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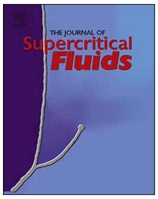

Development of a ferrocenyl-based MIP in supercritical carbon dioxide: Towards an electrochemical sensor for bisphenol A

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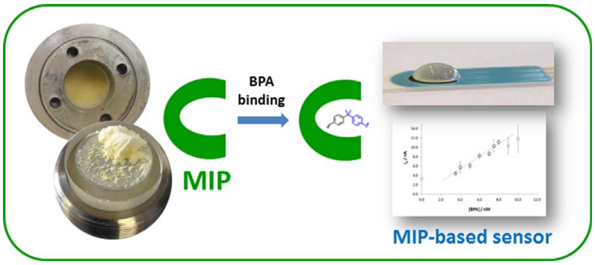
GRAPHICAL ABSTRACT



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ABSTRACT

This work describes the development of a molecular imprinted polymer (MIP)-based disposable sensor for Bisphenol A (BPA). Ferrocenylmethyl methacrylate (FMMA) was co-polymerized with ethylene glycol dimethacrylate (EGDMA) for the first time using supercritical carbon dioxide (scCO$_2$) as porogenic solvent. This polymer was developed with affinity for BPA by molecular imprinting technique and characterized by scanning electron microscopy (SEM), Fourier transform infrared spectroscopy (FTIR), average particle size diameter and particle size distribution. Binding performance was evaluated through affinity and selectivity tests in aqueous media. MIP performance as an electrochemical sensor was studied on commercial carbon screen-printed electrodes in the presence of BPA by differential pulse voltammetry. The results show the successful detection of the BPA characteristic irreversible oxidation peak, and the increase in the current intensity response with BPA concentration (4.7–8 nM), opening a route for the development of cost-effective disposable sensitive sensors for BPA using MIP.

1. Introduction

Molecular imprinting technology (MIT) has become a subject of an enormous research in the last years, with particular applications as chemical (or biological) sensors, artificial antibodies, solid-phase extraction and chromatographic separation [1]. One of the most efficient approaches to offer a synthetic route to artificial recognition systems is by molecular imprinting. Molecularly imprinted polymers (MIPs) are synthetic materials with artificially recognition sites to a specific target molecule. These materials are prepared by a polymerization reaction in the presence of a target molecule (template), appropriate funcional monomer(s) and a cross-linker. When the template is removed from the matrix leaves empty sites within the polymer matrix that have the precise spacial arrangement of the functional groups, thus with high affinity towards the template molecule [2]. The main advantages of these materials is their high selectivity and affinity for the target molecule used in the imprinting procedure, and their physical robustness, thermal stability compared with those of natural molecular recognition

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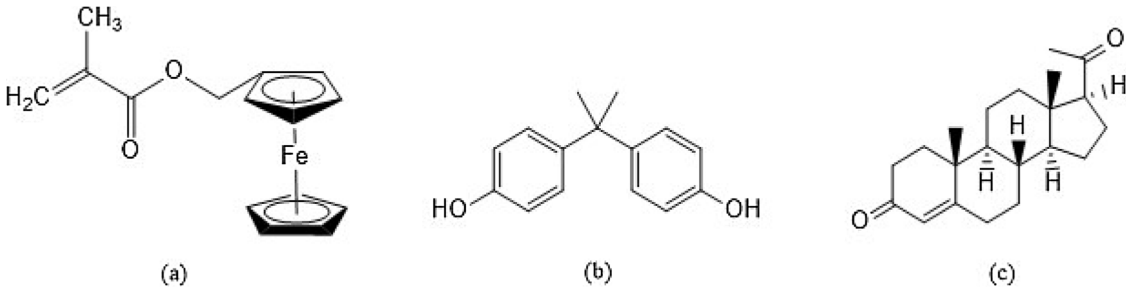

Fig. 1. Molecular structures of electroactive monomer FMMA (a); Bisphenol A (b) and Progesterone (c) used in the selectivity tests.

products (e.g., antibody), as well as low-cost and relatively simple preparation. Consequently MIPs have been used in different fields: solid-phase extraction [3], purification [4], catalysis [5], drug delivery [6], biological antibodies and artificial receptors [7,8] and in the development of electrochemical sensor systems [9–11].

The template used in this work was bisphenol A (Fig. 1a). BPA is a chemical widely used as a monomer in the production of plastics as polysulfone (PS), polycarbonate (PC) and epoxy resins [12–14]. Many studies showed that BPA has been found in products for children as baby bottles, resin coating of cans, drinking water bottles, medical devices, and food packaging [15] In the process of production, the addition of BPA makes the plastic products more transparent, durable and resistant. More than five million metric tons of BPA are produced worldwide each year [16].

