Korean J. Chem. Eng., **22**(2), 264-267 (2005)

Adsorption Isotherm of Ibuprofen on Molecular Imprinted Polymer

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(*Received 19 October 2004 • accepted 14 December 2004*)

Abstract−A molecular imprinted polymer (MIP) using (+)-(S)-2-(4-isobutylphenyl) propionic acid ((+)-(S)-ibuprofen) as the template and 4-vinylpyridine (4-VPY) as the functional monomer was prepared. Chloroform and acetonitrile were used as the porogen with ethylene glycol dimethacrylate (EGDMA) as the crosslinker and 2,2'-azobis(isobutyronitrile) (AIBN) as the initiator. Comparison of ibuprofen adsorption isotherm on molecular imprinted and blank polymers was made by the static method. The adsorption equilibrium data were correlated into the Freundlich, Langmuir, Sips (Langmuir-Freundlich) and Radke-Prausnitz isotherm models, respectively. By a nonlinear regression analysis, the experimental parameters in the equilibrium isotherms were estimated and compared. The calculated data is well fitted with the experimented data. Through the analysis, the ibuprofen imprinted polymer showed higher adsorption ability than blank polymer.

Key words: Adsorption Isotherm, Molecular Imprinted Polymer, Ibuprofen, HPLC

INTRODUCTION

The adsorption isotherm is a basic thermodynamic property of separation processes and it is the relationship between the concentration of the solute in the stationary phase and that in the mobile phase. The parameters of the adsorption isotherm can be determined by fitting the model to the experimental data. By this way, it is possible to predict the individual band profile of separated sample components under various conditions and to optimize the separation condition.

The technique of molecular imprinting consists of the self-assembly of a functional monomer and a template molecule in solution followed by the co-polymerization of the functional monomer and an excess of an appropriate crosslinking monomer. After removing of the small molecule, the resulting network polymer exhibits a significantly higher affinity for the molecule used as the template than for similar molecules, including closely related isomers [Zhou et al., 1999; Sajonz et al., 1998; Owens et al., 1999; Chen et al., 2001; Zhang et al., 2001, 2002]. MIP have been applied to chiral separation [Schweitz et al., 1997], solid extraction [Wang et al., 2004], biomimic sensor [Yano et al., 1999] and membrane separation [Park et al., 2004]. MIP can be prepared by both the covalent and the non-covalent method, whereas the latter has been widely used in recent years because of the ease with which that method can be performed [Wang et al., 2004]. The most successful non-covalent imprinting systems are based on commodity methacrylic monomers, such as methacrylic acid (MAA), because their carboxyl group is the most commonly hydrogen-bonding and acidic functional group in molecular imprinting when cross-linked with EGDMA.

MIPs have been shown to be useful as separation materials in the extraction of certain active components from herbs, beverages and spiked human plasma. This utility, which is based on their shape, size, and functionality selectivity, strong affinity on rebinding target compounds, the significantly low cost for preparation and the workability in organic solvents, calls for finding a proper template to improve their selectivity and affinity.

Although the selectivity is usually high, the imprinted polymers are generally associated with a poor chromatographic efficiency and the elution of broad and asymmetric peaks [Sllergren et al., 1995]. One of the attributions of the poor performance may be the non-specific binding which comes from incomplete monomer-template association and nonequivalence of the different binding sites. Another reason for such poor performance is slow mass transfer. Mass transfer limitations result in peak broadening and asymmetry. A key to improving the performance of imprinted polymers would thus be either to achieve a narrower site distribution or to increase the accessibility of binding sites. The former requires chemical modifications, whereas the latter can be affected by changing the polymer morphology. In order to clearly understand the influence of such modifications, an investigation of the thermodynamic is necessary which involves the measuring of the adsorption equilibrium isotherms.

In this work, an imprinted polymer stationary phase by using ibuprofen as the template, 4-VPY as the functional monomer and EGDMA as the crosslinker was developed. Furthermore, isotherms of ibuprofen on the imprinted and blank polymers were determined by using static method.

