Mass transfer in a special type of nanomaterials: MIPs

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This study presents data regarding the mass transfer in a new type of nanomaterials: molecularly imprinted polymers (MIPs). MIPs are polymers with very high affinity for the substance used for their imprinting (called template). The preparation technique of MIP pearls is new and a mass transfer study inside these new materials is imperative. Adsorption isotherms were obtained experimentally for MIP pearls and for the corresponding NIP (non-imprinted polymer) in different conditions of temperature, solvent flow and initial concentration. The obtained curves were fitted, as incipient study, with a function that characterizes the dose response in pharmaceutics and chemistry.

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1. Introduction

Molecularly imprinted polymers (MIPs) are among today's most debated types of advanced polymeric materials due to their repeatedly confirmed affinity for the target molecule on the scientific scene and due to their expansive area of applications: medicine [1], environment [2], analytical and separation techniques [3], catalysis [4], pharmaceutics, sensors [5] and more. A molecularly imprinted polymer is a polymer that formed in the presence of a molecule that is extracted afterwards, thus leaving complementary molecular cavities behind with specific electronic surroundings.

Similar methods that are interested in shape memory, nanomanipulation and templating the materials are abundant in literature [6-9], but MIP concept remains one distinctive and in continuous evolution.

The pharmaceutical field enriched with many selective materials based on MIPs, one of the recent studies dealing with the detection of sildenafil and vardenafil (inhibitors of phosphodiesterase type 5 – PDE5) in herbal dietary supplements [10]. The incidental excessive use of this drugs may alter seriously the health, this being the reason of concern regarding their detection. The detection of these molecules is very difficult due to the complex mixtures in which they can be found. Magnetic MIPs based on 2-trifluoromethyl acrylic acid (TFMAA) and ethylene glycol dimethacrylate (EGDMA) were successfully applied for the separation of the target substances from herbal mixtures.

The separation technique based on MIPs, so called MISPE (molecularly imprinted solid phase extraction), was applied to separate a bioactive ingredient in the traditional Chinese medicine, podophyllotoxin (PPT), from complex phytoextracts of Dysosma versipellis, Sinopodophyllum hexandrum and Diphylleia sinensis [11]. The known pharmacological activities of PPT are: antitumoral, antiviral, inhibitor of reverse transcriptase (a way to combat HIV), immunomodulatory, hemostasis, detoxification and detumescence. The MIP for PPT was obtained by precipitation polymerization under microwave heating of the mixture: acrylamide as monomer, ethylene glycol dimethacrylate and divinylbenzene as crosslinkers, acetonitrile as porogen and AIBN as initiator. The SPE column packed with PPT MIP showed limits of detection between 0.12–0.18 $\mu g \cdot mL^{-1}$ and the recovery of template was in the range of 89.5–91.1%.

In this study, acrylonitrile (AN)-acrylic acid (AA) MIPs selective to diosgenin, prepared by phase inversion method [12] were used to perform mass transfer experiments (adsorption and extraction).

2. Experimental

For the adsorption studies were used AN: AA 80:20 copolymer pearls (Fig. 1), imprinted with diosgenin (MIP) and non-imprinted (NIP). The template is extracted from MIP pores using ethanol (it works good also with methanol and chloroform), but ethanol was chosen due to less toxicity reasons. Adsorption was done also from ethanol solutions of diosgenin.

