Recognition Properties of Poly(vinylidene fluoride) Hollow-Fiber Membranes Modified by Levofloxacin-Imprinted Polymers

Nai-Ci Bing, Zhen-Liang Xu, Xue-Jun Wang, Zuo-Guo Yang, Hu Yang

Chemical Engineering Research Center, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, People's Republic of China

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ABSTRACT: Through the use of thermal polymerization, poly(vinylidene fluoride) (PVDF) hollow-fiber membranes modified by a thin layer of molecularly imprinted polymers (MIPs) were developed for the selective separation of levofloxacin. To demonstrate the changes induced by thermal polymerization, PVDF hollow-fiber membranes with different modification degrees by repeated polymerization were weighed. The total weight of the imprinted membranes increased by 14 μg/cm^2 after a five-cycle polymerization. An increase in the membrane weight indicated the deposition of an MIP layer on the external surface of PVDF hollow-fiber membranes during each polymerization cycle, which was also characterized by scanning electron microscopy. MIP membranes with different degrees of surface modification provided highly selective binding of levofloxacin. Both hollow-fiber MIP membranes and nonimprinted membranes showed enhanced adsorption of levofloxacin and ofloxacin gradually with an increase in the modification degrees of PVDF hollow-fiber membranes to a maximum value followed by a decrease. These results indicate that thermal polymerization indeed produces an MIP layer on the external surface of PVDF hollow-fiber membranes and that it is feasible to control the permeability by repeated polymerization cycles. Different solvent systems in the permeation experiments were used to understand the hydrophobic interaction as one of the results of the binding specificity of MIP membranes. Selective separation was obtained by multisite binding to the template via ionic, hydrogen-bond, and hydrophobic interactions. J Appl Polym Sci 106: 71–76, 2007

Key words: chiral; membranes; separation techniques

INTRODUCTION

Since Wulff and Sarhan[1] put forward the molecular imprinting concept, this new kind of technique for preparing highly crosslinked macroporous materials with antibody-like specific binding sites for target molecules (templates) has grown and developed at a rapid pace. Because of the advantages of higher selectivity, superior stability, and lower price,[2] molecularly imprinted polymers (MIPs) have been applied in a broad range of fields, including chromatographic stationary phases,[3,4] sensor technology,[5,6] and solid phase extraction,[7,8] and as catalytically active polymers in organic synthesis.[9] Nowadays, there is increasing focus on the introduction of molecular imprinting technology to membrane separation, which is easy to establish on an impressively large scale and integrate with other separation or reaction processes.

Correspondence to: Z.-L. Xu (chemxuzl@ecust.edu.cn).
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An MIP membrane is a membrane either composed of MIPs or containing MIPs,[10] in which a selective transport process can be realized by template binding to MIP sites. Consequently, some technically challenging and commercially attractive separations, including the separation of chiral drugs[11,12] or biomolecules,[13] can be realized with this kind of novel molecule-selective membrane. MIP membranes are always prepared as thin polymer films on the surface of support membranes[14] or as free-standing membranes either from previously synthesized conventional MIPs[15] or from the simultaneous formation of an MIP structure and membrane morphology.[16] A much more general approach for the synthesis of thin polymer films on the surface of support membranes is heterogeneous photografting[17,18] or thermal copolymerization[19] on the surface of flat membranes, and only a few attempts toward synthesizing hollow-fiber MIP composite membranes have been reported.[20] Studies on the morphology and permeability/transportability of MIP membranes are always focused on flat membranes by photografting and living free-radical polymerization.[21–23] However, a detailed analysis of the morphology, modification degree, and binding mechanism of imprinted membranes has not yet been

performed for hollow-fiber MIP composite membranes by thermal polymerization.

In this work, hollow-fiber MIP composite membranes for the selective separation of levofloxacin were obtained by thermal polymerization. The main work was focused on detailed investigations of the morphology structure, modification degree, and transport characterization of well-defined membranes prepared from different modifications. At the same time, the separation mechanisms of MIP membranes were studied with different solvent systems.