BPA is an endocrine disruptor that puts in risk public health. Long-term exposure to bisphenol A may induce negative health effects, like increase the risk of heart and liver diseases, diabetes, and cancer, being also a recognised pollutant of water effluents [17,18]. Consequently, to help preventing the noxious effect of BPA there is a high demand for new analytical techniques that allow the detection of this compound *in situ*. Several analytical methods have been developed for BPA measurement, such as: liquid chromatography–mass spectrometry (LC/MS) [19], gas chromatography–mass spectrometry (GC/MS) [20], capillary electrophoresis [21], spectrophotometric [22], chemiluminescence detection [23], immunoassay detection [24] and electrochemical sensors [10,25,26].

The use of a sustainable and clean technology with a green solvent, such as $scCO_2$, allows the implementation of greener processes with lower environmental impact. $ScCO_2$ is a GRAS solvent (Generally Recognised As Safe), has low reactivity and toxicity, it is highly available in high purity and its critical point is relatively easy to achieve (31 °C and 7.4 MPa). Near the critical point small variations in pressure and temperature result in significant variations in density and properties density-dependent [27,28]. Comparing with the traditional organic solvents, $scCO_2$ is also considered as an excellent solvent extraction method and can be used to extract unreacted monomers, initiator and other types of residues from polymerizations. When it is used as solvent for MIP synthesis, at the end of the reaction and template desorption the reactor is depressurized and the polymer is obtained completely solvent-free since CO_2 is released as gas, remaining in the cell a very pure polymer, obtained as a homogeneous dry powder, that does not need further purification processes. Moreover, $scCO_2$ is apolar and does not interfere with the template-monomer complex, which results in a strongly impact on the structure formation of MIPs and further affect the recognition and separation of the MIPs for template molecules. The MIPs synthetized using $scCO_2$ are obtained as free-flowing powers, dry and pure, with controlled morphology and porosity [29,30].

In this work, we assess the viability of developing electrochemical disposable sensors based on MIPs synthesized with $scCO_2$ technology. The MIP was integrated into a disposable sensor and its behavior was studied by differential pulse voltammetry (DPV), using screen-printed electrodes and applying a simple and relatively inexpensive experimental procedure. In particular, the developed methodology is very simple, detecting BPA in water in low concentration range (3.2–8 nM), which opens up the future potential application in BPA detection in water bottles and water effluents amongst other media [31,32].

2. Materials and methods

2.1. Materials

Bisphenol A (2,2-bis (4-hydroxyphenyl) propane, BPA, 99% purity) as template, ethyleneglycol dimethacrylate (EDGMA, 98% purity) as cross-linker and 2,2′- Azobis(2-methylpropionitrile) (AIBN, 98% purity) as initiator and Progesterone (PRO, 99% purity) as analogue molecule were all purchased from Sigma-Aldrich. Ferrocenylmethyl methacrylate (FMMA, 95% purity) as functional monomer was supplied by Fluorochem. Methanol (99.9% purity) and Acetonitrile HPLC grade (99.9% purity) were supplied by Carlo Erba reagents. Phosphate buffered saline (PBS) solution was prepared from PBS buffer tablets from Sigma-Aldrich. Carbon dioxide (N48, with purity higher than 99.998%) was purchased from Air Liquide. Electrochemical experiments were carried out using screen-printed carbon electrodes (SPE) from Dropsens. All chemicals and reagents were used without any further purification.

2.2. Synthesis of FMMA-based MIP polymers in $scCO_2$

The FMMA- based MIP was synthesized in a 33 mL stainless steel high-pressure cell equipped with two aligned sapphire windows, allowing visualization of the mixture and reaction, and also on an already elsewhere described setup [27]. In a typical MIP synthesis, FMMA (0.975 mmol), EDGMA (5 mmol), BPA (0.19875 mmol) and AIBN (1 wt % of total weight) were added to the cell. The cell was purged with a flow of CO_2 up to 1 MPa and was immersed in ultra-sound bath (Nahita, model 620/10) for 10 min to help the dissolution of solids. After this, the cell was immersed in a thermostatic water bath set to 65 °C to ensure that AIBN was at optimal initiation conditions. Temperature control was made using a controller (LAUDA, Model Alpha). Carbon dioxide was added up to 22 MPa and polymerization reactions proceeded for 24 h. At the end of the reaction the polymer was washed with a fresh stream of $scCO_2$ for 1 h to ensure that all the unreacted reactants were removed from the final product. Non-imprinted polymer (NIP) synthesis was followed identical procedure, with exception that no template was added to the reactional mixture.

2.3. BPA- desorption in $scCO_2$

After the polymerization reaction, the removal of the template from the matrix is a critical step in molecular imprinting process, in order to turn the specific sites available for future re-binding in the final application. The use of supercritical fluid extraction can increase at least 10-fold the diffusion coefficient, being most appropriate for extraction of relatively non-polar compounds from solid matrices [33]. To ensure that the synthetized MIP had no template (BPA) entrapped, a high pressure apparatus similar to that described by Soares da Silva et al.