Preparation of (*S*)-Ibuprofen-Imprinted Polymer and Its Molecular Recognition Study

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ABSTRACT: Two molecularly imprinted polymers (MIPs) were prepared using (*S*)-ibuprofen as the template molecule as well as methacrylic acid (MAA) or 4-vinylpyridine and ethylene glycol dimethacrylate (EGDMA) as the functional monomer and crosslinker, respectively. Free radical polymerization was carried out at 4°C under ultraviolet (UV) radiation. The MIPs thus obtained were ground into 25–44 μm, which were slurry packed into analytical columns. The template molecules were removed by acetic acid/methanol solution (1:9, v/v). high-performance liquid chromatography (HPLC), with UV detection, was used to evaluate the binding performance of the MIP for the template. The selectivity of (*S*)-ibuprofen and naproxen on the host–guest system were assessed using acetonitrile-based mobile phases. The limits of detection of ibuprofen and naproxen were found to be 0.1844 mmol/L and 0.3264 mmol/L, while the limits of quantitation were 0.6262 mmol/L and 1.0909 mmol/L, respectively. The stationary phase was applied successfully to the commercial tablet analysis. Ibuprofen and naproxen were extracted from tablets with acetonitrile; analysis results showed a good relative standard deviation (RSD) of 0.81–1.24% and accuracy from −4.01 to +2.98% for ibuprofen as well as an RSD of 0.59–0.86% and accuracy from −4.01 to −2.01% for naproxen. © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 102: 2972–2979, 2006

Key words: molecularly imprinted polymers; HPLC; selectivity; host–guest system; commercial tablet analysis

INTRODUCTION

Ibuprofen [2-(4-isobutylphenyl) propionic acid] is a nonsteroidal antiinflammatory, antipyretic drug widely used in the treatment of pain and inflammation. This compound exists in two forms, *R*- and *S*-ibuprofen, which differ in their therapeutic and pharmacological properties. *S*-(+)-ibuprofen exhibits pharmacological effects by inhibition of cyclooxygenase (COX), while *R*-(−)-ibuprofen appears to be inactive.[1] Ibuprofen is metabolized primarily in the liver, and the major metabolites are 2-hydroxy-ibuprofen and 2-carboxy-ibuprofen.[2]

Because this is a commonly used drug, a variety of techniques are available for the determination of this compound in pure form or pharmaceutical samples, including high-performance liquid chromatography (HPLC),[3,4] gas chromatography-mass spectrometry (GC-MS),[5] supercritical fluid chromatography,[6] nuclear magnetic resonance (NMR) spectrometry,[7] infrared (IR) spectrophotometry,[8] capillary electrophoreses,[9] and potentiometry.[10] The European Pharmacopoeia used an acid–base titration method to determine the content of ibuprofen in pharmaceutical preparations.[11] Haginaka et al.[12] prepared molecularly imprinted polymers of uniform size for (*S*)-ibuprofen by a multi-step swelling and thermal polymerization method that has been used successfully in the analysis of pharmaceutical samples.

We report a method for measuring ibuprofen and naproxen concentration in pharmaceutical samples using a simple molecular imprinting technique. Wulff and Sarhan[13] introduced the technique in 1972, which was further developed by Arshady and Mosbach[14] in 1980. From 1990 to now, more than 250 review papers on molecularly imprinted polymers have described the principles, chemical properties, methods of preparation, effect of external factors polymers during synthesis,[15,16] as well as its applications, including uses as an antibody and receptor mimics for assays,[17] separation and screening of compounds of biological origin,[18] and membrane separations.[19] The molecularly imprinted polymers obtained have been used successfully for the resolution of drug molecules,[20,21] controlling drug release,[22] steroids,[23] DNA molecules,[24] nucleotide base,[25] and amino acids.[26] The advantages of the method described in the present study in over frequently reported ones include the ease of sample preparation and excellent mechanical

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TABLE I
Composition of Polymers Synthesized in This Study*

Polymer	Ibuprofen (mmol)	MAA[a] (mmol)	4-Vinylpyridine[b] (mmol)	EGDMA (mmol)	AIBN (mmol)
P1	—	0.45	—	18.42	0.23
P2	—	—	0.45	18.42	0.23
P3	0.45	0.45	—	3.88	0.06
P4	0.60	0.30	—	5.50	0.07
P5	0.68	0.22	—	8.73	0.11
P6	0.18	0.72	—	18.42	0.23
P7	0.45	—	0.45	3.88	0.06
P8	0.60	—	0.30	5.50	0.07
P9	0.68	—	0.22	8.73	0.11
P10	0.18	—	0.72	18.42	0.23

* 5 ml chloroform used as solvent.
[a] pH of solution during synthesis is 3.55 ± 0.05.
[b] pH of solution during synthesis is 6.47 ± 0.05.

and chemical stability. It is particularly suitable for the separation of molecules similar in size and shape.

