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Hybrid molecularly imprinted poly(methacrylic acid-TRIM)-silica chemically modified with (3-glycidyloxypropyl)trimethoxysilane for the extraction of folic acid in aqueous medium

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ABSTRACT

In the present study a hybrid molecularly imprinted poly(methacrylic acid-trimethylolpropane trimethacrylate)-silica (MIP) was synthesized and modified with (3-glycidyloxypropyl)trimethoxysilane (GPTMS) with posterior opening of epoxy ring to provide hydrophilic properties of material in the extraction of folic acid from aqueous medium. The chemical and structural aggregates of hybrid material were characterized by means of Fourier Transform Infrared (FT-IR), Transmission Electron Microscopy (TEM), Scanning Electron Microscopy (SEM), Thermogravimetric analysis (TGA) and textural data. Selectivity data of MIP were compared to non-imprinted polymer (NIP) through competitive sorption studies in the presence of caffeine, paracetamol or 4-aminobenzamide yielding relative selectivity coefficients (k′) higher than one unit, thus confirming the selective character of MIP even in the presence of structurally smaller compounds than the folic acid. The lower hydrophobic sorption by bovine serum albumin (BSA) in the MIP as compared to unmodified MIP proves the hydrophilicity of polymer surface by using GPTMS with opening ring. Under acid medium (pH 1.5) the sorption of folic acid onto MIP from batch experiments was higher than the one achieved for NIP. Equilibrium sorption of folic acid was reached at 120 min for MIP, NIP and MIP without GPTMS and kinetic sorption data were well described by pseudo-second-order, Elovich and intraparticle diffusion models. Thus, these results indicate the existence of different binding energy sites in the polymers and a complex mechanism consisting of both surface sorption and intraparticle transport of folic acid within the pores of polymers.

1. Introduction

Molecularly imprinted polymers (MIPs) are well known materials that allow the molecular recognition in different applications of analytical sciences such as preconcentration methods [1], optical and electrochemical sensors [2,3], preparation of stationary phase for liquid chromatography [4], solid phase extraction [5], drug delivery systems [6] and catalytic systems [7], resulting in improved selectivity to procedure. Ion imprinted polymers (IIPs) have also been widely used in the field of separation with outstanding features in terms of selectivity [8,9]. MIPs or IIPs are polymerized by means of radicalar reaction of functional monomer and cross-linking reagent in the presence of the target analyte, resulting in trapping template analyte in the cross-linked polymer matrix. Upon removal of target analyte, cavities possessing a shape and an arrangement of functional groups corresponding to that of the analyte will be formed [10]. The selective feature of MIPs depends upon interactions between template and functional monomers such as non-covalent (hydrogen bonding, dipole–dipole), semi-covalent, covalent or hydrophobic ones [11]. It is well known that MIPs have outstanding molecular recognition ability in organic solvents, mainly in the same porogenic solvent used in the synthesis. Therefore, once MIPs are water-incompatible, their practical application in aqueous solution mostly fail to show specific template binding, probably due to non-specific interactions between small analytes and binding sites of polymer, and the presence of hydrophobically driven bonds [12,13]. Furthermore, the selective performance of MIPs in biological samples such as blood, serum, milk and plasma can be drastically affected by the sorption of macromolecules such as proteins onto their surface [14]. In this sense, some efforts aiming at obtaining water-compatible MIPs with hydrophilic surface have been reported for controlling the adhesion of biomolecules. In aqueous medium, both hydrophilic surface of the MIPs and proteins are hydrated by water molecules and, thus, the presence of water at the interface will prevent or diminish the sorption of proteins [15]. The most common approach for preparing MIPs with hydrophilic surface is based on use of hydrophilic comonomers such as 2-

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hydroxyethyl methacrylate (HEMA) [16], glycerol monomethacrylate (GMMA) and glycerol dimethacrylate (GDMA) in the synthesis [17,18]. Despite their significant success to produce water-compatible MIPs, these comonomers, which contain hydroxyl groups, can also interact with template by means of hydrogen bonds formation, thus decreasing the formation of imprinting sites. Another approach for obtaining water-compatible MIPs relies upon the use of acrylamide, methacrylamide and 3-acrylamido-N,N,N-trimethylpropan-1-aminium chloride (AMTC) as hydrophilic functional monomer [19,20], but no evidence has been reported on the exclusion of macromolecules by the MIPs.