EXPERIMENT

1. Chemicals

Ibuprofen and 4-vinylpyridine (4-VPY) were bought from Sigma (St Louis, MO, USA). Ethylene glycol dimethacrylate (EGDMA) was purchased from Fluka (Buchs, Switzerland). 2,2'-azobis(isobutyronitrile) (AIBN) was produced by Junsei Chemical Co. Ltd. (Japan) and refined before use. Methyl alcohol, acetonitrile and chloroform were from Pure Chemical Co., Ltd (Ansan, Korea). Acetic

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acid (analytical grade) was from Oriental Chemical Industries (Incheon, Korea). All the other solvents used in the experiment were HPLC or analytical grade. Distilled water was filtered with a vacuum pump (Division of Millipore, Waters) and filter (HA-0.45, Division of Millipore, Waters) before use. All the samples were filtered by using a filter (MFS-25, 0.2 μm TF, WHATMAN, U.S.A.) before injection into the HPLC system.

2. Liquid Chromatography

The chromatography system consisted of a Waters 600 s Multisolvent Delivery System and Waters 616 liquid chromatography (Waters Associates, Milford, MA, U.S.A.), Rheodyne injector (20 μl sample loop), a variable wavelength 2487 UV dual channel detector. Data processing was carried out with a Millenium 3.2 consistingof HP Vectra 500PC. In adsorption analysis, the chromatographic condition was the flow rate 0.7 ml/min, injection volume 0.5 μl, UV wavelength 220 nm. The C_{18} column (25-35 μm particles, 100 Å pore sizes, 4.6×250 mm) from RS tech Corporation, methanol : acetonitrile : water=85 : 15 : 5 (vol%) as the mobile phase, were used to determine the free concentration of the compound in the static method.

3. Preparation of the Polymers

1.5 mmol ibuprofen, 5.0 mmol 4-VPY were dissolved in 5 ml chloroform in a glass flask; 0.1 g AIBN was dissolved in 5 ml acetonitrile in another glass flask; the above two solutions into the experiment test tube were combined and mixed, then 30 mmol EDMA was added into the solution. The solution was put into a sonication bath for 10 min to dissolve the chemical well, purged with helium for 10 min to remove oxygen, and then the test tube was sealed under vacuum. After that, polymerization was performed in a water bath with the temperature maintained at 60 °C for 24 h. The polymerized monolith was put in the oven to dry and then ground into particles. The particles were passed through a 35 μm sieve and by repeated suspending in water to remove the small particles, and therefore the particle sizes of 25-35 μm were obtained. The dried particles were packed into a 3.9×150 mm stainless steel HPLC column. First, a solution of methanol : acetic acid=90 : 10 (vol%) was used to remove the template molecule; then the residual acetic acid was removed with methanol. For comparison, blank polymer was prepared with the same procedure but in the absence of the template.

4. Static Method

The static method was performed on the manufactured polymer particles. 30 mg of the ibuprofen imprinted and blank polymer was put into 10 ml flasks, respectively. Then 3.0 ml of ibuprofen solution with the concentration of 0.15 to 2 mmol/L was added. The mixture was left alone at room temperature for 72 h and then the supernatant was collected and filtered (0.2 mm). The concentration of free ibuprofen in the solution was determined by the C_{18} column at room temperature. Absorbed ibuprofen on the molecular imprinted and blank polymers was calculated by subtracting the free concentrations from the initial concentrations of ibuprofen.

RESULTS AND DISCUSSIONS

1. Determination of the Density and the Volume of Stationary Phase of the Polymers

The ibuprofen imprinted and blank polymers were packed into the stainless steel column (3.9×150 mm) for calculation of density and the dead volume. To determine the adsorption isotherm of the polymers, the density and the volume of the stationary phase were first calculated. The volume of the stationary phase was determined by timing the hold-up time of the column and the flow rate. The hold-up time was measured with acetone as the marker. The volume of the stationary phase for ibuprofen imprinted and blank polymer columns was 0.015 ml, respectively. The densities of polymers were obtained by the weight of the particles divided by the volume of the particles. The volume of the particles was obtained by the volume of the column minus the void volume. The calculated density and volume of the stationary phase are expressed in the Table 1.

