Environmental Technology & Innovation 10 (2018) 102–110

Contents lists available at ScienceDirect

Environmental Technology & Innovation

journal homepage: www.elsevier.com/locate/eti

# Determination of *N*-nitrosamines in water by nano iron-porphyrinated poly(amidoamine) dendrimer MCM-41 generation-3 through solid phase membrane tip extraction and HPLC

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ARTICLE INFO

*Article history:*
Received 19 October 2017
Received in revised form 13 November 2017
Accepted 1 February 2018
Available online 5 February 2018

*Keywords:*
Nitrosamines
Iron porphyrin solid-phase membrane tip extraction
HPLC
Water analysis

ABSTRACT

This study described a method comprising solid-phase membrane tip extraction (SPMTE) with nano iron-porphyrinated poly(amidoamine) dendrimer Mobil Composition Matter-41 Generation-3 (FeP-Dend-MCM-41-G3) and high-performance liquid chromatography for analysis of *N*-nitrosamines in water samples (tap, lake, and hospital water). The studied carcinogenic nitrosamines were *N*-nitrosopyrrolidine (NPYR), *N*-nitrosomorpholine (NMOR), and *N*-nitrosopiperidine (NPIP). Nano FeP-Dend-MCM-41-G3 SPMTE was evaluated in terms of efficiency for the extraction of nitrosamines from waste, lake, and tap water samples. The suitability of the chromatographic system for the separation of nitrosamines was also established. The capacity factor, $k'$ for NMOR, NPYR, and NPIP were 1.67, 2.50, and 6.75, respectively, with excellent selectivity factors (NMOR-NPYR, 1.497 and NPYR-NPIP, 2.70) and resolution, $R_s$ (NMOR-NPYR, 1.81 and NPYR-NPIP, 6.00). Under the optimized conditions, the proposed method showed good relative recovery within 84%–100% and acceptable reproducibility with intra- and inter-day relative standard deviations of $<11.8\%$. The method also showed good linearity within 1–1000 ng/mL, high enrichment factor (71–406), and low detection limits ($<5.7$ ng/L). The limits of detection and quantification for nitrosamines were within 0.6–0.75 ng/mL. Overall, the proposed method was efficient and required only small amounts of the adsorbent and organic solvent and, thus, contributed toward green chemistry.



## 1. Introduction:

*N*-Nitrosamines are well-known carcinogens and mutagens for the animals and human beings (Wishnok, 1977; Grebel and Mel Suffet, 2007). These compounds impose health risks even in trace amounts (ng/L) (Ali et al., 2009; Instrumental

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https://doi.org/10.1016/j.eti.2018.02.004
2352-1864/

methods, 2006; Ali and Aboul-Enein, 2004, 2003; Barnes and Magee, 1954; Mhlongo et al., 2009; U.S. Environmental Protection Agency, 1980). Nitrosamines are widespread in the environment (Padhye et al., 2009; Nawrocki and Andrzejewski, 2011; Qu et al., 2013; Hartmetz and Slemrova, 1980; Wang et al., 2011) and even produced in the stomach by the reactions of secondary amines and nitrite. Considering the presence of nitrosamines in drinking (Wang et al., 2011; Charrois and Hrudey, 2007; Jurado-Sánchez et al., 2012; Luo et al., 2012; Schnute and Wang, 2010; Zhao et al., 2006), treated (Jurado-Sánchez et al., 2012; Cheng et al., 2006; Zhou et al., 2009; Bin et al., 2011; Zhao et al., 2008), and different surface waters (Wang et al., 2011; Cheng et al., 2006; Zhao et al., 2008; Tomkins et al., 1995; De Ridder et al., 2012; Kaserzon et al., 2011; Pozzi et al., 2011), researchers have developed excellent qualitative and quantitative analytical methods for the extraction, analysis, detection, and removal of nitrosamines from water. Typical nitrosamines found in water are *N*-nitrosodimethylamine (NDMA) (Charrois and Hrudey, 2007; Chen et al., 2010; Ripolles et al., 2011), *N*-nitrosomorpholine (NMOR) (Ripolles et al., 2011), *N*-nitrosopyrrolidine (NPYR) (Zhao et al., 2006; Ripolles et al., 2011), *N*-nitrosopiperidine (NPIP) (Zhao et al., 2006; Ripolles et al., 2011), and *N*-nitrosodiphenylamine (NDPhA) (Zhou et al., 2009). These compounds are also present as disinfectant by-products in drinking water (Zhou et al., 2009; Eaton and Briggs, 2000) and listed in the United States Environmental Protection Agency (EPA) Drinking Water Contaminant Candidate List (U.S. Environmental Protection Agency, 1980). The California Department of Health Services set 10 ng/L as the notification level for NDMA, *N*-nitrosodiethylamine (NDEA), and *N*-nitrosodi-*n*-propylamine (NDPA) (U.S. Environmental Protection Agency, 2001). Nitrosamine analysis is often based on denitrosation reaction (Rostkowska et al., 1998; Xu et al., 2010). Rostkowska et al. (1998) reported that nitrosamines are metabolically activated upon degradation to biologically active derivatives. This phenomenon occurs in the liver, lung, and nasal tissues, where nitrosamines are denitrosated by a reductive process. Appel et al. (1979) demonstrated two main paths for nitrosamine binding on cytochrome P450; namely, binding to protein pocket site near heme (iron center) and direct contact with iron center.