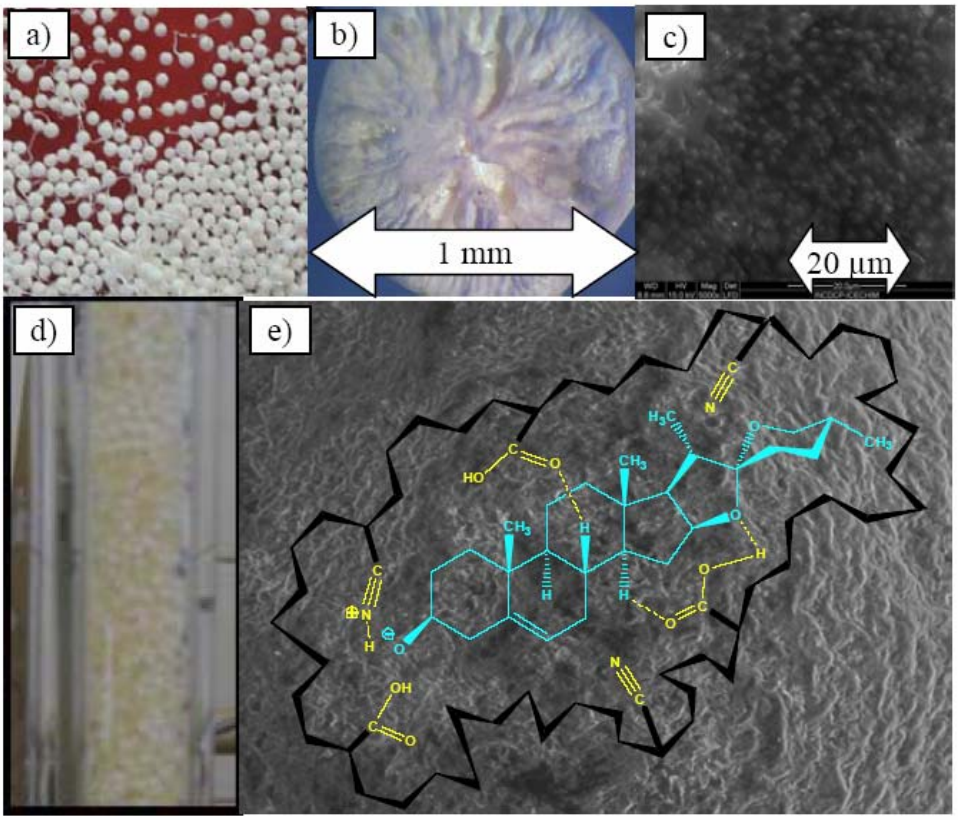

Fig. 1. MIP pearls. a) dried pearls; b) section in a MIP pearl; c) SEM for a MIP pearl; d) glass column packed with MIP pearls; e) theoretical binding of the template (diosgenin) inside the copolymer matrix.

18.5 g AN:AA 80:20 of copolymer pearls (firstly MIP, and then NIP) were used to fill up a glass column as packing bed with the dimensions: height (h_p) = 445 mm and diameter (d_i) = 10 mm. The bed of polymeric pearls is limited by two small beds (30 mm) of glass spheres (1 mm diameter). The inferior bed has two functions: one, to support the pearls and second, to uniformly distribute the upward mobile phase, while the superior one has the function to keep the pearls inside the column. The volume of the fixed bed is 0.035 L, while the medium bed density of polymeric pearls is 528 g/L.

The temperature was maintained constantly during the adsorption – extraction experiments with the help of a VEB MLW thermostat bath. In order to choose the extraction conditions, extraction experiments were conducted at three temperatures: 25ºC, 45ºC, and 60ºC. The adsorption/rebinding experiments were performed at 25ºC. Two flows were used for both extraction (extraction flow - EF) and adsorption (adsorption flow - AF) experiments: 3 mL/min and 6 mL/min. The gathered volume for each sample was 1 mL. For the adsorption experiments, two different diosgenin concentrations in the initial solution were used: 0.2w% and 0.3w% (weight percent). The concentration was calculated using the signals obtained from an HPLC with refractive index detector (RID).

3. Results

Experimentally were obtained curves that explain the mass transfer phenomenon in MIP and NIP, when three parameters are varied: the solvent velocity through pearls bed, the temperature and, for the adsorption case, the initial concentration of the diosgenin solution. The diagram that gives the evolution of diosgenin concentration in the effluent out of the pearls bed represents the breakthrough curve that characterizes the experiment. The breakthrough curve is specific to MIP and NIP and depends also on the initial concentration and the solvent flow.

Firstly, it is necessary a conversion of the HPLC signal in terms of concentration. The HPLC gives graphical signal with an area that can be calculated by integration. The first degree equation c(w%)=f(A) can be used to calculate any diosgenin concentration, if the area exists.

$$c(w\%) = 9.5 \cdot 10^{-7} \cdot A - 0.00107 \qquad (1)$$

The three consecutive extractions done at 25ºC, 45ºC, and 60ºC and at 6 mL/min solvent flow showed that at 45ºC all the template is removed from all the pores (Fig. *2*). The validation was evidenced by the fact that the third extraction (at 60ºC) didn't contained diosgenin at all.