EXPERIMENTAL

Materials and instruments

Ofloxacin and levofloxacin (Scheme 1) were from Kun Shan Double-Crane Pharmaceutical Co., Ltd. (Kunshan, China). Ethylene glycol dimethacrylate (EDMA) was from Shanghai Coral Chemical Co., Ltd. (Shanghai, China). 2,2′-Azobisisobutyronitrile (AIBN) was purchased from Shanghai Shisihewei Chemical Co., Ltd. (Shanghai, China). Methacrylic acid (MAA) was purchased from Shanghai Lingfeng Chemical Reagent Co. (Shanghai, China). Glacial acetic acid and chloroform, analytical-reagent-grade solvents, were all obtained from Shanghai No. 1 Reagent Co., Ltd. (Shanghai, China). Methanol (chromatographic grade) was acquired from Shanghai Fangkeweiqi Biochemical Product Co., Ltd. (Shanghai, China). EDMA and MAA were further purified with active carbon.

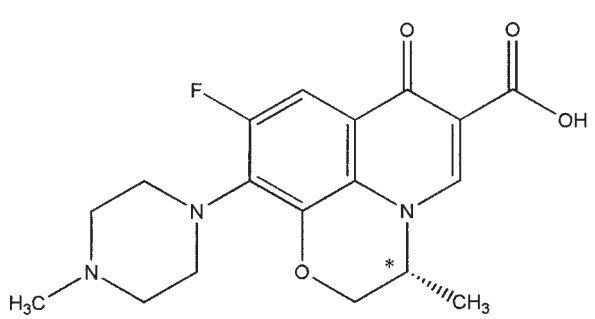
Poly(vinylidene fluoride) (PVDF) hollow-fiber membranes (self-made; porosity = 70%, pure water flux = 12 L/($m^2 \cdot h \cdot Bar$), molecular weight cutoff with BSA67000 as a standard solution = 94.7%).

A UV-762 spectrophotometer (Shanghai Precision & Scientific Instruments Co., Ltd., Shanghai, China) and a JSM-6360 LV scanning electron microscope (JEOL Ltd., Tokyo, Japan) were used.

Preparation of the hollow-fiber MIP composite membranes

To obtain a highly selective imprinted polymeric layer on the surface of a PVDF hollow-fiber membrane, the MIP recipe contained 1.0 mmol of levofloxacin, 4.0 mmol of MAA, 20 mmol of EDMA, and 0.2 mmol of AIBN in a chloroform solution. Prepolymerization solutions were mixed for 30 min with ultrasonic waves before being cast onto the initial membranes. The polymerization was performed through the heating of the membranes in a vacuum drying oven at 60°C for 48 h. Then, the membranes were washed with acetic/methanol (1:9 v/v) to extract the templates, rinsed with methanol to eliminate the residual acetic acid, and dried at room temperature. The concentration of levofloxacin was quantitatively determined by a UV-762 spectrophotometer to guarantee that the absorbance was less than 0.005 at 298 nm.

For comparison, nonimprinted membranes (without a template) were prepared under the same conditions.



Scheme 1 Formula of ofloxacin (*R*- and *S*-) and levofloxacin (*S*-). The asterisk denotes the chiral center.

Modification degrees of the PVDF hollow-fiber MIP membranes

PVDF hollow-fiber membranes with different modification degrees were obtained by repeated polymerization cycles. The procedures were repeated five times. The samples were dried and weighed. The change in the weight as a result of polymerization was measured by a BS110S electronic microbalance (readability = 0.1 mg, Beijing Sartorius Instrument and System Engineering Co., Ltd., Beijing, China). The modification degree was calculated from the weight difference between the MIP membrane and initial membrane. The reproducibility of the modification degree values for a series of samples prepared under identical conditions was ±10%. The final value was calculated as the arithmetic average of a series of samples prepared under identical conditions.