Adverse effects of chiral nonsteroidal antiinflammatory drugs (NSAIDs) are often seen because of the widespread use of these agents. In the present study, a molecularly imprinted polymer for (*S*)-ibuprofen has been prepared by a free radical polymerization method using methacrylic acid (MAA) or 4-vinylpyridine and ethylene glycol dimethacrylate (EGDMA) as a functional monomer and crosslinker, respectively. We have also examined the influence of the functional monomer-template molar ratio and the composition of mobile phase on the recognition characteristics of the resultant polymers. A series of (*S*)-ibuprofen imprinted polymers demonstrate that the (*S*)-ibuprofen and naproxen separation can be greatly enhanced by using the molecularly imprinted polymers as the stationary phase.

EXPERIMENTAL

Chemical and reagents

Methacrylic acid (MAA, 99%) and ethylene glycol dimethacrylate (EGDMA, 98%) were obtained from Merck (Darmstadt, Germany). 2.2′-Azo-bisisobutyronitrile (AIBN) was obtained from TCI (Tokyo, Japan). Methanol, ethanol, acetone, 4-vinylpyridine, sodium dihydrogen phosphate, and acetonitrile were of HPLC grade and obtained from TEDIA (Fairfield, OH). Chloroform and acetic acid were from RDH (Riedel-de Haen AG Seelze, Germany) and of GC grade, while (*S*)-ibuprofen and naproxen were purchased from Sigma (St. Louis, MO). All chemicals were of HPLC or analytical grade. MAA and EGDMA were distilled to remove the inhibitors before polymerization. Water is double deionized.

Synthesis of molecular imprinting stationary phase

MAA and 4-vinylpyridine were used respectively as the functional monomers to prepare the MIP by the noncovalent imprinting method. Briefly, (*S*)-ibuprofen, functional monomer, EGDMA, and AIBN were dissolved in 5 mL of chloroform in a conical Erlenmeyer flask. Table I shows the composition of polymers synthesized in this study. After degassing and nitrogen purging for 3 min, the flask was sealed and allowed to polymerize at 4°C for 24 h under UV (365 nm, 100-W lamp) irradiation. For each preparation of MIP, (*S*)-ibuprofen was used as the template. EGDMA was used as the crosslinking monomer and AIBN as the free radical initiator. After polymerization, solvent was removed. The product was dried in a vacuum oven for 12 h at room temperature. The resultant rigid polymer was finally ground into fine particles using a mortar and pestle. Polymer particles were to pass through a 25–44-μm sieve. The fraction of particles having an average size of 25–44 μm was collected for packing in chromatographic columns.

HPLC analysis

MIP particles were suspended in methanol (30 mL) by sonication for 3 min and placed in a slurry reservoir. The polymer particles were packed into 15-cm × 0.46-cm inner-diameter (ID) stainless steel columns using an air-driven fluid pump with acetone (300 mL) as the packing solvent. The weight of particles in each column was ~ 3.32 g. The columns were then washed online with methanol/acetic acid (9:1, v/v) at a flow rate of 0.5 mL/min to remove unreacted monomers until a stable baseline was reached.

An HPLC analysis (JASCO PU-2080 chromatograph equipped with a JASCO UV-2075 variable wavelength detector and a Peak ABC Chromatography Workstation Version 2.10 integrator) was performed isocratically with acetonitrile/PBS (pH 3.20 ± 0.01) at different ratios, and the UV detection was carried out at 220 nm and eluent. Solution (20 μL) of the

(*S*)-ibuprofen compound was injected and eluted isocratically at a flow rate of 0.5 mL/min. The void volume of the column was determined by the injection of toluene. Separation factors (α) and capacity factors (K') were calculated according to: $\alpha = K'_{\text{ibuprofen}}/K'_{\text{naproxen}}$, where $K'_{\text{ibuprofen}}$ and K'_{naproxen} were the capacity factor of ibuprofen and naproxen. The capacity factors were determined as $K'_{\text{naproxen}} = (t_{\text{naproxen}} - t_o)/t_o$ and $K'_{\text{ibuprofen}} = (t_{\text{ibuprofen}} - t_o)/t_o$, where t_{naproxen} and $t_{\text{ibuprofen}}$ were the retention times of naproxen and ibuprofen, and t_o was the elution time of the void marker, which was determined by the injection of toluene.