Table 1. Properties of blank polymer and MIP determination of equilibrium adsorption concentration

Property \ Polymers	Blank polymer	MIP
Volume of column (ml)	1.79	1.79
Void volume (ml)	1.22	1.20
Packing weight (g)	1.14	1.19
True density (g/ml)	2.02	2.01

After the ibuprofen solution and the stationary particles were mixed for 72 hours, the adsorption equilibrium could be obtained between the two phases. The free concentration of ibuprofen in the liquid phase was quantitatively determined by HPLC. The calibration curve (peak area (Y) vs. concentration (X)) was constructed in the range of 0.05 to 2 mmol/L. The calibration equation was

$$Y=367354.62X-130142.26,\ r^2=0.9985$$

The absorbed concentration of ibuprofen (C_s) for MIP and blank polymers was as follows:

$$C_s=(C_0-C_m)\times\frac{Vm}{Vs} \quad (1)$$

where C_s is the absorbed concentration, C_0 is the initiator concentration, C_m is the free concentration, and Vm and Vs are the volume of the mobile phase and the volume of the stationary phase, respec-

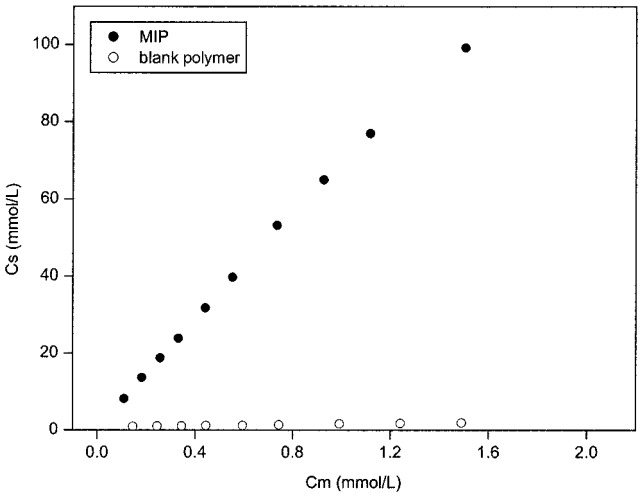

Fig. 1. The adsorption isotherm of ibuprofen on molecular-imprinted and blank polymers.

tively. C_s is calculated from this procedure, and then the experimental parameters were estimated and compared with the equilibrium isotherms by nonlinear regression analysis.

2. Determination of Adsorption Isotherms

Fig. 1 illustrates the adsorption isotherm plots ibuprofen on molecular imprinted and blank polymers. One can see from the figure that the ibuprofen-imprinted polymer shows significantly higher adsorption ability for the template than the blank polymer.

This experiment data were fitted to the following adsorption isotherm models:

$$C_s = aC_m^{1/n} \quad (2)$$

$$C_s = \frac{aC_m}{1+bC_m} \quad (3)$$

$$C_s = \frac{aC_m^n}{1+bC_m^n} \quad (4)$$

$$C_s = \frac{aC_m}{1+bC_m^n} \quad (5)$$

Where a, b and n are parameters. These adsorption isotherms are the Freundlich, Langmuir, Sips and Radke-Prausnitz equations, respectively. The parameters fitted by four adsorption isotherm models can be seen in Table 2. From the parameters listed in Table 2, it can be seen that the ibuprofen-imprinted molecular polymer shows higher affinity to the target molecule than blank polymer. The ibuprofen-imprinted polymer shows higher saturation capacity for the template than that of blank polymer.

One can also see that the three parameter equations (Sips and Radke-Prausnitz), Eq. (4) and (5), have the better correlation results than that of two parameter equations of (Freundlich and Langmuir), Eq. (2) and (3). The regression coefficients of Radke-Prausnitz adsorption isotherm model Eq. (5) are 0.9999 for ibuprofen-imprinted and 0.9724 for blank polymer, respectively. Whereas for Langmuir adsorption isotherm, Eq. (3), the regression coefficients are 0.9997 and 0.8579, respectively.

The experimental and calculated data are shown in Fig. 2. The known Cm and Cs were fitted to obtain the four equilibrium equations.

