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Adsorption of Berberine Hydrochloride, Ligustrazine Hydrochloride, Colchicine, and Matrine Alkaloids on Macroporous Resins

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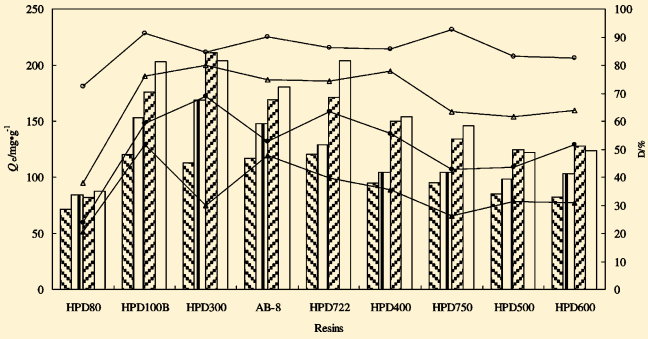
Supporting Information

ABSTRACT: This research aims at identifying suitable resin adsorbents for efficient separation and purification of alkaloids from plant materials. The adsorption properties (equilibrium, kinetics, and column breakthrough) of four alkaloid model compounds (berberine hydrochloride, ligustrazine hydrochloride, colchicine, and matrine) on selected macroporous resins were studied. The adsorption equilibrium capacities and desorption ratios of the four model compounds on nine different macroporous resins were measured and compared. It was observed that the resins with a low polarity and high surface area offered a high adsorption capacity for all alkaloids. The pseudo-second-order adsorption rate equation fit well all the kinetic data, and the Langmuir and Freundlich isotherm equations correlate well the adsorption isotherms on the four resins. Among the nine resins studied in this work, the HPD300 resin was identified as the most promising adsorbent for alkaloids separation and purification because of its excellent adsorption and desorption properties for all four alkaloid compounds. The adsorption breakthrough experiment on the HPD300 resin using a mixture solution containing all four model compounds further confirmed the effective separation of alkaloids on the HPD300 resin.



1. INTRODUCTION

Alkaloids are a group of natural organic compounds that contain mostly basic nitrogen atoms in a heterocyclic ring.[1] Alkaloids represent one of the most widespread classes of natural products, which derive from at least 158 botanical families including cryptogams, phanerogams, mono- and dicotyledons.[2] Over 10 000 alkaloids have been isolated from natural resources and the number of alkaloids increases about 100 per year.[3] Alkaloids exhibit a range of biological and pharmacological activities and many alkaloids are the bioactive ingredients of medicinal plants and traditional Chinese medicine.[2] Statistically, alkaloids comprise about 15.6 % of the known natural products and almost 50 % of the plant-derived natural products of pharmaceutical and biological significance.[4] To date, alkaloids are still the potential natural products in drug discovery, and purification of alkaloids remains a popular topic in natural products research and development.[5] However, alkaloids generally exist in multi-component mixtures with a low concentration in the natural resource. Furthermore, the alkalinity and structural diversity of alkaloids make their isolation and purification especially the simultaneous separation of multiple alkaloids a very challenging task.[2]

Berberine hydrochloride (benzo[*g*]-1,3-benzodioxolo[5,6-*a*]-quinolizinium, 5,6-dihydro-9,10-dimethoxy-, chloride), ligustrazine hydrochloride (pyrazine, 2,3,5,6-tetramethyl-, hydrochloride), colchicine (acetamide, *N*-[(7*S*)-5,6,7,9-tetrahydro-1,2,3,10-tetramethoxy-9-oxobenzo[*a*]heptalen-7-yl]-), and matrine (1*H*,5*H*,10*H*-dipyrido[2,1-*f*:3′,2′,1′-*ij*][1,6]naphthyridin-10-one, dodecahydro-, (7a*S*,13a*R*,13b*R*,13c*S*)−) are four typical alkaloid compounds that belong to isoquinoline derivative alkaloids, organic amine derivative alkaloids, pyrazine derivative alkaloids, and pyridine derivative alkaloids, respectively, their chemical structures are shown in Figure 1. These alkaloids have exhibited different biological activities and a wide range of pharmacological effects. Berberine hydrochloride has a variety of pharmacological effects such as anticancer action, antibiotic property, and anti-inflammatory effect.[6,7] Ligustrazine hydrochloride is widely used to cure cardiovascular diseases in China.[8] Colchicines is used for the treatment of acute gout flares and the prophylaxis of gout flares,[9] and matrine has a wide spectrum of pharmacological actions including hepato-protective activity on acetaminophen-induced hepatotoxicity in mice, and proapoptotic activity in gastric carcinoma cells and leukemia cells.[10]