The mobile phases were prepared by adjusting the pH of a 0.05 mol/L sodium dihydrogen phosphate solution and mixing this with acetonitrile to the desired proportion (3 : 2, v/v).

Linearity

The linearity was calculated over the concentration range 1.23–4.13 mmol/L for naproxen and 0.97–4.85 mmol/L for ibuprofen by assaying two or three times at each concentration. In the concentration range, a wavelength of 220 nm was used for the chromatographic peak detection.

Preparation of ibuprofen® and NAP® sample solutions

For the analysis of ibuprofen and naproxen, 20 tablets (each containing 250 mg IBUP and 200 mg NAP) were accurately weighed and grind to fine powder. A weighted portion of the powder equivalent to the suitable amount of drug was transferred to a 250-mL flask and 150 mL 0.05 mol/L sodium dihydrogen phosphate solution was added, which together with acetonitrile made up a total of 250 mL. It was sonicated for 15 min. The solution was then centrifuged at 1000*g* for 15 min to yield a clear supernatant solution. A portion of the solution was filtered through a disposable 0.45 μm filter.

RESULTS AND DISCUSSION

Characterization of the (*S*)-ibuprofen-imprinted polymer

The conversion of polymerization has 80.52–82.69%. The polymer materials were ground into powder and the fraction have a particle size of 25–44 μm. Particle size of > 25 μm provided the higher separation factor for EGDMA/MAA imprinted polymer than that of sizes < 25 μm.[27] Although the MIP particles for packing were irregular in shape and had a wide size distribution, the 15-cm-long columns possessed a linear curve of volumetric flow rate versus pressure.

For comparison, noncovalent imprinted polymers were prepared using either MAA or 4-vinylpyridine as the functional monomer. A series of highly crosslinked MIPs were synthesized for chromatographic evaluation. Polymer P1 contains EGDMA and MAA, while P2 contains EGDMA and 4-vinylpyridine; these polymers have no templates and serve as the blank for the noncovalent imprinted polymers. The addition of MAA to P3–P6 provides an insight into the formation of templates, and functional monomer assemblies. P7-P10 is noncovalent MIPs in which 4-vinylpyridine was used in place of MAA.

Effect of solvents and template/monomer ratio

It is clear that the polarity of solvents or eluents used in the imprinting analyses affects the specificity of the polymers. Acetonitrile and chloroform are the most commonly used solvents for imprinting. Generally, MIPs prepared by noncovalent method in a relatively nonpolar organic solvent exhibit better recognition property than those prepared using a polar organic solvent.[28] Acetonitrile is more polar than chloroform: the dielectric constant for acetonitrile is 36.64, while that for chloroform is 4.81.[29] Previous works have shown that when hydrogen bonding or ionic interactions between the imprinting molecule and the carboxyl monomers are involved, MIPs made in acetonitrile exhibit only very weak enantiomeric recognition and in some cases no recognition at all.[30] In this study, chloroform is successfully used as solvent for preparing polymer-introduced recognition sites for (*S*)-ibuprofen.

The ratio of template to functional monomer (T/M ratio) affects apparently the selectivity and sensitivity of MIPs with respect to the number of recognition sites.[31,32] To find the optimum conditions for preparing molecularly imprinted polymers, We synthesized a series of highly crosslinked MIPs that were composed of various mole ratios of (*S*)-ibuprofen to functional monomers and examined the effect of stoichiometry on selectivity (Table II).