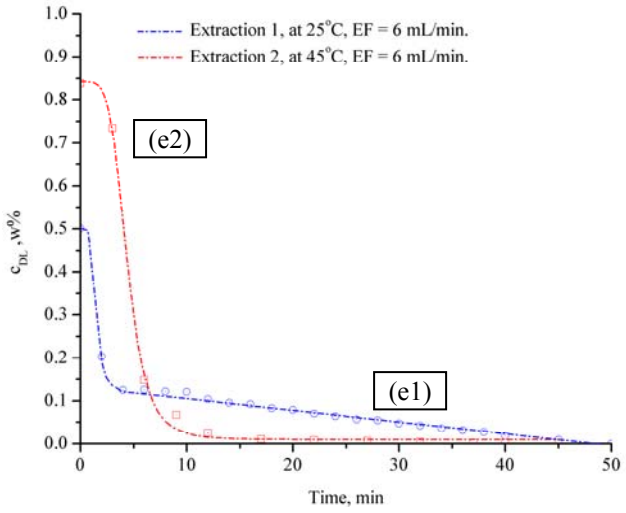

Fig. 2. Consecutive extraction of the template, with ethanol, at two temperatures (25ºC and 45ºC).

At 25ºC the extraction is not complete. When the temperature is raised (at 45ºC), the extraction goes deeper into the pores and the template is completely removed.

The experimental data will be fitted with equations, so every curve will receive a number (e1,e2,e3,…), meaning that the equation 1, 2, 3… is fitting that curve. A table with the equations' parameters will be presented in section 4. Discussions.

The binding capacity of the imprinted polymers with varying concentrations of the analyte was evaluated in comparison with the non-imprinted copolymer pearls. For both types of polymer the initial template concentration was 0.2 w%, the solution flow was 3 mL/min and the extraction flow also 3 mL/min. The adsorption isotherms for these experiments are presented in Fig. 3.

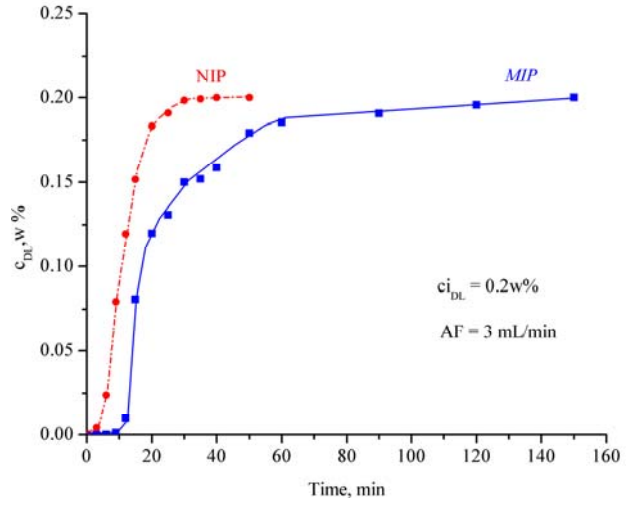

Fig. 3. Breakthrough curves for MIP and NIP, adsorption flow (AF) 3 mL/min.

The Figs. 3 and 4 show the differences between the breakthrough curves for the selective polymer (MIP) and the non-selective polymer (NIP). It is clear that the binding capacity of the imprinted polymer is higher than the one for the non-imprinted. This is due to those N binding sites that are formed inside a MIP. A polymer prepared in the mentioned manner is porous, so even the non-imprinted pearls can adsorb template molecules. Another difference is that the breakthrough for NIP starts sooner (2 min) than in MIP (7 min), the reason being the higher number of pores and binding sites in MIP.

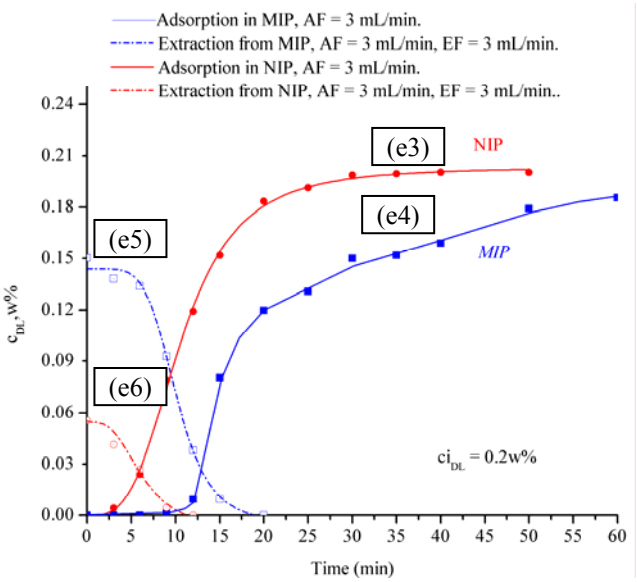

Fig.4. Adsorption and extraction of the template in MIP and NIP (AF-adsorption flow, EF-extraction flow).