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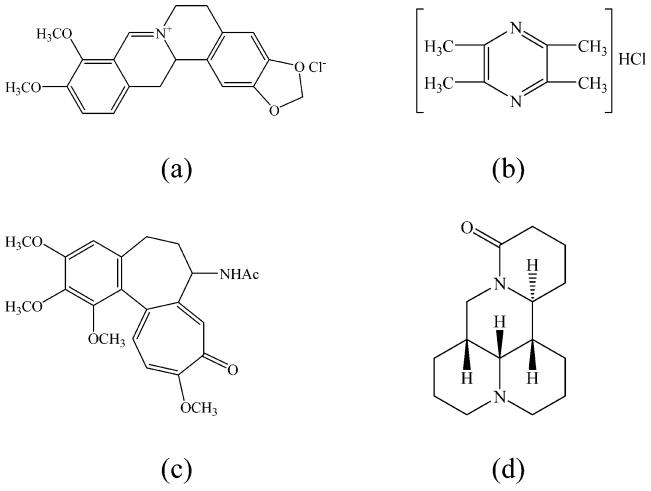

Figure 1. Chemical structures of berberine hydrochloride (a), ligustrazine hydrochloride (b), colchicines (c), and matrine (d).

The physical and chemical techniques that have been successfully applied in separation and purification of alkaloids include liquid−liquid extraction, precipitation,[3] membrane filtration,[3,11] adsorption,[12−17] and chromatography methods such as high-performance liquid chromatography,[5,17,18] centrifugal partition chromatography (CPC),[19] and high-speed counter-current chromatography.[2,20−26] Among those methods, adsorption is probably the most widely used and the most effective process for separation and purification of alkaloids. Silica gel (SiO_2), alumina (Al_2O_3), activated carbon, and resin are the commonly used adsorbents for alkaloids purification using column chromatography.[15] Relatively, macroporous resins are extensively applied as solid-state extraction materials for adsorption, separation, and purification of bioactive substances due to their stable phys-chemical structure, moderate equilibrium adsorption capacity, high adsorption selectivity, diverse surface chemical structure, and feasible regeneration for repeated use.[16,27] They have been widely used in separation and enrichment including flavonoids,[28,29] polyphenols,[15,30] alkaloids,[16,31,32] saponins,[33,34] and other active compounds extracted from plant materials. The separation achieved in the macroporous adsorbents is based on the differences of adsorbent affinity toward the adsorbate molecules, which basically depends on the molecular weight, polarity of the adsorbate molecules, and so on.[16,35] Different alkaloids have diverse chemical structures, distinct molecular weights, and different hydrophobicities and polarities, so proper macroporous resins are selected to separate different kinds of alkaloids based on the different affinities between resins and alkaloids.

Some alkaloids have been successfully separated and purified from herbal materials by using macroporous resins, such as sanguinarine and chelerythrine in *Macleaya cordata (Willd) R. Br.*,[16] tertiary alkaloids in *Corydalis yanhusuo*,[31] vinblastine and vincristine in *Gatharanthus Roseus*,[36] and puerarin in *Pueraria lobata*.[37] However, the existing separation and purification of alkaloids on macroporous resins were mostly used for the isolation of one or two alkaloid compounds from natural plant extracts, or total alkaloids extraction from herbal materials, and these processes are only applied to a few limited plant materials.

The objectives of this work are to study the adsorption equilibrium, kinetics, and column breakthrough of different kinds of alkaloids on selected resins to identify suitable resin adsorbents and to develop an efficient process for separation and purification of alkaloids from different kinds of plant materials using macroporous resins. Berberine hydrochloride, ligustrazine hydrochloride, colchicine, and matrine were identified as the model compounds according to their different structures, different existing states, and their wide range of applications. Nine resins were selected as the resin adsorbents according to their physical, surface chemical, and pore structures. Limited experimental adsorption data of the same alkaloid compounds on those nine resins are currently available in the literature,[38,39] while none of them was tested at identical conditions of this study. The information obtained in this study is important for selecting the resin adsorbents for separation and purification of different kinds of alkaloids from plant materials.