HPLC analysis revealed that polymers P6 and P10, with mole ratios 1:4 (template to functional monomer), exhibited greater separation properties than was observed for the other polymers. Similar effects have previously been observed by Andersson.[33] An excess of monomers in relation to the template would form complexes [Fig. 1(A)], thus producing the affinity and selective binding sites. Polymers, P3–P5 and P7–P9, have higher T/M ratio than P6 and P10 may form the states of complexes [Fig. 1(B) and (C)] or template self-association. High T/M ratio cannot afford the formation of optimal complexes or

TABLE II
Effect of the Ratio of Template to Functional Monomer on Selectivity

Polymer[a]	Template/Functional monomer (mole ratio)	Capacity factor		Separation factor α
		$K'_{ibuprofen}$	$K'_{aproxen}$	
P3	1:1	No resolution		
P4	2:1	26.13	22.14	1.18
P5	3:1	27.16	22.26	1.22
P6	1:4	19.32		1.40
P7	1:1	No resolution		—
P8	2:1	59.27	45.24	1.31
P8	3:1	59.34	43.63	1.36
P10	1:4	60.83	41.77	1.46

[a] The void volume of each column was about 37.84% by the injection of toluene; retention time of toluene was 1.88 min.

high number of affinity binding sites in the limited presence of MIPs, so there is a decrease in selectivity.

P1–P10, with EGDMA content ranging from 80% to 95%, is high-degree crosslinking polymers. EGDMA serves as crosslinker and controls the morphology, fixed binding sites, and stable mechanics of the polymer matrix. At higher degrees of crosslinking, the polymer chain is less mobile, and thus helps retain the integrity of the recognition sites. Our results show that P3 and P7 (Table II) have no separation; the separation factor decreased with a decrease in crosslinking, indicating that the optimum amount of template in the study is about 1% of the total amount of monomers.

Comparison of functional monomers

The functional monomers must strongly interact with the template before and during polymerization to achieve a high yield of imprinted binding sites. Lu et al.[34] used UV-Vis spectroscopy and NMR to calculate the association constant of interactions between functional monomers and template. In this study, MAA and 4-vinylpyridine were used as functional monomers for forming a template-monomer complex prior to polymerization in the noncovalent imprinting method. The most widely applied functional monomer is MAA. It has been shown to interact via hydrogen bonds with carboxyl group on the print molecules [Fig. 2(A)]. 4-vinylpyridine contains an electrophilic

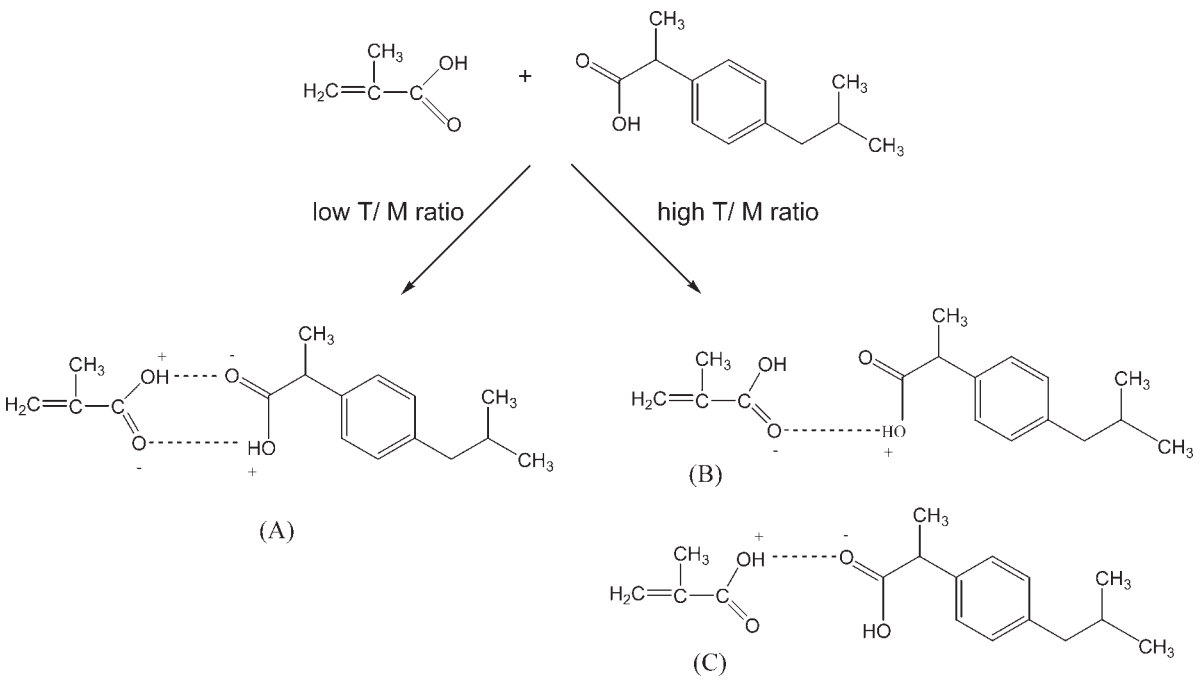

Figure 1 Effect of template: monomer ratios (T/M) on the state of complexes in the pre-polymerization.

