A Kinetic Consideration on the Selective Adsorption and Molecular Recognition by Molecularly Imprinted Polymer

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Received April 6, 2007

This article presents an original work on kinetically studying the selective adsorption and recognition by molecularly imprinted polymer (MIP). With S-naproxen as template, the imprinted polymer was prepared. The result indicates that the prepared polymer shows a more complicated sorption toward S-naproxen than toward its enantiomer R-naproxen. The rate constant in the case of template appears to be a variable. There are also significant deviations from the idealized Langmuir model. Related information indicates that these, in logic, can be a result of biomimic structural and functional complements between imprint and the template, which makes the polymer capable of selectively recognizing the imprint species.

Key Words : Molecularly imprinted polymer, Adsorption, Kinetics

Introduction

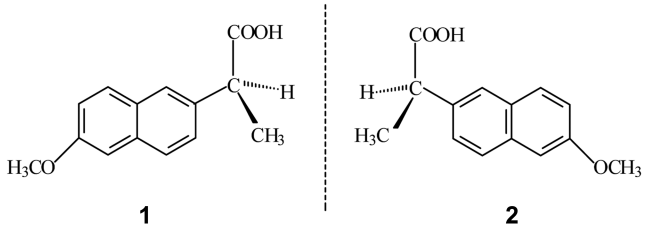
Biomimic recognition has been an active field in the present research.[1-3] Recently, this field is significantly advanced by the so-call 'molecular imprinting' technique.[4,5] Comparable to the recognition of some natural biomolecules such as antibody-antigen, receptor-ligand or enzyme-substrate, the molecular imprinting recognizes a special substrate basing on the same principle. For this reason, the molecularly imprinted polymer (MIP) is also called as 'antibody-like mimic'.[6,7] To fabricate a structural and functional complement between imprint and template, this methodology uses usually molecular self-assembly to position the groups of functional monomer around an inducible template.[8] Subsequently, a photo- or thermal polymerization in the presence of cross-linker is performed to fix this organized architecture. The template imprinted is then removed from the polymer, leaving behind binding sites complementary to the imprint species in terms of the shape and position. Owing to these features, quite some potential applications by MIP have been exploited, such as selective adsorption,[9] chromatographic separation,[10] solid extraction,[11] drug release,[12] chemical sensing[13] and catalysis[14] and so on.

As commonly known, the selective adsorption and molecular recognition by MIP, in essence, is a result of structural and functional complements between imprint and the template. Thus, differing from the general adsorption driven by thermodynamic entropy, the adsorption by MIP involves usually more influential factors, particularly the complementary interaction. Moreover, the reorientation of substrate within the imprint toward binding sites due to the mutual induction is also anticipated to have effect on this process.[15] In addition, the molecules adsorbed earlier can sterically hinder the later adsorption due to its size in itself. Owing to these reasons, the intrinsic mechanism by MIP can not be simply told from one or two qualitative and quantitative relationships of adsorption amount. It is also actually rough to deem the rate constant as a fixed-value in the presence of inter- or intra-molecular interactions.[16,17] Regarding the complexity of MIP adsorption, it appears to be necessary to discuss the mechanism with kinetic opinion since it can present not only the general information in dynamic process but also insight into the probable essence of these interactions. In literature, as noted, some endeavors have been tentatively made on this topic.[18-20] However, most of them are limited to theoretical, modal or principial level. Almost no specialized work has conducted to discuss this mechanism of molecular recognition in the presence of these interactions.