2. EXPERIMENTAL SECTION

2.1. Adsorbents and Adsorbates. The adsorbents used in this study are macroporous resins that were purchased from Cangzhou Bon Adsorber Technology Co., Ltd. (Hebei, China). The structural parameters of these resins are summarized in Table 1. Before use, these resins were first soaked in ethanol for 24 h and then washed with distilled water until no residual ethanol can be detected. Meanwhile, they were washed with 1.37 mol·kg^{-1} of hydrochloric acid and 1.25 mol·kg^{-1} of sodium hydroxide alternatively and finally immersed in distilled water.

All four alkaloid model compounds (berberine hydrochloride, ligustrazine hydrochloride, colchicine, and matrine) used in this study have a 98$^+$ % purity. Berberine hydrochloride was purchased from Shanghai Darui Finechem Ltd. (Shanghai,

Table 1. Physical Properties of the Tested Macroporous Resins, Including the Matrix, Functional Groups, Particle Diameter, Average Pore Diameter, BET Surface Area, and Polarity

				particle diameter	average pore diameter	BET surface area	
number	resins	matrix	functional groups	mm	nm	$m^2 \cdot g^{-1}$	polarity
1	HPD80	styrene	none	0.30 to 1.25	8.0 to 8.5	350 to 400	nonpolar
2	HPD910	styrene	ester	0.30 to 1.25	8.5 to 9.0	450 to 550	nonpolar
3	HPD100B	styrene	none	0.30 to 1.25	12.0 to 16.0	500 to 580	nonpolar
4	HPD300	styrene	none	0.30 to 1.20	5.0 to 5.5	800 to 870	nonpolar
5	AB-8	styrene	ester	0.30 to 1.25	13.0 to 14.0	480 to 520	weak-polar
6	HPD722	styrene	ester	0.30 to 1.25	13.0 to 14.0	485 to 530	weak-polar
7	HPD450	styrene	ester	0.30 to 1.20	9.0 to 11.0	500 to 550	weak-polar
8	HPD750	styrene	ester	0.30 to 1.20	8.5 to 9.0	650 to 700	medium-polar
9	HPD500	styrene	cyano	0.30 to 1.20	5.5 to 7.5	500 to 550	polar

China), colchicine and ligustrazine hydrochloride were provided by Nanjing Zelang Medical Technology Co., Ltd. (Nanjing, China) and matrine was purchased from Shanghai Tauto Biotech Co., Ltd. (Shanghai, China), their chemical structures are displayed in Figure 1 and their IUPAC systematic names and CAS registry numbers were listed in Table S1 in the supplementary document. The mobile phase reagents including methanol and acetonitrile are of high-performance liquid chromatograph (HPLC) grade and were obtained from Merck, and all other chemicals are analytical grade reagents.

2.2. HPLC Analysis of Alkaloid Compounds. An Agilent 1100 liquid chromatographic system was used to determine the concentrations of alkaloids. The HPLC column was a Phenomenex-C18 (250 mm × 4.6 mm, 5 μm), the flow rate was 0.6 $cm^3 \cdot min^{-1}$ and the column temperature was maintained at 303 K. The mobile phases, detection wavelengths, calibration curves, and linearity test ranges for the four model compounds were listed in Table S2 in the Supporting Information with the relative standard deviation ($n = 6$) less than 0.8 %. The mobile phase for the mixed sample was 0.05 $mol \cdot kg^{-1}$ monopotassium phosphate aqueous solution−methanol, and the gradient elution conditions were shown in Table S3 with the relative standard deviation ($n = 6$) less than 1 %. The HPLC profile of a mixture sample is displayed in Figure 2.

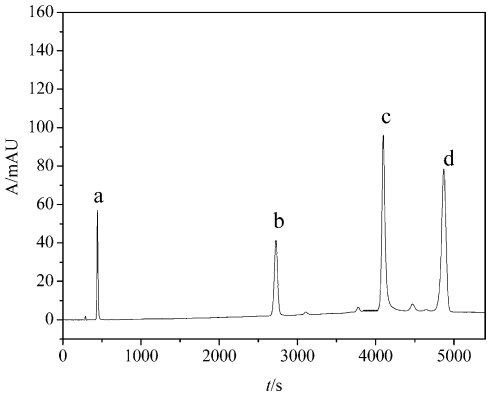

Figure 2. A HPLC profile of an alkaloid mixture sample of matrine (a), ligustrazine hydrochloride (b), berberine hydrochloride (c), and colchicine (d).