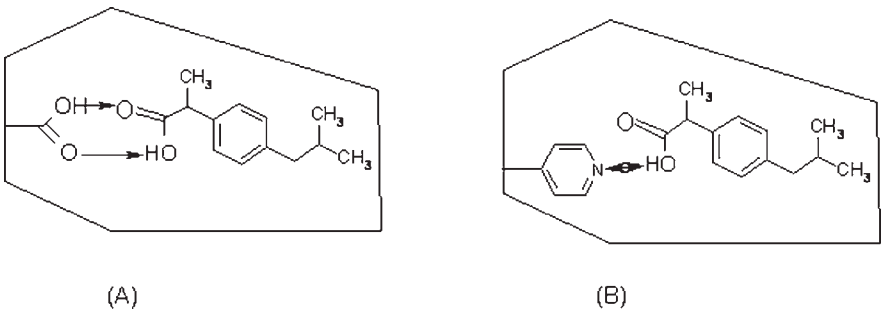

Figure 2 Binding sites for (*S*)-ibuprofen in the molecularly imprinted polymers. Polymers prepared by the methods of noncovalent imprinting use methacrylic acid (A) or 4-vinylpyridine (B) as the functional monomer.

group used as the functional monomer that initiates ionic interaction between the recognition sites of the polymer and imprinted molecules [Fig. 2(B)]. The low-temperature polymer synthesized using 4-vinylpyridine was slightly yellow in bulk, but it turned into white powder after drying and grinding. After removal of the template, the bound pyridine on the 4-vinylpyridine-based MIP seemed to have a stronger interaction with the hydroxyl group of (*S*)-ibuprofen. An examination of the data in Tables III and IV reveals that the imprinted polymer P10 has higher capacity factor values than the polymer P6. This observation supports that templates containing basic groups or acidic groups are usually best imprinted using acidic, i.d., MAA, and basic, i.d., vinylpyridine, functional monomers.[27,32] This is very important in order to enhance the imprinting effect that must match the cavity created by template printing with the functionality of the functional monomers in a complementary fashion.

Influence of mobile phase composition on the separation of (*S*)-ibuprofen and naproxen

In this study, polymers P6 and P10 had better separation using the acetonitrile-based mobile phase. Since (*S*)-ibuprofen employed in this work has a simple structure, the mobile phase played a very important role in the separation of (*S*)-ibuprofen and naproxen. A mobile phase with higher polar substances was used to compete with the MAA or pyridine residues in the polymers and weaken the specific polar interaction of substrates with the imprinting cavity of the stationary phase. To investigate the role that acetonitrile played in the recognition and binding of template molecule to MIP, chromatographic runs were carried out using different acetonitrile content levels in the mobile phase.

As shown in Figure 3, a mixture of (*S*)-ibuprofen and naproxen was well resolved by an eluent of 40% acetonitrile in buffer solution and sharp peaks were obtained. This indicates that using a higher concentration of acetonitrile could significantly reduce the separation factor. It is believed that acetonitrile molecules would displace the target molecules, in competition with the immobilized MAA and bind to the stationary phase and finally template molecules eluted out from the column.

Although the particles were irregular in shape and dispersed in size, for our system of (*S*)-ibuprofen-MIP, the use of the acetonitrile-based mobile phase eliminated the tailing problem. The polarity of acetonitrile influences the partition of (*S*)-ibuprofen in the

TABLE III
Separation of (*S*)-Ibuprofen and Naproxen Using P6 Polymer as the Stationary Phase*

Concentration in sample (g/L)[a]		Retention time, min (capacity factor[b])		
(*S*)-ibuprofen	naproxen	(*S*)-ibuprofen	naproxen	α ($=K'_{\text{ibuproxen}}/K'_{\text{naproxen}}$)
0.5	0	51.58 (26.88)	—	—
0.5	0.1	51.56 (26.88)	37.28 (19.12)	1.40
0.9	0.1	51.58 (26.88)	37.23 (19.12)	1.41
0.7	0.3	51.95 (27.08)	37.59 (19.32)	1.40
0.5	0.5	54.77 (28.60)	39.24 (20.21)	1.41
0.3	0.7	52.39 (27.32)	37.42 (19.34)	1.41
0.1	0.9	53.16 (27.73)	38.25 (19.67)	1.40
0	1.0	—	37.63 (19.34)	—

* HPLC conditions (see the section on HPLC analysis).
[a] The volume of injected solution is 20 μL.
[b] Calculated using the average retention times for the nonretention compound (toluene), determined to be 1.85, 1.84, and 1.87 min, respectively.