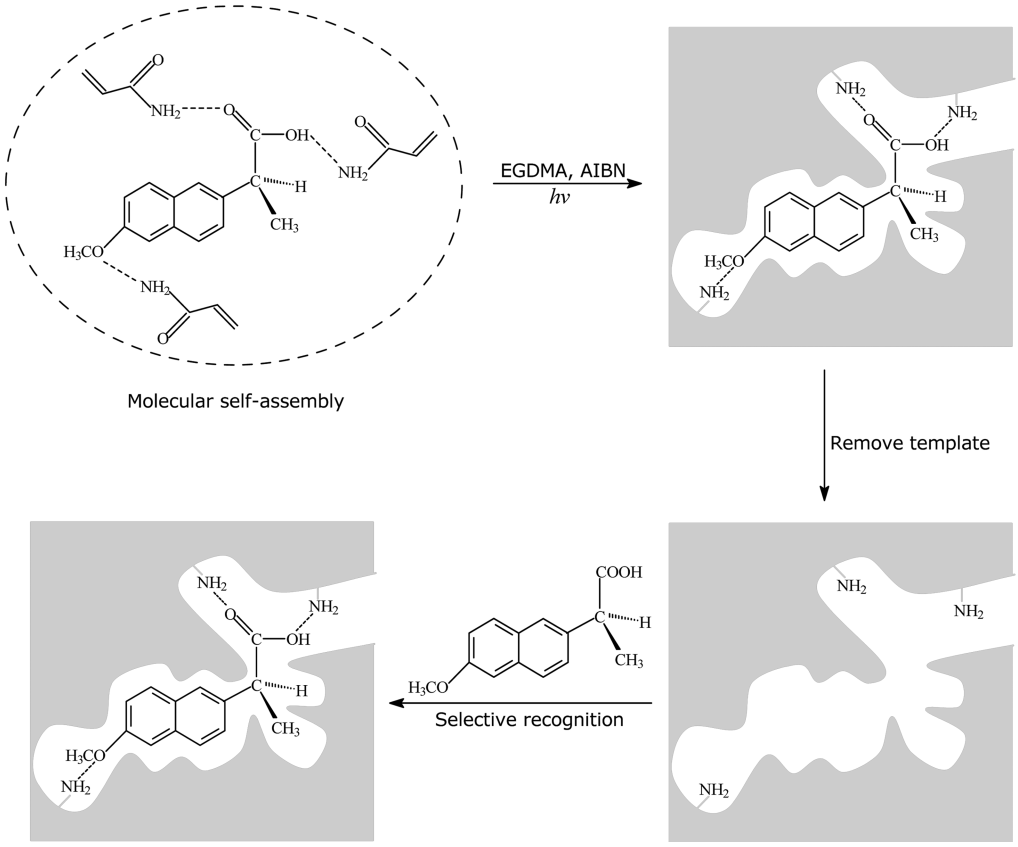
To the best of our knowledge, this article is the first work that specially contributes to discussing the adsorption mechanism of MIP in the presence of these interactions. With S-naproxen as template (**1**; Scheme 1), the imprinted polymer was prepared and used as adsorbent for S-naproxen. Based on classic kinetics or models, the adsorption mechanism was discussed. For a contrastive study, the enantiomer S-naproxen (**2**; Scheme 1) was selected as control. The aim is to present a complementary study to the general understanding on molecular recognition by imprinted polymers.

Experimental Section

Materials and Regents. Both S- and R-naproxens were purchased from Zhejian Xianju Pharmaceutic Plant (China).



Scheme 1. Formula structures of S- and R-naproxens.



Scheme 2. Schematic presentation of the preparation and molecular recognition of MIP.

Ethylene glycol dimethacrylate (EGDMA) was obtained from Acros Organics (Belgium). Acrylamide and 2,2'-azobis (isobutyronitrile) (AIBN) were purchased from Peking Chemical Reagent Plant (China). All other chemicals concerned are commercially available products of reagent.

Preparation of MIP. To help learning, Scheme 2 presents a technical outline for the preparation of MIP.[21] 0.3529 gram (1.53 mmol) of S-naproxen, 6.06 gram (30.6 mmol) of EGDMA, 40 milligram (0.24 mmol) of AIBN and 0.308 gram (5.6 mmol) of acrylamide were dissolved in tetrahydrofuran (THF) (10 mL). After deoxygenation with sonication and nitrogen, the system was irradiated under ultraviolet light (365 nm) at 0 ^{o}C for 24 h. The resulted polymer (MIP precursor) was crushed roughly and subsequently treated by the mixture of THF and acetic acid (in a volume ratio of 9:1) with many cycles to remove the template imprinted. The final polymer (*i.e.* MIP) was dried in a vacuum vessel (20 ^{o}C) and then ground into 40-50 mesh for further study.