Almost all the experimental and calculated data were on the diagonal neighborhood. This indicates that these experimental data are well fitted to the four equations. Fig. 3 shows the plot of the experimental data of ibuprofen on the molecular imprinted polymer fitted by the Radke-Prausnitz Eq. (5). It shows that the experimental data fits to the Radke-Prausnitz equation quite well.

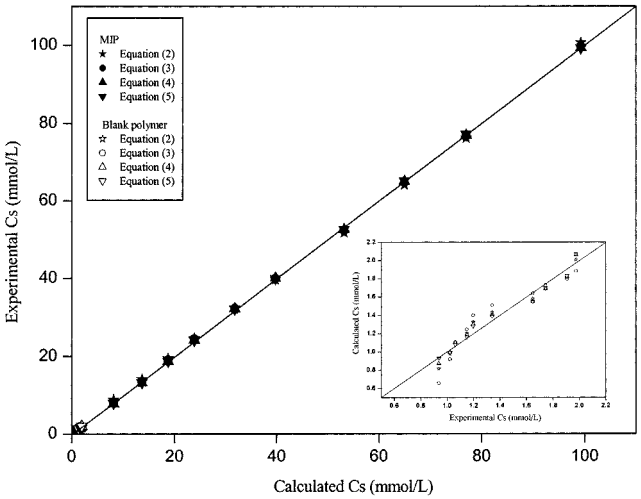

Fig. 2. Comparison of experimental and calculated concentrations of ibuprofen on the molecular imprinted and blank polymer.

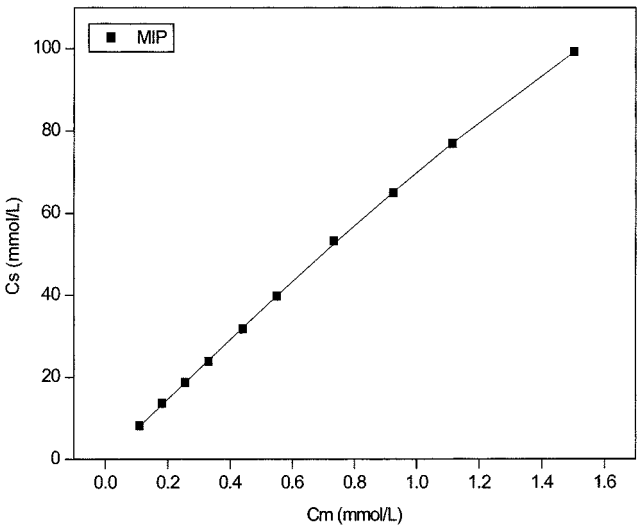

Fig. 3. Adsorption isotherm of ibuprofen fitted by Radke-Prausnitz equation.

Table 2. Parameters in adsorption isotherm of ibuprofen imprinted and blank polymer

Adsorption isotherm \ Parameters		a	b	n	Regression coefficient
MIP	Freundlich	68.88	-	1.08	0.9990
	Langmuir	76.59	0.10	-	0.9997
	Sips	81.81	0.17	1.05	0.9999
	Radke-Prausnitz	73.35	0.05	2.05	0.9999
Blank polymer	Freundlich	1.59	-	2.91	0.9557
	Langmuir	6.43	2.91	-	0.8579
	Sips	0.41	−0.74	0.10	0.9635
	Radke-prausnitz	−6.56	−5.21	0.49	0.9724

CONCLUSIONS

In this work the static method was experimentally implemented to measure the adsorption isotherm of ibuprofen by the prepared molecular imprinting polymer. The adsorption experiment data were fitted by four isotherm equations, Freundlich, Langmuir, Sips and Radke-Prausnitz. Results showed that the experiment data fit well to the four equations. The Radke-Prausnitz isotherm was the best-fit model to the experimental data among the four isotherm models. The regression coefficient is 0.9999 and 0.9724 in the MIP and blank polymer, respectively. The high saturation capacity and high selectivity of the developed molecular imprinted polymer is important for the preparation of the drug with high purity. The polymer is also stable and can be reproducibly synthesized, which is an attractive feature for further applications.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the financial support of Center for Advanced Bioseparation Technology.

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