2.3. Determination of Adsorption Isotherm and Desorption Ratio. An amount of 0.25 g of resins was accurately weighed and introduced in 250 cm^3 of aqueous sample solution in a conical flask. The initial concentration of the four samples, berberine hydrochloride, ligustrazine hydrochloride, colchicine, and matrine, was set to be ($8.07 \cdot 10^{-4}$, $2.32 \cdot 10^{-3}$, $5.01 \cdot 10^{-4}$ and $1.21 \cdot 10^{-3}$) $mmol \cdot kg^{-1}$, respectively. The flasks were then shaken at a constant speed (150 rpm) for 28 h at 303 ± 1 K in a SHZ-82A oscillator (Changzhou Nuoji Equipment Co., Ltd., Jiangsu, China) until the equilibrium was reached; the equilibrium concentration of the sample was determined and the equilibrium adsorption capacity of the alkaloids on the resin was calculated as

$$Q_e = (C_0 - C_e)\frac{M \cdot W_i}{W} \quad (1)$$

where C_0 is the initial concentration of the sample ($mmol \cdot kg^{-1}$), C_e is the equilibrium concentration of the sample ($mmol \cdot kg^{-1}$), W_i is the weight of the solution (g), M is the relative molecular weight of the alkaloids, Q_e is the equilibrium adsorption capacity of the alkaloids on the resin ($mg \cdot g^{-1}$), and W is the weight of the dry resin (g).

After the equilibrium adsorption, the resins were filtered and purged with a small quantity of deionized water (< 10 cm^3). After that, they were statically desorbed with 50 cm^3 of 14.07 $mol \cdot kg^{-1}$ of ethanol aqueous solution for 8 h at 303 ± 1 K. The concentration of the alkaloids in the desorption solution was detected and the desorption ratio was calculated with the following equation as

$$D = \frac{C_d W_d}{(C_0 - C_e)W_i} \quad (2)$$

where C_d is the concentration of the alkaloids in the desorption solution ($mmol \cdot kg^{-1}$); W_d is the weight of the desorption solution (g); D is the desorption ratio (%).

2.4. Adsorption Kinetics. For measuring the adsorption kinetics of alkaloids on the resins, about 0.25 g of the resin adsorbents (HPD100B, HPD300, AB-8, and HPD722) was mixed with a 250 cm^3 alkaloid aqueous solution at an initial concentration of ($8.07 \cdot 10^{-4}$, $2.32 \cdot 10^{-3}$, $5.01 \cdot 10^{-4}$ and $1.21 \cdot 10^{-3}$) $mmol \cdot kg^{-1}$ for berberine hydrochloride, ligustrazine hydrochloride, colchicines, and matrine, respectively, in a 500 cm^3 conical flask with a stopper. The flask was then continuously shaken in the thermostatic oscillator at 303 K until the adsorption equilibrium was reached, and the uncertainty of the temperature was ± 1 K. During the shaking process, 3.0 cm^3 of aqueous solution was withdrawn at a given interval, and the concentration of the alkaloids solution at the contact time t was determined and the adsorption capacity at the contact time t was calculated as

$$Q_t = (C_0 - C_t)\frac{M \cdot W_i}{W} \quad (3)$$

where C_t is the concentration of the alkaloids at the contact time t ($mmol \cdot kg^{-1}$); Q_t is the equilibrium adsorption capacity of the alkaloids at the contact time t ($mg \cdot g^{-1}$).

2.5. Dynamic Adsorption of an Alkaloid Mixture Sample. HPD300 resin was selected as the adsorbent for separation of the four alkaloids from an aqueous solution in this study. An amount of 3.0 cm^3 of wet HPD300 resin was densely packed in a glass column (8 mm × 500 mm), and deionized water was continuously rinsing the column before the dynamic experiment. The alkaloid mixture solution containing berberine hydrochloride, ligustrazine hydrochloride, colchicine, and matrine (their initial concentrations were preset to be $2.69 \cdot 10^{-4}$ $mmol \cdot kg^{-1}$, $5.79 \cdot 10^{-4}$ $mmol \cdot kg^{-1}$, $2.50 \cdot 10^{-4}$ $mmol \cdot kg^{-1}$ and $4.03 \cdot 10^{-4}$ $mmol \cdot kg^{-1}$, respectively) was passed through the resin column at a flow rate of 0.0025 $cm^3 \cdot s^{-1}$. The effluents from the resin column were collected, and the concentrations of all four alkaloids, C, were monitored by a HPLC until the effluent concentrations approached the feed concentrations.