Evaluation of the thin-layer MIP composite membranes

A module with a certain membrane area was connected to the membrane separation device (Fig. 1). The selectivity of the membranes toward levofloxacin and ofloxacin was investigated by the measurement of the amounts of the target molecule in the permeate solution during the filtration tests. A 100-mL solution of levofloxacin/ofloxacin in methanol was filtered through the membranes under 25°C and 1 bar. The specificity of the MIP composite membranes to the target molecule was determined by the division of the permeation capacity of the MIP composite membranes by the permeation capacity of the nonimprinted membranes. In all tests, a levofloxacin/ofloxacin concentration of 0.02 mmol/L in methanol was applied. The concentration of the solution was monitored by a UV spectrophotometer at 298 nm. All permeation experiments were carried out in triplicate, and the final

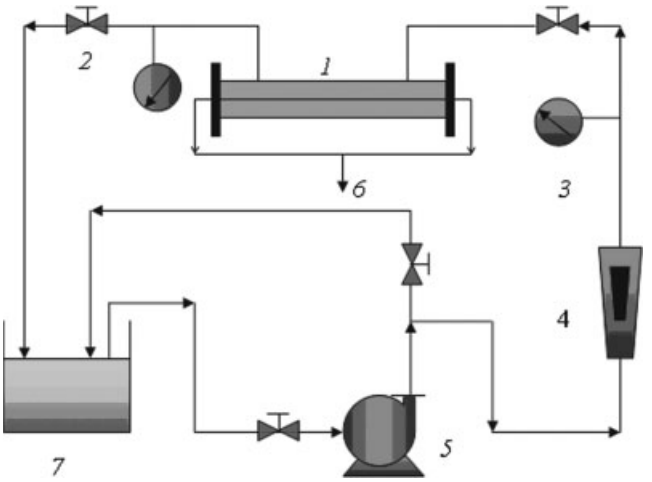


Figure 1 Testing equipment for molecularly imprinted composite membranes: (1) module, (2) valve, (3) pressure gauge, (4) flow meter, (5) pump, (6) permeate, and (7) feed tank.

adsorption capacity was calculated as the arithmetic average.

Morphology of the thin-layer MIP composite membranes

Scanning electron microscopy (SEM) was used to visualize the external surface and cross-section morphology images of both the initial and modified membranes after the membranes were broken in liquid nitrogen to avoid destroying the structure of the cross sections of the hollow fibers. All samples were sputter-coated with gold before the analysis.

RESULTS AND DISCUSSION

Modification degree of the hollow-fiber MIP composite membranes

The relationship between the changes in the modification degree of the membranes (MIP composite membranes and nonimprinted membranes) and the times of the polymerization cycles is shown in Figure 2. The total weight of the MIP composite membranes increased by 14 $\mu g/cm^2$ after a five-cycle polymerization. The membrane weight increased after every cycle, and this indicates that a new layer was repeatedly produced on the external surface of the membrane during each polymerization cycle. Because a PVDF membrane is practically inert in a polymerization solution and generated radicals, the MIP layer could be considered the deposition process on the external surface of a PVDF hollow-fiber membrane. It has been concluded that the amount of the synthesized polymers on the surface of the membranes can be controlled by the repetition of the polymerization cycle. It is also noted that an MIP composite membrane has a lower modification degree than a nonimprinted membrane has. This difference might be due to the formation of a supramolecular complex between the monomers and the template that influences the kinetics of the copolymerization.[24]

Membrane performance of the modified hollow-fiber MIP composite membranes

As previously reported,[20,25] the molecular sieve effect of MIP composite membranes is responsible for the accessible specific cavities of the top skin layer. Therefore, the separation of the solution is dominated by the number of specific cavities in the top layer. To test the effect of the top layer on the MIP composite membranes under enantioseparation conditions, evaluation experiments were performed in which both levofloxacin and ofloxacin were applied simultaneously to differently modified membranes.

