in routine monitoring programs in Europe, and especially in France, information about the contamination level with these emerging DBPs is very limited.

2. Materials and methods

2.1. *Chemicals, standards and preparation of stock solutions*

Individual standard solutions (2000 mg L^{-1} in methanol) of N-nitrosamines were purchased from LGC Standards (Wesel, Germany). The main physico-chemical characteristics of the studied molecules as well as their toxicity are shown in Table 1.

Acetonitrile (LC–MS grade) and formic acid (>95%) were obtained from J.T. Baker (Deventer, Netherlands). Methanol and GC-grade dichloromethane were purchased from Fischer Scientific-Bioblock (Illkirch, France). Acetic acid (100%) was supplied by Acros Organics (Noisy-le-Grand, France). All