An interesting approach to obtain water-compatible MIPs was described by Puoci and coworkers [21]. In this work the authors used glycidilmethacrylate (GMA) as pro-hydrophilic co-monomer, which interferes less in the pre-polymerization complex formation. Upon polymerization of methacrylic acid (MAA) in the presence of caffeine as template and divinyl benzene as cross-linking reagent, epoxide ring opening from GMA with perchloric acid was performed for the hydrophilic modification of polymeric surface. The synthesis of organic polymer was based on bulk method, which leads to the formation of irregular particle sizes due to the milling process and low amount of recognition sites.

According to considerations mentioned previously and bearing in mind that few studies have reported the preparation of water-compatible polymers through chemical imprinting technology, the purpose of the present study was to synthesize a new water-compatible organic/inorganic hybrid molecularly imprinted poly(methacrylic acid-TRIM)-silica using 3-(glycidyloxypropyl)trimethoxysilane (GPTMS) as pro-hydrophilic comonomer for the sorption of folic acid (FA). Some reports have demonstrated the great advantages of hybrid organic–inorganic polymers including high physical and chemical stability, good textural and morphological features and uniform particle sizes, very important features in sorption process, but neither of them exploits the synthesis of MIP with external hydrophilic layer [22–24]. Folic acid has been chosen as template since it is a water-soluble vitamin, thus MIPs here synthesized can be explored as a good sorbent for this molecule. Additionally, studies dedicated to synthesis of MIPs for FA have been few exploited mostly due to larger size of molecule, which can hinder the creation of selective binding sites in the MIP.

2. Experimental

2.1. Chemicals

Chemicals-folic acid (2S)-2-[[4-[(2-amino-4-oxo-1 H-pteridin-6-yl)methylamino]benzoyl]amino]pentanedioic acid (FA), methacrylic acid (MAA), trimethylolpropane trimethacrylate (TRIM), 2,2′-azoisobutyronitrile (AIBN), tetraethoxysilane (TEOS), 3-(glycidyloxypropyl)trimethoxysilane (GPTMS), vinyltrimetoxysilane (VTMS), caffeine, paracetamol, 4-aminobenzamide and bovine serum albumin (BSA) were purchased from Sigma-Aldrich® (Steinheim, Germany) and used without prior purification. The solvents and acids (acetic acid, hydrochloric acid, acetonitrile (ACN), methanol and ethanol) were also purchased from Sigma-Aldrich®. All the solutions were prepared in ultra-pure water obtained from a Milli-Q® purification system (Millipore®) (Massachusetts, USA).