TABLE IV
Separation of (*S*)-Ibuprofen and Naproxen Using P10 Polymer as the Stationary Phase*

Concentration in sample (g/L)[a]		Retention time,min (capacity factor[b])		
(*S*)-ibuprofen	naproxen	(*S*)-ibuprofen	naproxen	α ($=K'_{ibuprofen}/K'_{naproxen}$)
1.0	0	120.60 (64.19)	—	—
0.9	0.1	127.41 (67.87)	86.03 (45.50)	1.49
0.7	0.3	114.40 (60.83)	79.13 (41.77)	1.46
0.5	0.5	131.58 (70.12)	93.73 (49.66)	1.41
0.3	0.7	131.69 (70.18)	86.54 (45.77)	1.53
0.1	0.9	132.67 (70.71)	85.74 (45.34)	1.56
0	1.0	81.98 (43.31)	—	—

* HPLC conditions (see the section on HPLC analysis).
[a] The volume of injected solution is 20 μL.
[b] Calculated using the average retention times for the nonretention compound (toluene), determined to be 1.83, 1.89, and 1.85 min, respectively.

stationary phase and the selectivity for (*S*)-ibuprofen on the column was thus evident.

Separation of (*S*)-ibuprofen and naproxen on molecularly imprinted polymers

Results from the liquid chromatography of (*S*)-ibuprofen on imprinted polymers prepared by noncovalent method using either MAA or 4-vinylpyridine as the functional monomer are shown in Figures 4 and 5. No separation is achieved on the blank polymers (P1 and P2). The separation, as shown in the chromatographic peaks, was very good. As shown in Figures 4 and 5, every component has the same retention time when eluted in mixture or pure compound. For either pure (*S*)-ibuprofen or naproxen, the peak area eluted alone was found to be almost linearly related to that eluted in mixture. In Figure 4(C) and (D), in concordance with the fact that the amount of pure (*S*)-ibuprofen sample is nearly the same (*S*)-ibuprofen in the mixture sample. Other similar cases can also be found in Figure 5. Chromatographic separation using these MIPs was reproducible and each data point reported in these figures was an average taken from two to four runs for each combination of solute concentrations. For different combinations of (*S*)-ibuprofen and naproxen concentrations with a total of 1 g/L (Tables III and IV), the peak retention times for both compounds were nearly constant, the time for naproxen ranged within 37.23–39.24 min, while that for (*S*)-ibuprofen ranged within 51.58–54.77 min when using P6 polymer as the stationary phase. When using P10 as the stationary phase, the time of naproxen ranged within 79.13–93.73 min, while that for (*S*)-ibuprofen ranged within 114.40–132.67 min. Chromatographic results indicate that the imprinted molecule was retained in the column because of the possible hydrophilic interaction between the template and the stationary phase. This phenomenon is very clear, since a polar compound acetone could also be retained in the column with a retention time of 4.18 min; however, toluene was thus considered as the nonretained component with retention time of 1.85 min because the stationary phase did not contribute to the favorable retention of hydrophobic substances.

Tables III and IV indicated that the separation factor for (*S*)-ibuprofen from naproxen was almost constant at various concentrations in samples when using P6 and P10 as the stationary phase, respectively. Although the common phenomenon in MIP systems is the elution of peaks that were broad with a little tailing, our results showed that the separation factor was very good. In a comparison with (*S*)-ibuprofen and naproxen, the volume of injected solutions was 20 μL, naproxen had a small increase in retention time with sample load, while the retention of (*S*)-ibuprofen was strongly dependent on the sample loading. The maximum retention time observed