3. RESULTS AND DISCUSSION

3.1. Adsorption Capacity and Desorption Ratio. The adsorption capacity and desorption ratio of four alkaloid compounds on nine macroporous resins at 303 K are summarized in Figure 3. The initial feed concentrations of berberine hydrochloride, ligustrazine hydrochloride, colchicine and matrine are ($8.07 \cdot 10^{-4}$, $2.32 \cdot 10^{-3}$, $5.01 \cdot 10^{-4}$, and $1.21 \cdot 10^{-3}$) $mmol \cdot kg^{-1}$, respectively. As shown in Figure 3, the resins tested in this work exhibited significantly different

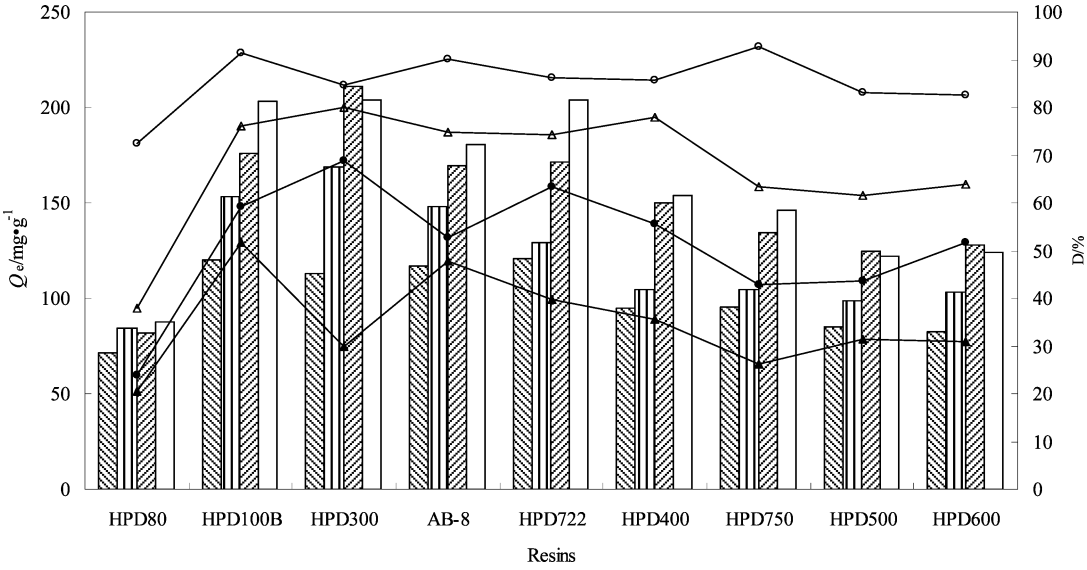

Figure 3. Adsorption capacities and desorption ratios of alkaloids on nine resins at 30 °C (with the initial concentrations of berberine hydrochloride, ligustrazine hydrochloride, colchicine, and matrine of $8.07 \cdot 10^{-4}$ mmol·kg^{-1}, $2.32 \cdot 10^{-3}$ mmol·kg^{-1}, $5.01 \cdot 10^{-4}$ mmol·kg^{-1}, and $1.21 \cdot 10^{-3}$ mmol·kg^{-1}, respectively): left to right stripes, adsorption capacity of berberine hydrochloride; vertical stripes, adsorption capacity of ligustrazine hydrochloride; right to left stripes, adsorption capacity of colchicine; white bars, adsorption capacity of matrine; ▲, desorption ratio of berberine hydrochloride; ●, desorption ratio of ligustrazine hydrochloride; ○, desorption ratio of colchicine; △, desorption ratio of matrine.

equilibrium adsorption capacities and desorption ratios for the four alkaloid compounds. Overall, the adsorption on the polar resins was much weaker than that on the nonpolar or weak-polar resins, which in turn implies that the four alkaloid compounds are weakly polar compounds according to the polarity matching principle, and nonpolar (HPD100B and HPD300) or weakly polar (AB-8 and HPD722) resins are suitable for the adsorptive separation and purification of the four alkaloid compounds.