Xu et al. (2010) reported that the reaction of nitrosamines with ferric and ferrous porphyrins involve ferric porphyrin and yields ferric nitrosamine complexes. The functional group NN=O of nitrosamines form N-binding or O-binding mode to iron porphyrins leads to the binding of nitrosamine ligands to the iron center. This binding event is a key criterion for nitrosamine extraction with iron porphyrins.

SPE has been extensively used with different types of solvents to analyze nitrosamines in drinking water and wastewater samples. Activated carbon-based sorbents, such as LiChrolut EN and Ambersorb 572, are commonly used in nitrosamine analysis. Charrois and Hrudey (2007) detected 2–180 ng/L NDMA, 2–4 ng/L NPYR, and 1.0 ng/L NMOR in drinking water samples by using diallydimethylammonium chloride cationic polymer (poly-DADMAC). Zhao et al. (2006) used LC-MS method coupled with Ambersorb 572 to quantify NPYR, NPIP, and NDPhA in drinking water, with a method detection limit of 0.1–10.6 ng/L. Ripolles et al. (2011) reported a pre-concentration step by off-line SPE using charcoal EPA 521 cartridges and liquid chromatography coupled with tandem mass spectrometry triple quadrupole analyzer for nitrosamine analysis. High recovery and low limits of detection (LOD) were obtained within the range of 1–8 ng/L in different water samples. Rostkowska et al. (1998) developed a solid-phase microtip extraction fiber for the extraction of seven nitrosamines (NDPA, NMOR, NPYR, NPIP, NDBA, *N*-nitrosometylethylamine and NDEA). Nitrosamines were analyzed by gas chromatography–mass spectrometry (GC–MS) instruments. The detection limits of nitrosamines were within 30–890 ng/L. This method was modified by Xu et al. (2010) to obtain lower detection limits, namely, 3.2–3.5 ng/L for NDMA, NDEA, and *N*-nitrosodi-*n*-propylamine and 15.2 ng/L for NMOR. These methods suffer from drawbacks, such as long chromatographic run time, use of costly solvents, and poor extraction efficiency. Therefore, scholars must develop alternative methods to address these issues and determine nitrosamine compounds in water at low concentration levels.

The most commonly detected nitrosamines, NPIP, NMOR (Group 2B), and NPYR (Group B2) are considered as possible carcinogens to humans (U.S. Environmental Protection Agency, 1980). In contrast to NDMA; which is the most commonly detected nitrosamine; NPIP, NMOR (Group 2B), and NPYR (Group B2) are found in wastewater and drinking water. However, this group of nitrosamine has not been investigated. Therefore, the occurrence or detection levels of NPIP, NMOR, and NPYR must be assessed considering that different regions provide different conditions for the formation of nitrosamines (Kadmi et al., 2015).

In this work, a comprehensive analysis was performed to determine the extraction capabilities of nanoFeP-Dend-MCM-41-G3 through solid-phase membrane tip extraction (SPMTE). The capabilities of the adsorbent in extracting nitrosamines rely on ferric nitrosamine complexes formed from iron porphyrin bound to nitrosamines (Xu et al., 2010; Appel et al., 1979). This extraction method is specific to nitrosamines, simple to perform, and can achieve high recoveries in the wastewater samples (See et al., 2010). The extracted nitrosamines were analyzed by HPLC using UV detector. Complete calibration data extraction, optimization, and analysis were performed. The developed method was successfully applied to the determination of selected nitrosamines in tap water, wastewater, and lake water samples in Johor Bahru (Malaysia).

## 2. Experimental

### 2.1. Chemicals and reagents

Three *N*-nitrosamine compounds (NPYR, NPIP, and NMOR; Table 1) were chosen those commonly found in water (National Toxicology Program, 2011; National Center for Biotechnology Information, 0000; John et al., 2009). Their generic structures, prevalence, physical properties, and cancer potency are also listed. The NPIP and NMOR standards (5000 μg/mL)