The extraction curves offer more information about the mass transfer inside the prepared materials. The elution from NIP is faster (it ends in 12 min) because the pores are fewer and not selective. The imprinted pearls retained a higher quantity of template by physically bounding the diosgenin molecules using hydrogen bonds or Van der Waals forces.

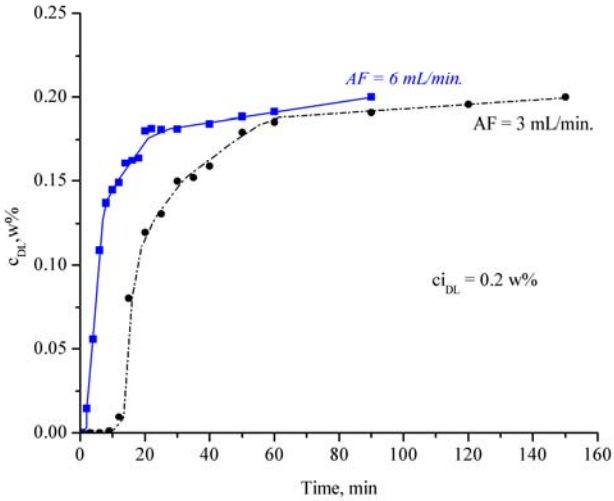

Fig. 5. Breakthrough curves for MIP at two adsorption flows (AF) and initial concentration 0.2w%.

The Figs. 5 and 6 describe the influence of the solution flow through the AN:AA MIP. The adsorption experiments were carried out from the same 0.2% solution, but at two different flows (3 mL/min and 6 mL/min) (and 25ºC).

Fig. 5 is showing that a higher flow leads to a better adsorption of template inside the selective pores. More, a bigger flow equals a faster breakthrough of the pearls bed.

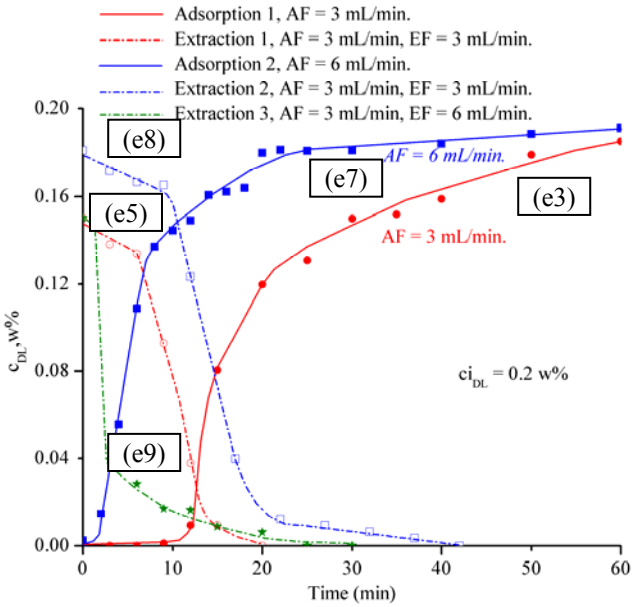

Fig. 6. Adsorption and extraction of the template in MIP at ci_{DL} = 0.2 w%.

After adsorption, the extraction (at 45ºC) of template from pearls is going similarly in the two cases, at 3 mL/min. But at 6 mL/min, the shape of elution curve is changing. The extraction is faster in the first 5 min, corresponding to the superficial binding sites, but after that the elution is slower, similar to previous cases, and the template elutes from the deepest pores. The extraction is total in all cases, fact proved by a second extraction experiment, at higher temperature (60ºC).