Figure 3 shows the change in the permeation concentrations of levofloxacin and ofloxacin across differently modified MIP composite membranes and nonimprinted membranes. Both modified MIP composite membranes and nonimprinted membranes showed enhanced levofloxacin and ofloxacin permeation. The difference in the permeation concentration between MIP composite membranes and nonimprinted membranes prepared under identical conditions (specificity of the membranes) gives information regarding the specific binding of recognizing sites to the imprinting molecules. As shown in Figure 3, the specificity of the membranes increases gradually with an increase in the modification degree of the membranes to a maximum value followed by a slight decrease. The increase in the repeated polymerization cycle can lead to an increase in the thickness of the membrane top skin layer. The imprinted layer formation and growth

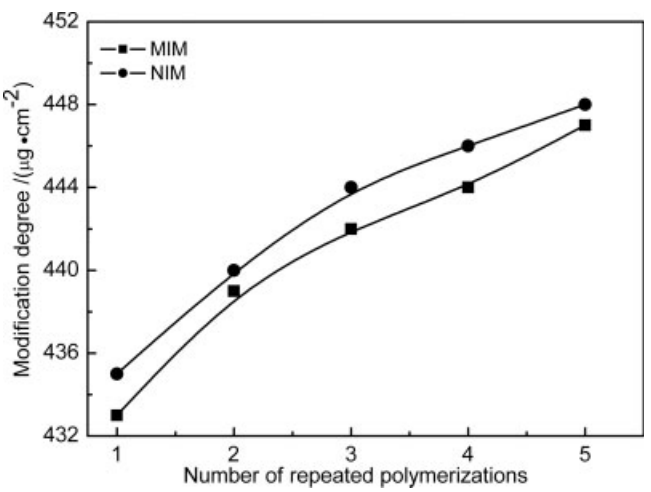


Figure 2 Change in the modification degree by repeated polymerization. MIM:MIP, composite membrane; NIM, nonimprinted membrane.

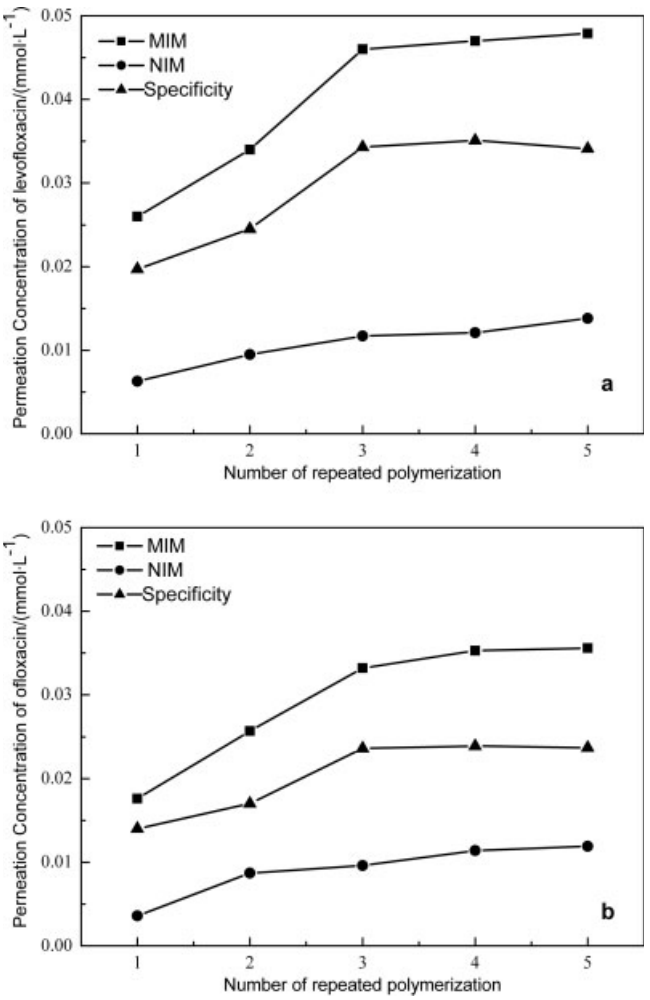


Figure 3 Effects of different cycles of thermal polymerization on the permeation concentration of (a) levofloxacin and (b) ofloxacin.

influence the specific template binding. On the one hand, the deposition of an imprinted layer can remedy the defect of the membrane surface; on the other hand, with increasing deposition of the imprinted layer, there are many more recognition sites available for the template when it passes through the membrane, and the pore size of the MIP composite membranes will decrease.[20] The largest permeation concentration and select factor were observed for MIP composite membranes in a four-cycle polymerization, as shown in Figure 3. Further casting caused a reduction in the permeation capacity of the membranes to both levofloxacin and ofloxacin. This phenomenon may be ascribed to an overly dense polymeric network created on the membrane surface, which is not favorable for the template diffusing through the longer recognition channel.