With increasing surface polarity of the resin, the equilibrium adsorption capacities of ligustrazine hydrochloride and colchicine decreased, and the adsorption on the nonpolar resins (HPD100B and HPD300) was shown to be relatively superior. In addition, it is observed that the equilibrium adsorption capacities increased with increasing Brunauer–Emmett–Teller (BET) surface area of the resins. The HPD300 resin has the largest adsorption capacity among all the resins, which implies that the BET surface area is the predominant factor influencing the adsorption of ligustrazine hydrochloride and colchicine from an aqueous solution.

On the other hand, the weakly polar resins (AB-8 and HPD722) were proven to be more effective for the adsorption of berberine hydrochloride and matrine from aqueous solutions. Although the BET surface area of AB-8 and HPD722 was a little smaller than that of HPD100B and much smaller than that of HPD300, the equilibrium adsorption capacities of berberine hydrochloride and matrine on AB-8 were quite comparable to those of HPD722 and HPD300, and HPD722 had larger adsorption capacities than those of HPD100B and HPD300, which suggested that a polarity match between the functional groups on the surface of the resin adsorbents and the polar groups of adsorbate molecules (methyoxy, carbonyl, amino groups) is also a significant factor for achieving an effective adsorption. In addition, although HPD300 has the highest BET surface area among the three nonpolar resins (HPD80, HPD100B, and HPD300), HPD100B exhibited the largest adsorption capacity toward berberine hydrochloride and matrine, which might result from the different pore size of the resins. As shown in Figure 1, the molecule size of berberine hydrochloride and matrine was obviously larger than that of ligustrazine hydrochloride and colchicine, while the average pore diameter of HPD300 was the smallest (5 nm to 5.5 nm). The relatively smaller pore size of HPD300 might result in a more difficult diffusion of berberine hydrochloride and matrine in the pores of the resins, inducing a relatively smaller capacity. In conclusion, the resins with a relatively low polarity and a high BET surface area offered the largest adsorption capacities for the four alkaloids, while other physical properties, especially the average pore size of the resin adsorbents should also be considered during the selection of proper resins.

When 14.07 mol·kg^{-1} of ethanol aqueous solution was applied as the desorption solvent, the desorption ratios of the four compounds from the resins were quite different. In general, the desorption ratio of colchicine was the highest compared to those of the other three alkaloids for all resins, followed by matrine, and the desorption ratio of berberine hydrochloride was the lowest, which might be due to the different structures of the four alkaloid compounds and the surface chemistry of the resin absorbents. A weak affinity between the resins and the adsorbate molecule could result in a high desorption ratio. The van der Waals' force (hydrophobic interaction) is the main mechanism for the adsorption of nonpolar or weakly polar adsorbate on the nonpolar or weakly polar adsorbent. Hence, the desorption ratio of colchicine is the highest among the four compounds. Furthermore, because both berberine hydrochloride and ligustrazine hydrochloride were alkaloid salts, the present experimental results also implied a strong affinity of resins toward the alkaloid salts. Of course, the much smaller solubility of the alkaloids salts in the desorption solvent than in water induces their lower desorption ratios.[3]

3.2. Adsorption Kinetics on the Resins. By considering both adsorption capacity and desorption ratio for all four alkaloid compounds, HPD100B, HPD300, AB-8, and HPD722

