Synthesis of nano-sized molecularly imprinted polymer for selective extraction of Paracetamol

Golaleh Sheykhaghai1*, Moayad Hossainisadr1, Mehrdad Mahkam3, Kani Seyednezami2

1. Department of Chemistry, Since and Research Branch, Islamic Azad University, Tehran, Iran
2. Department of Chemistry, Mahabad Branch, Islamic Azad University, Mahabad, Iran
3. Chemistry Department, Faculty of Science, Azarbaijan Shahid Madani University, Tabriz, Iran

Corresponding author: Golaleh Sheykhaghai

ABSTRACT: A molecularly imprinted polymer nanoparticle (MIP-NPs) for the selective extraction of Paracetamol is described. MIPs were prepared by suspension polymerization in silicon oil in the presence of methacrylic acid (MAA) as a functional monomer, ethylene glycol dimethacrylate (EGDMA) as a cross-linker, 2, 2-azobisisobutyronitrile (AIBN) as an initiator and Paracetamol as a template molecule. The MIP-NPs were characterized by scanning electron microscopy (SEM) and thermo gravimetric analysis (TGA). Imprinted Paracetamol were eliminated from MIPs by acetic acid in methanol (20:80 V/V %) as an eluting solvent. Measurements of Paracetamol extracted from MIP-NPs compared with Tizanidine (TZD) showed that the imprinted polymer acts selectively.

Keywords: molecularly imprinted polymer, solid phase micro-extraction (SPME), solid phase extraction (SPE), Paracetamol, Tizanidine

INTRODUCTION

Molecularly imprinted polymers (MIPs) are synthesized by creating a three–dimensional polymeric matrix around a template molecule [1]. The most common methods of synthesis include: precipitation polymerization, mini- and micro- emulsion polymerization, core –shell (with subsequent grafting), suspension polymerization in silicon oil and living radical polymerization processes, such as atom transfer radical polymerization (ATRP) and reversible addition–fragmentation chain transfer polymerization (RAFT) [1,2]. In contrast to bimolecular, MIPs are stable at low and high pH, pressure and temperature (<180°C) [3-6]. MIPs nanoparticles have high surface area to volume ratios; thus, imprinted cavities are more easily accessible by the templates [7, 8]. So far, prepared MIPs nanoparticles have been widely used for specific purposes, as enzyme substitutes [9,10], drug delivery systems (DDS) [11,12], antibody substitutes [13-16], capillary electro chromatography [17-20], electrochemical sensors [21-23], solid phase extraction (SPE) [24-25], solid phase micro extraction (SPME) [26,27], stir bar sorptive extraction (SBSE) [28,29], dispersive liquid-liquid micro extraction (DLLME) [30], quartz crystal microbalance [31], biomimetic sensors [31, 32] and membrane separation [33]. The purpose of this research was to prepare the molecularly imprinted polymer nanoparticles by suspension polymerization in silicon oil method for selective extraction of paracetamol. Measurement of Paracetamol obtained from MIPs –NPs compared with TZD showed that the imprinted polymer has acted selectively.

MATERIAL AND METHODS

Experimental

Reagents and solutions

Methacrylic acid (MAA), ethylene glycol dimethacrylate (EGDMA), 2,2- azobisisobutyronitrile (AIBN) were purchased from merck chemical company, The drugs used in this study (Paracetamol and TZD) were obtained from daroupakhsh Co. (Tehran, Iran). All the other chemicals used in this study were of analytical reagent grade obtained from Merk (Germany). A stock standard solution of target analyte (Paracetamol) was prepared from methanol containing 1000 mg L⁻¹ of the drug. The working solution (5 mg L⁻¹) was prepared daily with an appropriate dilution of Paracetamol stock.
**Instrumentation**

A double beam spectrophotometer (UV-Vis) Perkin Elmer model lambda 25 was used for all measurements. The thermo gravimetric analysis (TGA, model PL, UK) was used to determine the thermal properties of synthesized polymers, scanning electron microscopy (SEM, LEO 1430 VP, UK) was used to characterize the nano-sized MIPs. The FT-IR spectra in KBr were recorded by a Spectrum RXI (Perkin Elmer, USA).