Evaluation of Adsorption Isotherms. In a batch format, the adsorption experiment was performed in a thermostatic apparatus (30 ^{o}C).[22] The substrate S-naproxen was dissolved in THF (totally 10 ml). The solid content of MIP was 19.6 mg/ml in each operation. The sample solutions (in identical quadruple) were stirred for 45h (except for additional statement). The change of substrate concentration before and after adsorption was spectrophotometrically monitored at 348 nm. The adsorption amount per gram MIP was obtained from the mass balance of substrate, and finally the average value of quadruple was presented. For a purpose of contrast, the adsorption isotherm of R-naproxen was also determined under comparable conditions.

Results and Discussion

Revelation of Imprint. Figure 1 presents the infrared spectrum of prepared MIP. There are two main absorption-bands existing in the spectrum, distributing respectively 3200-3600 within and 2800-3100 cm^{-1}. In basic condition, as already displayed,[23,24] the absorption band ranged from 3200 to 3600 cm^{-1} can be related to the stretching of amido. The peek within 2800-3100 cm^{-1} may be responsible for the stretching of C-H. For a purpose of clarification, we also enclose the spectra of MIP precursor, S-naproxen and a blank control prepared without S-naproxen in Figure 1. As observed, there is similarity existing in both spectra of S-naproxen and the MIP precursor. After washing, the spectrum of MIP is almost the same level as that of blank control. Figure 2 presents the SEM images of MIP and the blank control. The blank control shows a relatively smooth surface. However, there are obviously some cavities existing within the MIP. These strongly indicate that an imprint is formed within the prepared MIP. After removed template, as also observed, the spectrum of MIP shows no visible difference from that of the blank control. This reveals that almost all templates are removed from the precursor, which

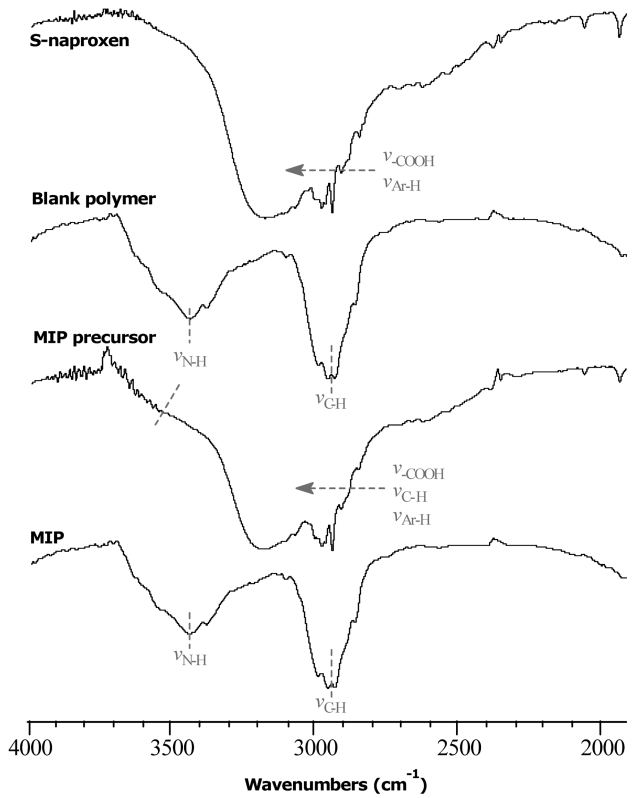
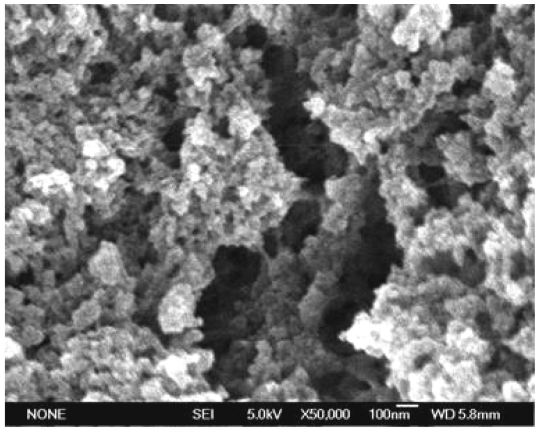
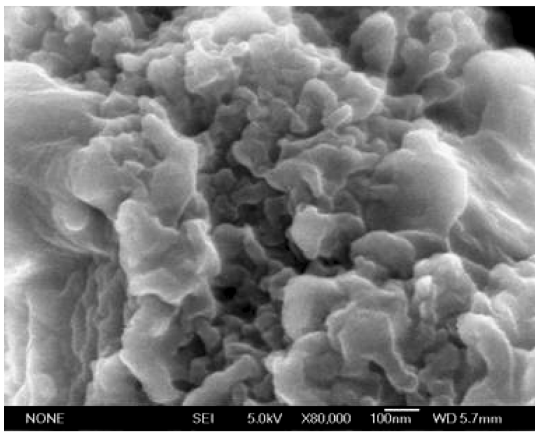