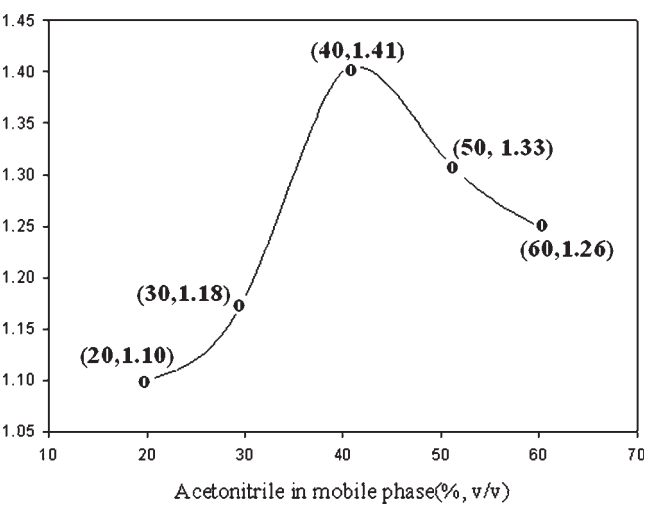

Figure 3 Effect of acetonitrile content in acetonitrile-based mobile phase on the separation factor and P6 particles as the stationary phase

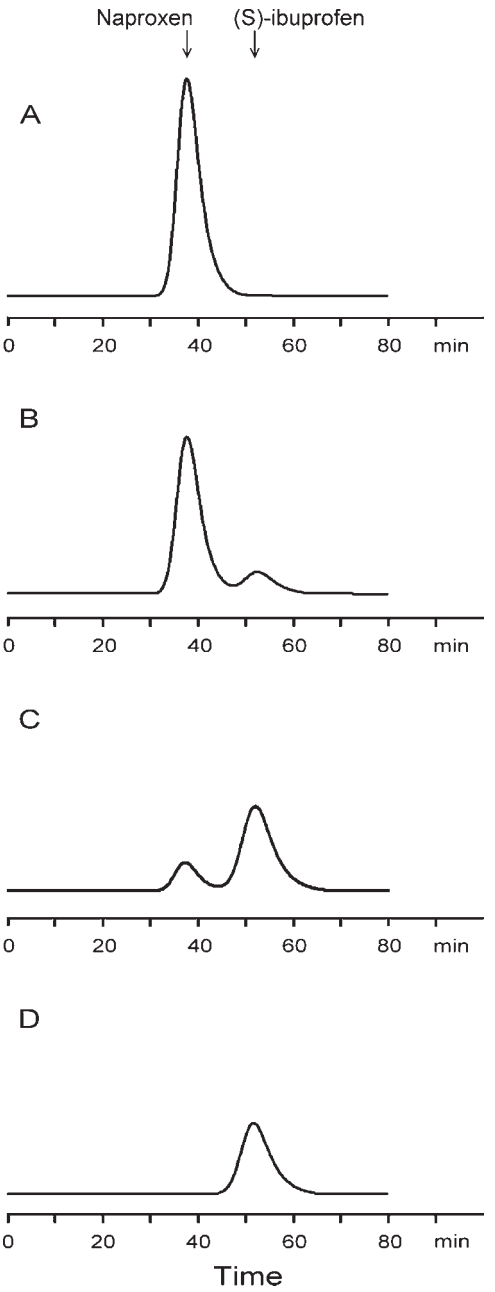

Figure 4 HPLC separation of (*S*)-ibuprofen and naproxen used P6 as the stationary phase. Concentration of naproxen in sample was 1g/L (A) and a mixture of 0.3g/L (*S*)-ibuprofen and 0.7g/L naproxen (B), a mixture of 0.5g/L (*S*)-ibuprofen and 0.1g/L naproxen (C), concentration of (*S*)-ibuprofen in sample was 0.5g/L (D).

was present at medium sample loading. As shown in Tables III and IV, a decrease in retention of (*S*)-ibuprofen molecules was obtained with a heavy sample load of the mixture but the separation factor was kept almost constant.

Linearity

Limits of detection (LOD) and of quantitation (LOQ), corresponding to signal-to-noise ratios of 3 and 10, respectively, were calculated from the linear regression analysis performed by plotting the analyte peak area versus the concentration of ibuprofen and naproxen. The separation of (*S*)-ibuprofen and naproxen will be very helpful for studying the pharmacological effect of each compound. According to the evaluation of peak areas, the chromatographic columns prepared in this study were effective for the quanti-

