Electrochemical detection of *N*-nitrosodimethylamine using a molecular imprinted polymer

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ABSTRACT

We report on the development of an impedimetric sensor towards the determination of *N*-nitrosodimethylamine (NDMA) in water samples. The approach presented herein is based on the usage of a molecular imprinted polymer (MIP) as the recognition element in conjunction with a glassy carbon electrode (GCE) as the electrochemical transducer. To this end, the MIP particles were first synthesized by the precipitation polymerization method, and afterwards entrapped in an electropolymerized polypyrrole membrane. The developed sensor showed a selective response towards NDMA with a linear range from 10 to 230 $\mu g\,L^{-1}$ and a limit of detection of 0.85 $\mu g\,L^{-1}$; without showing significant response towards structurally-related compounds. The MIP gave an order of magnitude higher sensitivity for NDMA detection than the non-imprinted polymer (NIP). Lastly, the developed sensor was applied to the determination of NDMA in spiked drinking and recycled water samples, obtained from conventional treatment and disinfection systems, without showing any matrix effect.

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1. Introduction

Chemical disinfection is the most widely used technique to control waterborne pathogens and ensure water can reach the consumer tap safe from microbial contamination or free from any harmful/unpleasant compounds [1,2]. However, such treatments can also lead to the production of potentially harmful disinfection by-products (DBPs), which arise from the reaction of those chemical agents with certain organic matter in water.

Over the last years, a wealth of research has improved our understanding on the formation, potential health risks and control of DBPs [2]. It is now recognized that all chemical disinfectants form some potentially harmful by-products [2]. Consequently, the well-known adverse health effects of some DBPs have led to the establishment of maximum contaminant levels for those compounds and to research in regard to alternative disinfection agents [3,4].

The usage of alternative disinfection agents, such as chloramines, has shifted attention from already known chlorinated

DBPs such as trihalomethanes (THMs) or haloacetic acids (HAAs) to the so-called "emerging" DBPs [5]. Among those new emerging contaminants, nitrosamines, and more correctly *N*-nitrosodimethylamine (NDMA) are of greatest concern [6]. NDMA has been categorized as probably carcinogenic to humans (Group 2A) by the International Agency for Research on Cancer [2], exhibiting a 10^{-6} cancer risk level at 0.7 $ng\,L^{-1}$ [7]; whereas other studies involving over 300 different nitrosamines have demonstrated that about 90% of them also show carcinogenic activity [8].

Due to these health effects, the maximum allowed levels for nitrosamines are generally set at the low $ng\,L^{-1}$ level, a concentration that is difficult to be detected by conventional analytical methods [9,10]. NDMA is generally present at the low $ng\,L^{-1}$ level in chloraminated/chlorinated drinking waters, but despite the regulation efforts, it has been detected above permitted limits in different regions over the world, where values up to 100–200 $ng\,L^{-1}$ have been reported, and even found at much higher levels in wastewaters [7]. Additionally, human contact with NDMA is not limited to drinking water [11], but also to chlorinated swimming pool waters [12]. Walse et al. reported values in swimming pools and hot tubs at levels up to 429 $ng\,L^{-1}$ [12]. NDMA can also be found in cigarettes and food (e.g. smoked food such as bacon) [11].

Although several studies have tried to elucidate the formation mechanisms of NDMA and to identifying its precursors [7,13,14], much effort has also been devoted to NDMA detection. Nitrosamines pose analytical challenges for their accurate determination, the sample preparation playing a critical role (e.g. the commonly used solid-phase extraction) [10]. The most common analytical techniques in current use to detect NDMA include gas chromatography (GC) and liquid chromatography (LC), especially coupled with mass spectrometry (MS or MS-MS). However, these techniques require sophisticated lab instruments, skilled personnel, and involve time-consuming and expensive procedures.

Therefore, the in-field detection of NDMA still remains an issue, requiring the development of low-cost and miniaturized highly sensitive measurement systems. In addition, such systems should provide a rapid response with a low rate of false alarms. In this direction, the development of sensing devices based on the combination of molecular imprinted polymers (MIPs) with electrochemical transduction might represent an alternative solution [15,16].

MIPs, also known as artificial or plastic antibodies [17], are polymers formed in the presence of a template molecule (the molecule that we aim to determine), which at a later stage is removed from the polymeric matrix, leaving a complementary cavity in the polymer with affinity to the chosen template molecule. Thus, in this way, allowing to synthetize a low-cost artificial receptor with high selectivity towards a desired analyte, highly suitable for diverse analytical applications.