Figure 1. IR spectra of prepared materials.



a: MIP



b: Blank control

Figure 2. SEM images of prepared materials (a: MIP; b: Blank control).

thus presents a convenience for further study.

Time Profile and Adsorption Kinetics. Figure 3 presents the adsorption curves of MIP. An increase in adsorption time leads to a corresponding increase in adsorbance (the data labeled are the initial concentrations of substrate). The adsorbance of both enantiomers shows no visible difference at 40h from at 45h. This indicates that the adsorption can actually reach the equilibrium within *ca*. 40 hours. Thus, for the determination of isotherms, the choice of adsorption time such as 45h is appropriate and sufficient regarding the reach of equilibrium. As noted, although both S- and R-naproxens present extremely similar structure, the adsorbance of S-naproxen is obviously larger than that of R-naproxen. The MIP shows a preferential adsorption for the imprint molecule. As already mentioned, the molecular recognition by imprinted polymer, in essence, is a result of structural and functional complements between imprint and the temple. Since the S-naproxen can present a structural match to the binding framework, the preferential adsorption is expected. As also noted, the sorption presents initially a rapid adsorption and then the slow approach to a limiting value, displaying a typical feature of first-order kinetics. In view of this, the first-order kinetics is tentatively used to simulate this process:[25,26]

$$-\frac{dC}{dt} = kC$$

or

$$-\frac{d(1-\theta)}{dt} = k(1-\theta) \quad (1)$$

Here C is the concentration of substrate in solution, θ is the coverage degree and $(1-\theta)$ represents the uncovered portion of MIP. Integrating this Eqn will present:

$$\ln(1-\theta) = -kt \quad (2)$$

This Eqn. thus gives:

$$\ln\left(1-\frac{Q_t}{Q_m}\right) = -kt \quad (3)$$

Here Q_t and Q_m are respectively the actual and the maximal adsorbances of substrate. Clearly, basing on above Eqn, one would normally expect the diagram (plotting $\ln(1-Q_t/Q_m)$ versus t) to be a straight-line. As shown in Figure 4, the fittings in the case of R-naproxen are actually not bad (dashed). The correlation coefficient (R^2) can be better than 0.98. However, for the adsorption of S-naproxen, the rate constant appears to be variable and almost no linear correlativity exists in any one of these fittings. The best fittings (presumed lines) do not lead these lines to passing through these data points but result in scattered outlines. These reveal that the adsorption by MIP toward S-naproxen involves likely more influential factors than toward R-naproxen. Correlated to previous discussion, this observa-