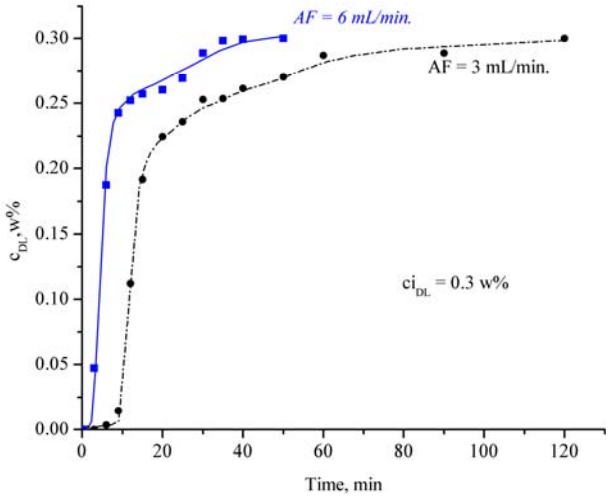

Fig. 7. Breakthrough curves for MIP at two adsorption flows (AF) and initial concentration 0.3 w%.

If the initial concentration of diosgenin in ethanol is raised from 0.2 to 0.3 w% and the adsorption-extraction experiments are repeated, the Figs. 7 and 8 are obtained.

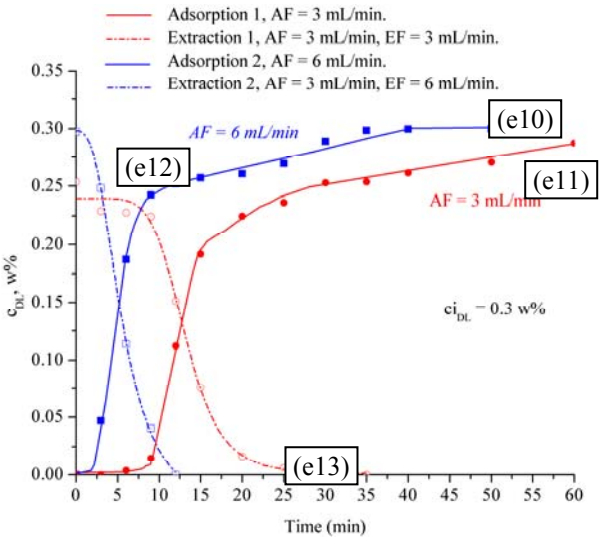

Fig. 8. Adsorption and extraction of the template in MIP at ci_{DL} = 0.3 w%.

4. Discussions

The 13 different curves obtained from the adsorption-extraction experiments are suitable for the mathematical evaluation. To study the mass transfer into these new materials (imprinted and non-imprinted) is an imperative task and this is the main purpose of the article.

The experimental data points were fitted, as the first step of study, using the existing functions in Origin Pro 8 (more then 40). For the mass transfer in AN:AA MIP pearls, one function was found to be suitable. It is a function that gives the logistic dose response in pharmacology and chemistry, y=f(x), equivalent to c_{DL}=f(t).

$$y = A2 + \frac{A1 - A2}{1 + \left(\frac{x}{x_0}\right)^p} \tag{2}$$

The calculated parameters (A1, A2, x_0 and p) are given in Table 1 for all 13 different isotherms obtained.

Table 1. Parameters of the obtained isotherms.

Equation	A1	A2	x_0	p
e1	0.499	-2	$2.2 \cdot 10^{6}$	0.135
e2	0.842	0.009	4.39	4.856
e3	-0.003	0.143	12.15	5.593
e4	$4 \cdot 10^{-4}$	0.059	5.03	2.454
e5	0.144	-0.005	10.12	5.385
e6	0.054	-0.009	6.26	3.114
e7	0.002	0.186	5.49	2.099
e8	0.174	0.004	13.79	6.235
e9	0.150	-0.065	2.56	0.354
e10	-0.003	0.279	4.84	2.920
e11	0.006	0.245	12.56	7.118
e12	0.298	-0.035	5.60	2.734
e13	0.239	$5.2 \cdot 10^{-4}$	13.17	6.225

5. Conclusions

From the conclusions that result from this study, the first one is that for extraction, higher temperature and velocity lead to a faster desorption of the template. Both temperatures, 45ºC and 60ºC, realize the extraction of the template from the copolymer matrix, but due to energetic reasons it is recommended the 45ºC value. The easiness of a total extraction is a real advantage in the MIP field, meaning that the binding sites are very accessible. Also the reproducibility of the adsorption-extraction experiments is very good (for triplicates), showing that the binding sites are active and working very well.

For adsorption experiments was observed that a higher concentration into the initial solution lead to a higher concentration of diosgenin in pearls.

A function was found to be able to correlate the experimental mass transfer data, but future studies are in work for a better description of the complex phenomenon inside the molecularly imprinted polymer pearls.

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