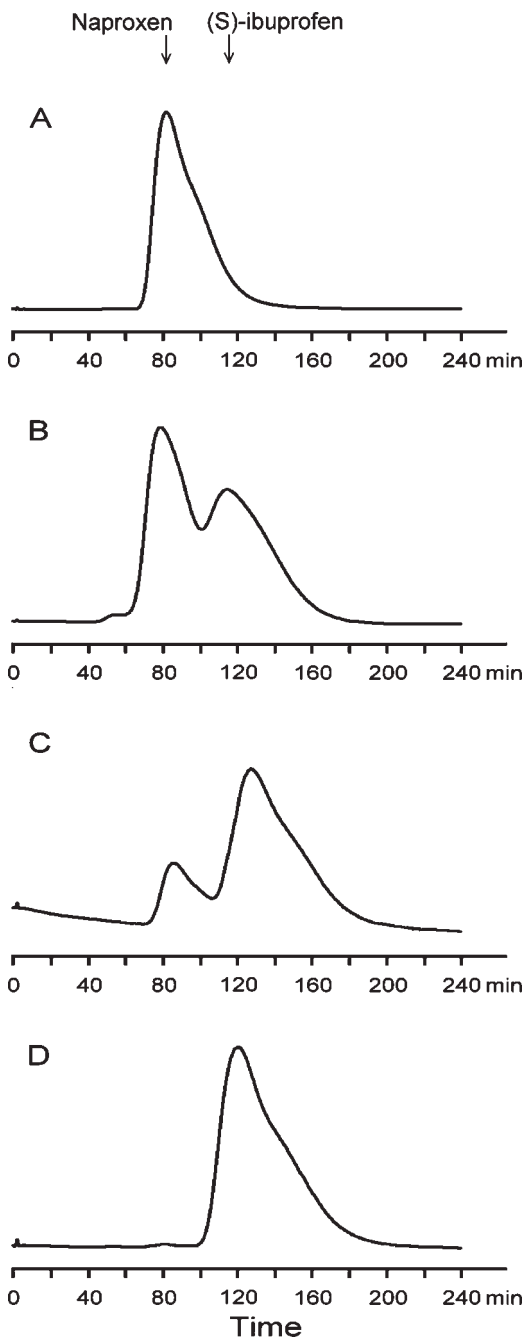

Figure 5 HPLC separation of (*S*)-ibuprofen and naproxen used P10 as the stationary phase. Concentration of naproxen was 1g/L (A) and a mixture of 0.3 g/L (*S*)-ibuprofen and 0.7 g/L naproxen (B), a mixture of 0.9 g/L (*S*)-ibuprofen and 0.1 g/L naproxen (C), concentration of (*S*)-ibuprofen in sample was 1.0 g/L (D).

TABLE V
Determination of Naproxen and Ibuprofen in Commercial Tablet

	Naproxen (mM)			Ibuprofen (mM)		
Parameters	1.652	2.066	2.479	1.941	2.427	2.912
Found (g/L)[a]	1.602	1.983	2.429	1.863	2.378	2.999
RSD (%)[b]	0.59	0.62	0.86	0.81	0.96	1.24
Accuracy(%)[c]	−3.02	−4.01	−2.01	−4.01	−2.01	+2.98

[a] Based on five replicate analysis.
[b] Relative standard deviation (RSD) values were estimated from repeatability.
[c] Accuracy (%) = [(found − added)/added] × 100.

tative analysis. A linear calibration of ibuprofen and naproxen could yield coefficients of determination (r^2) of 0.9979 and 0.9912.

Application of method to IBUP and NAP tablets

The same statistical approach was then applied to a synthetic mixture of the excipients of the dosage form to which quantities of naproxen and ibuprofen were known. The average weight of one ibuprofen tablet was 487.59 mg and as grade labeling, containing 250 mg of ibuprofen, while the average weight of one NAP tablet was 385.94 mg, containing 200 mg of naproxen and several excipients. Data for the variation in precision and accuracy are given in Table V, showing an R.S.D from 0.81 to 1.24% and accuracy from −4.01 to +2.98% for ibuprofen as well as an relative standard deviation (RSD) of 0.59–0.86% and accuracy from −4.01 to −2.01% for naproxen.

CONCLUSIONS

Molecular imprinting is a useful technique for the preparation of stationary phase selective for (*S*)-ibuprofen and naproxen. In the present study, we have used a simple molecule, (*S*)-ibuprofen, as the template for the preparation of MIP. These noncovalent imprinted polymers had the ability of recognizing the imprinting molecules and distinguishing the likely structure of substrates. The recognition and binding of template molecules involve interactions between the hydroxyl group of the template and the pyridine residues of 4-vinylpyridine or carboxyl group of MAA, host molecules in the MIP. Higher values of separation factor in the present work suggest that noncovalent molecular imprinting is a promising method for the separation of (*S*)-ibuprofen and naproxen.

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