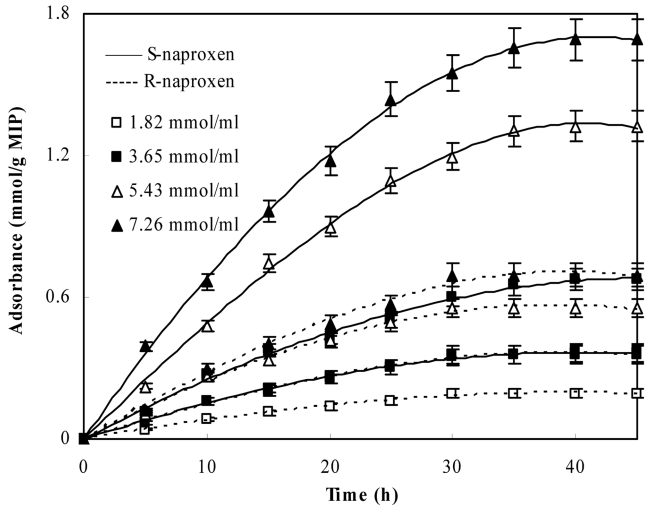


Figure 3. Adsorption curves.

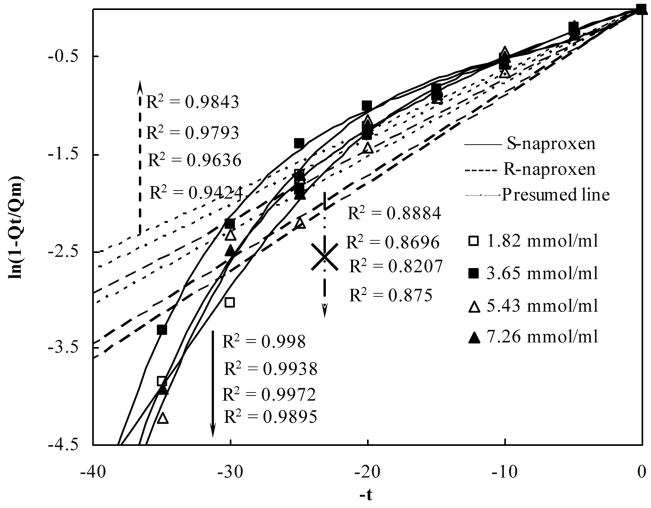


Figure 4. Fittings of first-order kinetics.

tion, in logic, can be due to the unique interaction between MIP and template. As commonly known, the specific induction of imprint toward S-naproxen makes the template capable of occupying priorly on the binding sites, followed by adsorbing over a relatively weaker surface. Furthermore, as time advances, the more molecules are adsorbed. The molecules adsorbed earlier can sterically hinder the later adsorption due to its size in itself. Owing to these reasons, the adsorption by MIP can not remain in a fixed state but is in a process of changing rate. As a result, the fitting from classic kinetics shows a deviation from the general process. Inspired by the mechanism of non-uniform adsorption as proposed by Temkin,[27,28] one would believe it more reasonable to regard the rate constant as a function of coverage degree than as a fixed value:

$$-\frac{d(1-\theta)}{dt} = Ae^{-\frac{E_a(\theta)}{RT}}(1-\theta) \tag{4}$$

Hereis $E_a(\theta)$ the function of activation energy and A is the pre-exponential factor. As presently known, the change of activation energy can be classified approximately into logarithmic and linear forms:[26,27]

$$E_a(\theta) = E_0 + \beta\theta \tag{5a}$$

$$E_a(\theta) = E_0 + \alpha\ln\theta \tag{5b}$$

Here E_0 is the initial activation energy, and α and β are the constants. Now, substituting both relationships into Eqn (4) would show:

$$\frac{d\theta}{dt} = Ae^{-\frac{E_0}{RT}}(1-\theta)e^{-\frac{\beta\theta}{RT}} \tag{6a}$$

$$\frac{d\theta}{dt} = Ae^{-\frac{E_0}{RT}}(1-\theta)\theta^{-\frac{\alpha}{RT}} \tag{6b}$$