2.2. Instruments

A liquid chromatograph model LC-20AT, Shimadzu® (Tokyo, Japan) equipped with a photodiode-array detector (PDA) was used to measure folic acid. The separation was carried out using a CLC-ODS column (250 mm × 4.6 mm id, 5 μm in particle size) and a guard column Phenomenex® (4.0 mm × 3.0 mm i.d., 5 μm in particle size). The mobile phase consisted of acetonitrile (ACN) and 0.266 mol L^{-1} acetate buffer (pH 2.8) whose separation was performed in gradient elution at 25 °C, from 15% to 24% ACN in 8.5 min and held for another 21.5 min. The flow rate was operated at 0.5 mL min^{-1} and the injection volume was 20 μL. The measurements of pH were performed using a pH meter Metrohm® 827 pH lab (Herisau Switzerland). Infrared (IR) transmission spectra (KBr pellets) of the polymers were recorded on a FT-IR 8300 spectrometer (Shimadzu®, Tokyo, Japan) in the range of 4000–400 cm^{-1}. An UV–Vis spectrophotometer Lambda 25 (Perkin Elmer®, Massachusetts, USA) was employed for the measurements of bovine serum albumin, caffeine, paracetamol and 4-aminobenzamide. A manifold system (Bio-Rad) with a capacity for 12 cartridges, coupled to a vacuum pump (Marconi® MA 2057, Piracicaba, Brazil) was used in the protein binding study. The morphology of the polymers was performed using a Philips® FEI Quanta 200 scanning electron microscope (SEM) at an accelerating voltage of 30 kV (FEI Company, Scientific and Technical Instruments, Oregon, USA). Before analysis, the samples were coated with a thin layer of gold alloy to minimize charging effects under electron beam irradiation using a Bal-Tec® MED 020 equipment. Analyses by transmission electron microscope (TEM) were performed using JEOL JEM-1400 microscope at an accelerating voltage of 120 kV (Tokyo, Japan). The samples were dispersed in ethanol under sonication for 20 min, followed by deposition of slurry onto copper grid and dried under vacuum. The surface area and average pore diameter, obtained respectively by multipoint BET (Brunauer, Emmett and Teller) and BJH (Barret, Joyner and Halenda) method, were determined from nitrogen adsorption experiments by means of the physical adsorption method using a Quantachrome® Model Nova 1200e automatic nitrogen gas adsorption instrument (Boynton Beach, Florida, USA). The samples were preactivated under vacuum at 85 °C for 5 h. Thermal analysis was performed on a TGA 4000 thermogravimetric analyzer (Perkin Elmer®, Massachusetts, USA). About 15 mg of polymer were heated from 30 to 900 °C at a scan rate of 10 °C min^{-1} under nitrogen atmosphere.

2.3. Synthesis of hybrid molecularly imprinted poly(methacrylic acid-TRIM)-silica chemically modified with (3-glycidyloxypropyl)trimethoxysilane

The synthesis of hybrid polymer was based on the precipitation method with some modification according to literature data [23]. 12 mmol of MAA were dissolved in 310 mL of ACN and mixed with 2.94 mmol of VTMS, 24 mmol TRIM and 600 mg of AIBN. Nitrogen gas was bubbled for 5 min and then the flask was sealed. The mixture was incubated for 1.5 h at 60 °C temperature and after this time, 2 mmol of FA dissolved in 100 mL of 3.0 mol L^{-1} HCl together with 52 mmol of TEOS were added to the mixture. The solution was polymerized at 60 °C during 24 h. Then, the hybrid polymer was dried and suspended in 300 mL of ethanol followed by addition of 48 mmol of GPTMS and 26 mL of 1.0 mol L^{-1} NaOH. This mixture was kept under stirring at room temperature for 24 h. The same procedure, but without a template, was performed to prepare the corresponding NIP (non imprinted polymer), as control materials. The epoxide ring grafted on the surface of hybrid polymer was opened in a similar way to Qi 2009 [25] with some modifications. For this task, 500 mL of 0.5% HCl solution were stirred with 10 g of hybrid polymer at 60 °C in a thermostatic bath during 36 h. The obtained material herein was named as MIP. The removal of folic acid from polymeric matrix of hybrid material was carried out by using a Soxhlet system with a mixture of methanol:acetic acid (90:10 *v*/*v*) until no template could be detected by HPLC-DAD.

2.4. Sorption kinetic study

The influence of stirring time on the kinetic sorption of folic acid onto polymers was evaluated by batch experiments. 50 mg of polymers in polyethylene flasks were stirred at 120 rpm for different time periods from 1 to 720 min with 40 mL of 10 mg L^{-1} folic acid under pH 1.5 in 0.01 mol KCl/HCl. Upon stirring time, the mixture was centrifuged and aliquots of supernatants were collected, filtered through a 0.45 μm