**Synthesis of molecularly imprinted polymer nanoparticles**

The schematic representation of the synthesis of MIP-NPs is shown in Fig. 1. In order to synthesis of MIP-NPs, suspension polymerization in silicon oil was used. Briefly, 0.1 mmol of Paracetamol, 5 mmol of MAA, 9.2 mmol of EGDMA and 0.02 g of AIBN were dissolved in 5 mL of methanol. The pre-polymerization mixture was added to the silicon oil and sonicated for 20 min. lastly; the system was reacted at 62°C for 24 h [34]. The non imprinted polymer nanoparticles (NIP-NPs) were synthesized using the same process of MIP-NPs, except the addition of the target molecule (Paracetamol).

**RESULTS AND DISCUSSION**

**Characterization of the synthesized MIP-NPs**

The resulting nano-sized MIPs were characterized by scanning electron microscopy (SEM). As it shown in Fig. 2, the average diameter of MIP-NPs was about 60 nm. The structure of MIP-NPs was investigated by FT-IR spectra. As it shown in Fig. 3, in all three spectra include: unleached MIPs, leached MIPs and NIPs, the strong stretching vibration band about 1720 cm$^{-1}$ is related to the $–\text{C}=\text{O}$ of the carboxylic acid group of methacrylic acid, that is typically located at the surfaces of the polymeric particles. A band at about 1610 cm$^{-1}$ for unleached MIP showed the $–\text{C}=\text{O}$, linked to Paracetamol (template), via coordination bonding. However, in the region of 1500-1700 cm$^{-1}$ for NIP, there are no observed bands.
The thermal stability of the synthesized MIP-NPs was investigated by TGA. Fig. 4. Indicates TGA plot for the MIP-NPs. TGA plot of imprinted polymer shows the two stage demolition behavior. The little weight loss about 140 °C (1.98 % weight loss) is due to physically combined water (first step demolition). The second stage of demolition viewed to happen at temperature range between 140 °C and 700 °C which is related to exclusion of remaining organic solvents and combustion of organic part (93.71 % weight loss).

Optimization of polymerization
The effect of solutions pH
To evaluate the effect of pH, working solutions by varying pH from 2 to 10 were examined. As can be seen from Fig. 5, the highest extraction efficiency of Paracetamol by MIP-NPs was 7. As a result, the pH of 7 was selected as optimized the pH.
The effect of molar ratios cross-linker to functional monomer

Molar ratios EGDMA to MAA for extraction Paracetamol from working solutions were examined using different volumes (1.6, 2.3, 3.9, and 1.84). As a result, 1.84 was the optimum molar ratio of EGDMA to MAA.

The effect of quantity of the template

To optimize the quantity of the template, several pre-polymer solutions containing different amounts (0.04-0.2 mmol) of Paracetamol were ready in 5 mL of methanol. Thus, 0.1 mmol was used as optimum quantity of the template.

The effect of elution solvent type and elution solvent volume on the extraction

In order to evaluate solvent type on the extraction Paracetamol (template) from MIP-NPs, several solvents: distilled water (100 V/V %), methanol (100 V/V %), acetic acid in methanol (10:90 V/V %), and acetic acid in methanol (20:80 V/V %) were studied. As a result, acetic acid: methanol (20:80 V/V %) were selected as the optimum elution solvent type. To investigate elution solvent volume different volumes from (2 to 10 mL) were examined. According to Fig. 6, 6 mL of acetic acid in methanol (20:80 V/V %) was selected as optimum elution solvent volume.

Selectivity

To evaluate selectivity of synthesized MIP-NPs toward Paracetamol, we have measured Paracetamol and TZD in city water samples at the concentration of 5 mg L$^{-1}$ of Paracetamol and TZD under optimum conditions. According to Figs 7a and 7b, synthesized MIP-NPs for Paracetamol has acted selectively.
Fig. 7. UV-Vis spectra of (a) Paracetamol by MIPs (b) TZD by MIPs

CONCLUSION

These experiments have conclusively demonstrated that: this method for the preparation of Paracetamol-MIP from methacrylic acid, ethylene-glycol dimethacrylate is very effective and simple for the selective SPME of Paracetamol. Other advantages: Low consumption of organic solvent. Also prepared MIP-NPs can be used repeatedly (8 times) with no significant decrease in its binding affinities.

REFERENCES


Y. Hu, J. Li, Y. Hu, G. Li, Development of selective and chemically stable coating for stir bar sorptive extraction by molecularly imprinted technique, Talanta 82 (2010) 464-470. [29]