In most cases of MIP adsorption, as commonly known, the utilization ratio of imprint is actually not high. This may be due to that the access of template to the innermost cavity is rarely available because of mutual induction along the cavity. As a result, the true coverage-degree is usually much less than 1. Hence, as a reasonable approximation, Eqns (6a) and (6b) can be sough into such forms:

$$\frac{d\theta}{dt} = ke^{-\frac{\beta\theta}{RT}} \tag{7a}$$

$$\frac{d\theta}{dt} = ke^{-\frac{\alpha}{RT}} \tag{7b}$$

Here k is a constant that includes various constant items. Now, treating both Eqns with integration and linearization will present:

$$Q_t = \mu\ln + \gamma \tag{8a}$$

$$\ln\frac{Q_t}{Q_m} = \eta\ln t + \lambda \tag{8b}$$

Here η, λ, μ and γ are the integral constants. Apparently, based on both Eqns/ (8a) and (8b), the important feature of molecular induction within MIP has been summarized. Thus, in logic, both Eqns are normally expected to fit the practical process better than the classic kinetics. As shown in Figures 5 and 6, there are significant improvements in these fittings. The improvement is quite remarkable in the case of template. The correlation coefficient (R^2) can be better than 0.95. This thus implies that both Eqns describe more characters and contents involved in MIP adsorption. Correlated to previous discussion, these can be a result of biomimic complements between template and the binding framework, which makes the polymer capable of preferentially adsorbing S-naproxen.

Adsorption Isotherms. Figure 7 presents the adsorption isotherms. An increase in substrate concentration results in a corresponding increase in adsorbance. Comparable to the time profiles, the imprinted polymer shows a preferential adsorption for the template S-naproxen. To simulate this

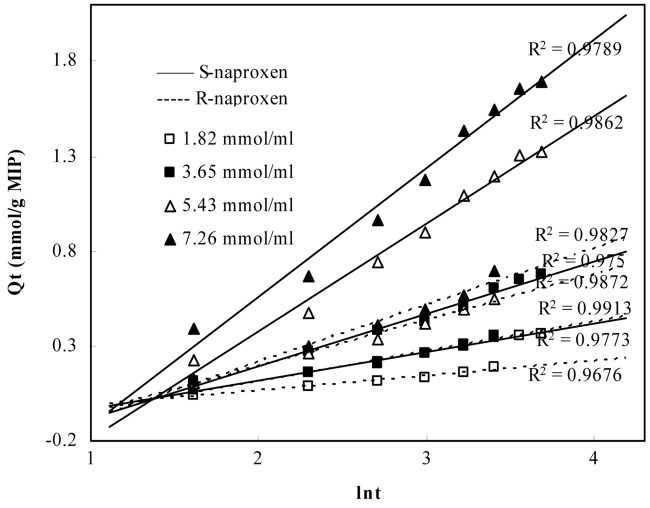


Figure 5. Fittings of Eqn. (8a).

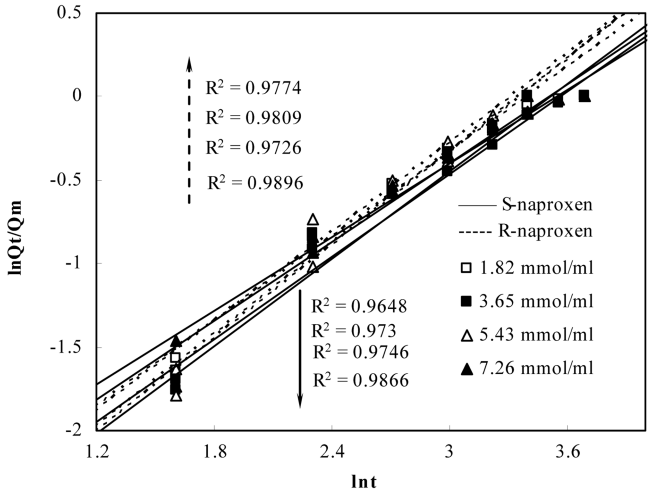


Figure 6. Fittings of Eqn. (8b).