As shown in Figure 3(a,b), MIP composite membranes show a higher permeation capacity toward levofloxacin than ofloxacin. Under the same conditions, nonimprinted membranes have much less permeation capacity for both levofloxacin and ofloxacin in comparison with MIP composite membranes. The different permeation performances of MIP composite membranes and nonimprinted membranes may result from different polymer morphologies in crosslinked polymerizations with or without template molecules. The presence of template molecules during polymerization makes the structures and porosities of the MIP composite membranes different from those of the nonimprinted membranes, and the recognition cavities in an orientation more suited for the high specific binding of levofloxacin.

MIP composite membrane permeation mechanism

In our previous study,[26] the high affinity of the levofloxacin-imprinted polymer was explained by mainly ionic and hydrogen-bond interactions due to the presence of the amino groups and carboxylic group in the crosslinked copolymer. However, hydrophobic interactions may have an additional impact on the separation of modified membranes with a levofloxacin-imprinted polymer. In this work, membrane permeation capacities in different solvents were studied, and this might contribute to understanding hydrophobic interactions in separation processes with MIP composite membranes.

As shown in Figure 4, the permeation studies showed higher levofloxacin diffusion through MIP composite membranes from a 90% methanol solution in water in comparison with a 100% methanol solution. For hydrophobic PVDF MIP composite membranes applied in this work, the permeation concentrations of levofloxacin from a 90% methanol solution in water and from a 100% methanol solution were 0.035 and 0.026 mmol/L, respectively, with a feed levofloxacin concentration of approximately 0.02 mmol/

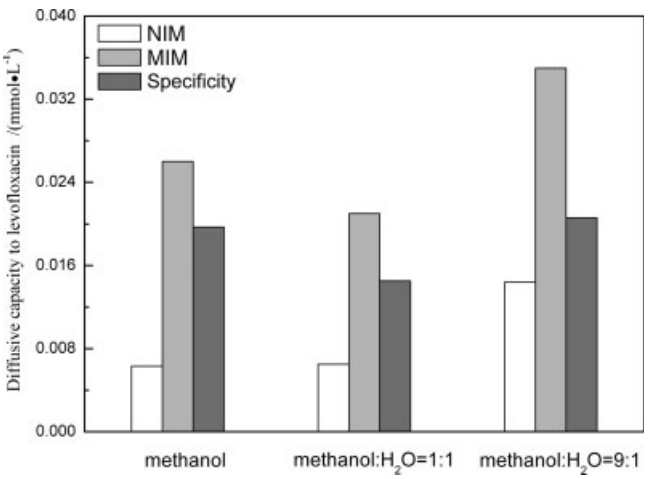


Figure 4 Changes in the diffusive capacity to levofloxacin in MIP composite membranes under different conditions.