In order to be used in sensing applications, MIPs prepared as particles or polymeric films have to be integrated with a transducer that converts the binding event into an analytical signal [14]. To this aim, different approaches based on the integration of MIPs with electrochemical transducers have been proposed in the literature [14,15], ranging from the ex-situ synthesis of MIP particles followed by their entrapment onto gels and deposition onto the electrode surface [18], to the in-situ electrosynthesis of MIP films from a monomer solution in the presence of the template molecule [15], as well as hybrid methods based on the entrapment of the MIP particles onto the transducer surface by electropolymerization of a conducting polymer solution [19,20]. The main advantage derived from the latter is the decoupling of the MIP synthesis and immobilization steps, thus allowing a better optimization of each step separately. Additionally, the electrosynthesis of the polymeric matrix also provides better control over the membrane thickness and adhesion, and constitutes a straight-forward solution for the usage of pre-established MIP formulations.

Based on the aforementioned, the aim of the present work is to demonstrate the applicability of electrochemical sensors for the rapid, selective and reliable detection of NDMA in drinking and recycled water samples. To this aim, the approach presented herein is based on the synthesis of a selective MIP towards NDMA to be used as a recognition element, its entrapment into an electrosynthethized polypyrrole (PPy) matrix, and its application for sensing purposes based on electrochemical impedance spectroscopy (EIS) measurements. After optimization of the experimental conditions, the developed MIP sensor was characterized; response features towards NDMA were compared with the responses obtained for analogous structural compounds, and with the NIP sensor, to evaluate MIP selectivity. Lastly, the sensor was applied to the determination of NDMA in spiked water samples.

2. Experimental

2.1. Reagents and solutions

All reagents used were analytical reagent grade and all solutions were prepared using deionized water from a Milli-Q system (Millipore, Billerica, MA, USA). Pyrrole (Py), *N*-nitrosodimethylamine (NDMA), methacrylic acid (MAA), ethylene glycol dimethyl acrylate (EGDMA), inhibitor remover columns, phosphate buffered saline (PBS) tablets, trimethylamine, *N,N*-dimethylformamide, *N,N*-dimethylacetamide and 4-(dimethylamino) pyridine were purchased from Sigma-Aldrich (St. Louis, MO, USA). 2,2′-azobis(2,4-dimethylvaleronitrile) (AIVN) was purchased from Wako Chemicals GmbH (Neuss, Germany). Potassium ferricyanide and potassium ferrocyanide were purchased from JT Baker (Deventer, Netherlands). Methanol (MeOH) and ethanol (EtOH) were purchased from Chem-supply (Port Adelaide, Australia). Aluminum oxide (activated, neutral) was purchased from Acros Organics (Geel, Belgium). Acetonitrile (ACN) was purchased from Scharlau (Barcelona, Spain).

Prior to its usage, Py was purified by filtering through a neutral alumina column to obtain a colourless liquid, then purged with argon and kept at 4 °C in darkness [21]. Additionally, the polymerization solution was purged with argon for 5 min prior to the electropolymerization. Similarly, MAA and EGDMA inhibitors were removed from the monomer solutions with the inhibitor remover pre-packed columns, and immediately used.

Carboxylic functionalized single-walled carbon nanotubes (SWCNTs) were kindly provided by Dr. N.M. Bandaru (School of Chemical and Physical Sciences, Flinders University, Australia).

2.2. Electrochemical system

All electrochemical measurements were carried out in a three-electrode cell, placed into a Faraday cage, by means of a CH Instruments 650e (Austin, TX, USA) potentiostat controlled with the provided software package (which was also used for the fitting of the impedance spectra).

The measurement cell was formed by a glassy carbon electrode (GCE, 3 mm diameter, BAS Inc., West Lafayette, IN, USA) as working electrode, a Ag/AgCl reference electrode (BAS Inc., West Lafayette, IN, USA) and a platinum wire as counter electrode.
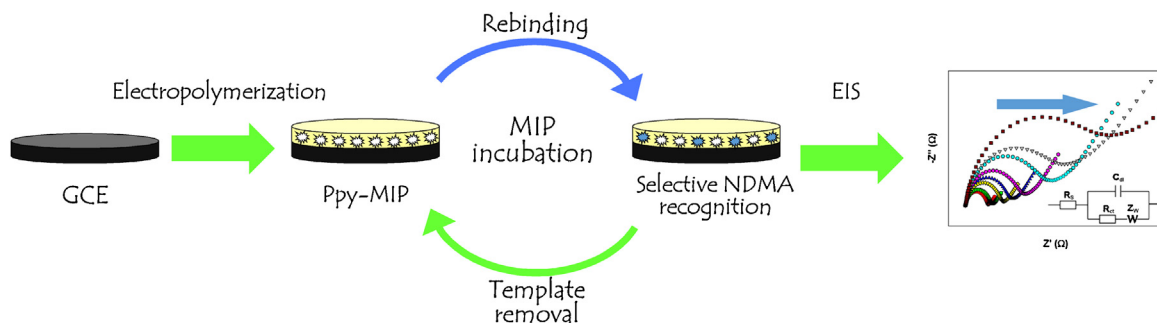

Fig. 1. Schematic of the MIP sensor preparation and approach for the detection of NDMA.