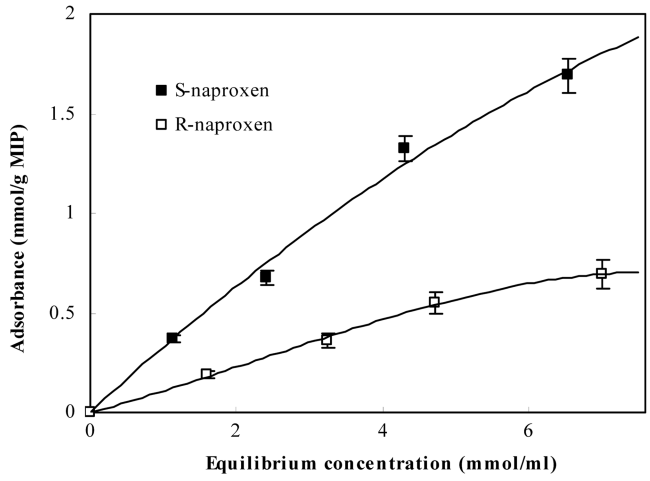


Figure 7. Adsorption isotherms.

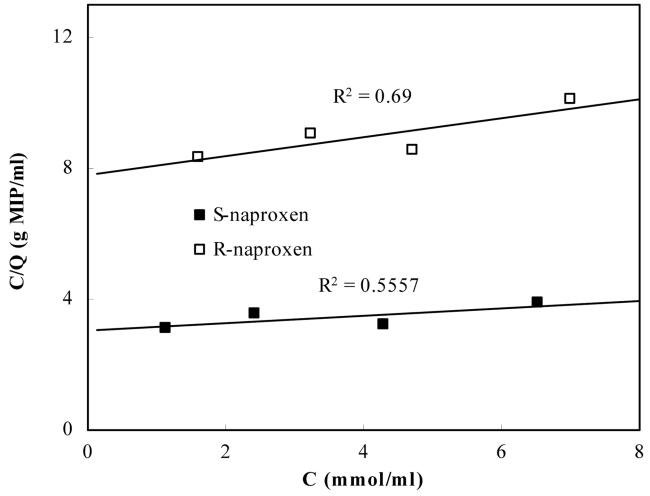


Figure 8. Fittings of Langmuir model.

process, the classic Langmuir model is tentatively used to fit the results:[29,30]

$$\frac{C}{Q} = \frac{1}{K_A Q_S} + \frac{1}{Q_S} C$$

or

$$\theta = \frac{k_a C}{k_d + k_a C} \tag{9}$$

Here C is the equilibrium concentration of substrate, K_A is the corresponding constant, and Q and Q_S are the actual and the saturated adsorbances. The subscripts '*a*' and '*d*' are related to the adsorption and the desorption. As commonly known, the Langmuir model is an idealized model and has held a dominative position in sorption. This model describes an ideal adsorption progressing over a smooth surface, which does not involve any intermolecular interaction of sorbate or surfacial ununiformity. According to this model, one would normally expect the diagram (plotting C/Q versus C) to be a straight line. As shown in Figure 8, the fittings for both enantiomers are not as good as expected. The correlative coefficient (R^2) is not larger than 0.69 regardless of the specific case. This reveals that the adsorption by imprinted polymer involves likely more factors in comparison to the general adsorption. As already explained, the specific adsorption and molecular recognition by MIP, in essence, is a result of inducted molecular memory. In the adsorption process, this inducted memory enables the polymer to specifically bind the template. Other factors including the reorientation of substrate toward binding sites and the steric interaction among sorbates are also expected to have effect on this process. Now, with this background, one can seek this idealized model into such a form (similar to the treatment in time profile):

$$\theta = \frac{k_a^0 e^{-\frac{E_\alpha(\theta)}{RT}} C}{k_d^0 e^{-\frac{E_d(\theta)}{RT}} + k_a^0 e^{-\frac{E_d(\theta)}{RT}} C} \tag{10}$$

Here the superscript '0' is related to the original rate

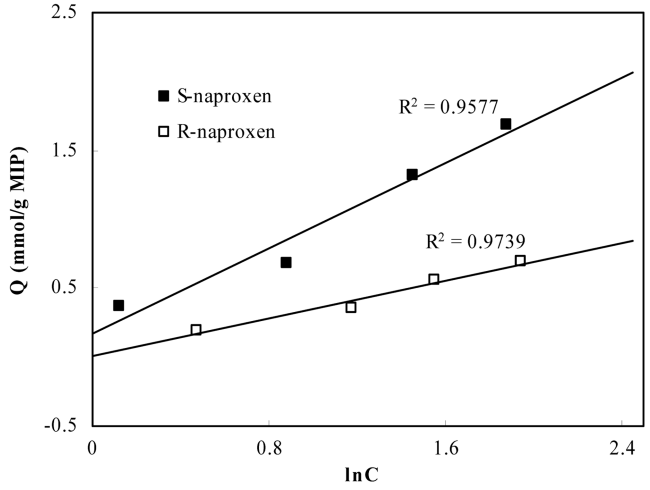


Figure 9. Fittings of Eqn. (12a).