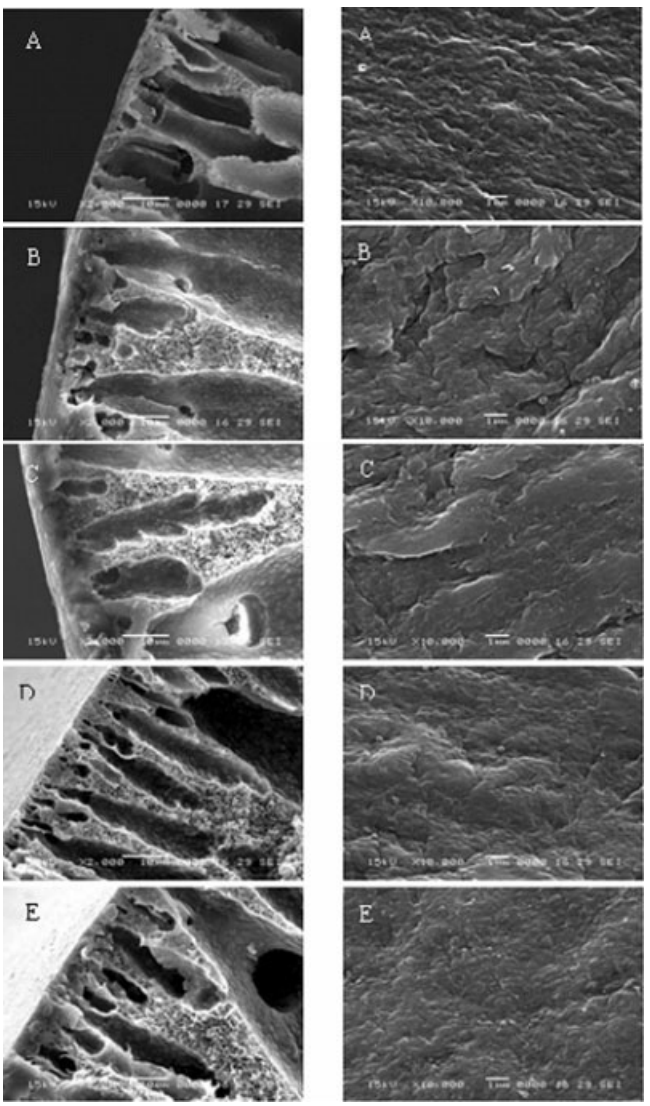


Figure 5 SEM photographs of cross sections and external surfaces modified with different cycle polymerizations: (A) initial membrane, (B,D) three-cycle polymerization (MIP membrane and eluted MIP membrane), and (C,E) five-cycle polymerization (MIP membrane and eluted MIP membrane).

L. This result indicates a contribution of the hydrophobic interactions to the levofloxacin binding and selective transport with MIP composite membranes. However, the permeation concentration seems to decrease upon a further increase in the water content in the feed resolution, and this can be explained in part by the fact that water is a relatively poor solvent for levofloxacin: more water in the solution leads to poor solubility of levofloxacin.

Hence, the binding specificity of MIP composite membranes is a result of both multisite binding to the template via ionic, hydrogen-bond, and hydrophobic interactions and the correct position of functional groups involved in binding imprints.

Membrane morphology of modified MIP composite membranes

When the levofloxacin-imprinted polymer protocols were cast onto the surfaces of PVDF membranes, there did not appear to be a clear polymer layer in a visual check after thermal polymerization. The membranes were still smooth and flexible, but a flavescent color was observed in the membrane surface. With an increasing modification degree, the membrane became rigid gradually. Figure 5 shows SEM photographs of the cross sections and external surfaces of different modified membranes. It is obvious from the SEM photographs [Fig. 5(A–C)] that the MIP membranes consist of a denser top layer gradually loaded onto the surface of the initial membranes. The gradually densely packed agglomerates of the imprinted polymer caused the membranes to be more rigid. A comparison of photographs A, D, and E suggests that the pores in the surface of the initial membrane were substituted by some small cavities after repeated polymerizations. The membrane morphology after multiple repeated castings looks smoother.

CONCLUSIONS

PVDF hollow-fiber membranes modified by a thin layer of MIPs were developed by thermal polymerization for the selective separation of levofloxacin. PVDF hollow-fiber membranes with different modification degrees by repeated polymerizations were weighed. The total weight of the imprinted membranes increased by 14 $\mu g/cm^2$ after a five-cycle polymerization. An increase in the membrane weight indicated a deposition of an MIP layer on the external surface of a PVDF hollow-fiber membrane during each polymerization cycle, as also demonstrated by SEM. MIP membranes with different degrees of surface modification provided highly selective binding of levofloxacin. Both MIP composite membranes and nonimprinted membrane showed enhanced adsorption of levofloxacin and ofloxacin gradually with an increase in the modification degrees of the PVDF hollow-fiber membranes to a maximum value followed by a decrease. These results indicate that thermal polymerization indeed produces an MIP layer on the external surface of hollow-fiber PVDF membranes and that it is feasible to control the permeability by repeated polymerization cycles. Changes in the solvent system in the permeation experiments were made to understand the hydrophobic interaction as one of the results of molecularly imprinted membrane binding specificity. Selective separation was obtained by multisite binding to the template via ionic, hydrogen-bond, and hydrophobic interactions.

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