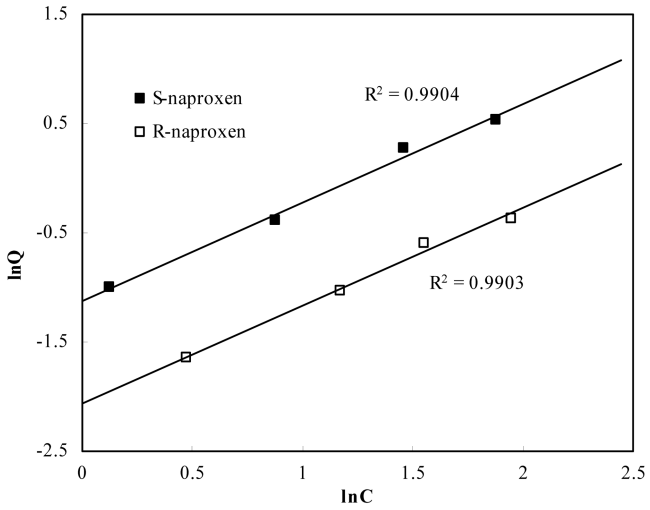


Figure 10. Fittings of Eqn. (12b).

constant and activation energy. Combining Eqns (5) with (10) will present:

$$\theta = \frac{RT}{\gamma}\ln(K_0 C) \qquad (11a)$$

$$\theta = K_0 C^{\frac{RT}{\mu}} \qquad (11b)$$

Here μ, γ and K_0 are constants. Now, treating both Eqns with transform of variable and linearization will present:

$$Q = \left(\frac{RTQ_S}{\gamma}\right)\ln C + \left(\frac{RTQ_S}{\gamma}\right)\ln K_0 \qquad (12a)$$

$$\ln Q = \left(\frac{RT}{\mu}\right)\ln C + \ln K_0 Q_S \qquad (12b)$$

As noted, Eqn. (12b) is exactly the expression of Freundlich model.[31] Although this model and its applicability toward many adsorptions have been well documented, the origin is empirical. In the present case, one can learn the probable internality. Some molecular interactions are additionally summarized in this model. Figure 9 and 10 present the fittings in tune with Eqns. (12a) and (12b). Relative to the idealized model, the fittings from both Eqns. (12a) and (12b) are obviously better. The fittings lead to the higher correlativity regardless the specific sorption. The improvement is quite remarkable in the case of template. The correlation coefficient (R^2) can be better than 0.95. These indicate that Eqns. (12a) and (12b) can summarize more features and contents involved in the practical adsorption. As already mentioned, the molecular recognition by MIP, in nature, is a result of induced molecular memory. Thus, differing from the general adsorption, the specific one by MIP involves obviously some molecular inductions. As a result, the practical adsorption shows a deviation from the idealized model.

Conclusions

This article presents important information on discussing the specific recognition by molecularly imprinted polymer (MIP). With kinetic backgrounds, the selective adsorption and molecular recognition were studied. Related study indicates that the specific adsorption by MIP is essentially different from a general adsorption. The adsorption by MIP leads to a changing rate constant. There are also significant deviations from the idealized Langmuir model. Inspired by the mechanism of non-uniform adsorption, we believe it more reasonable to regard the rate constant as a function of coverage degree than as a fixed value. It is also necessary to point out that these results are preliminary and that further work is necessary regarding a clearer understanding.

Acknowledgement. The authors want to thank NSFC (Grant No. 20603010) and Natural Science Foundation of Hubei Province for presenting financial supports to carry out this research work.

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