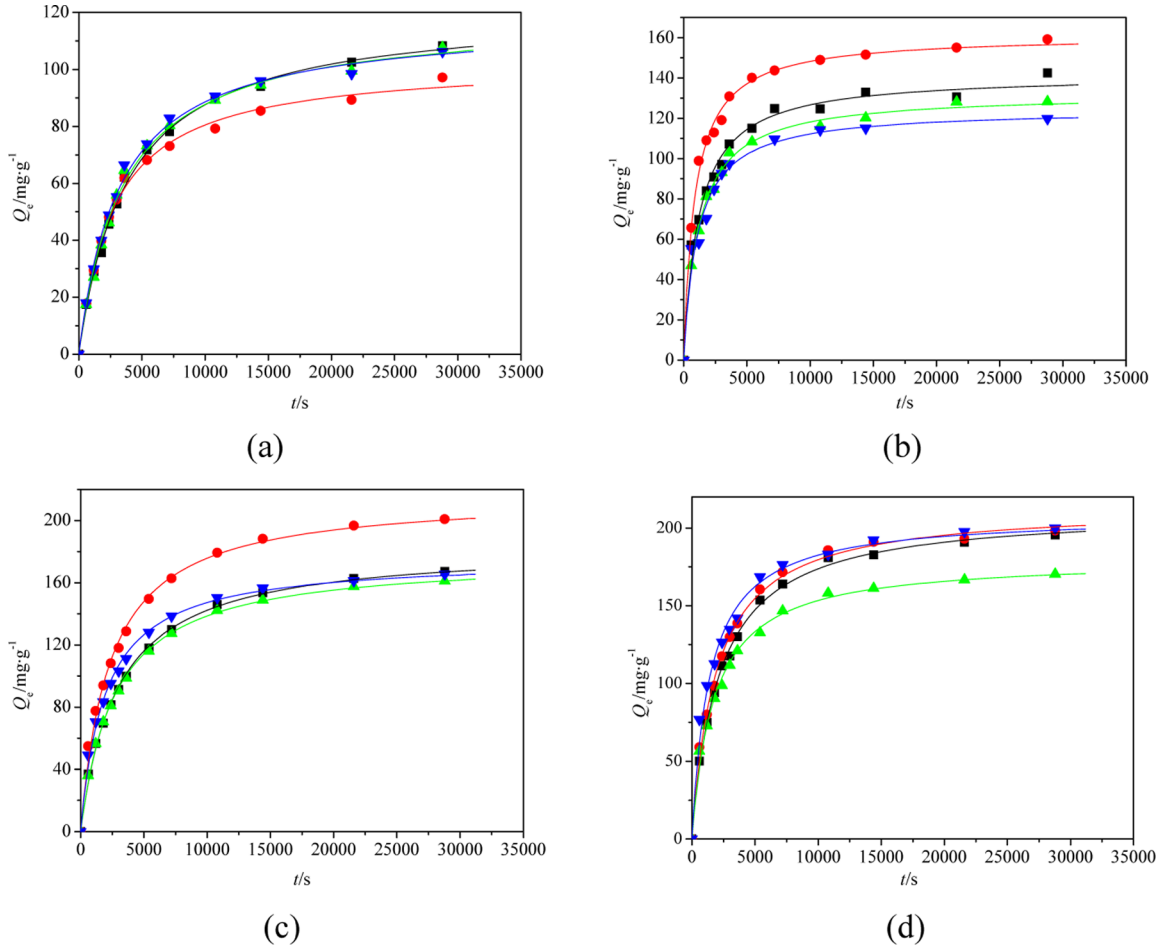

Figure 4. Adsorption kinetic curves for berberine hydrochloride (a), ligustrazine hydrochloride (b), colchicine (c), and matrine (d) on different resins at 30 °C: ■, HPD100B; ●, HPD300; ▲, AB-8; ▼, HPD722; −, pseudo-second-order.

were chosen for further kinetic and isotherm experiments. The adsorption uptake curves of berberine hydrochloride, ligustrazine hydrochloride, colchicine, and matrine on four different resins (HPD100B, HPD300, AB-8, and HPD722) were displayed in Figure 4. The adsorption rate is shown to be fast in the first 60 min (3600 s) (up to 60 % uptake), and then becomes slower, and the adsorption equilibrium was obtained within 360 min (21600 s). The kinetic results imply that these resins display an excellent kinetic property, which can be attributed to their open pore structures. In addition, it is observed that the HPD300 resin requires a much longer time to reach the adsorption equilibrium than other resins for a given alkaloid due to its smaller average pore diameter, confirming that the pore structure of the resin also plays an important role in the adsorption in addition to the BET surface area. As compared to the required time to equilibrium for a specific alkaloid on these resins, the equilibrium was established after about 120 min (7200 s) for ligustrazine hydrochloride and about 180 min (10800 s) was needed for colchicines and matrine, whereas the equilibrium can be reached after around 360 min (21600 s) for berberine hydrochloride, which is indicative of their different molecular size.

The adsorption kinetic data can be analyzed using different kinetic models. One of most widely used kinetic models is the pseudo-second-order equation in the following format:[40,41]

$$\frac{t}{q_t} = \frac{1}{k_{p2}q_e^{\,2}} + \frac{1}{q_e}t \tag{4}$$

where k_{p2} is the pseudo-second-order rate constant (g·mg^{-1}·s^{-1}), q_t (mg·g^{-1}) and q_e (mg·g^{-1}) are the adsorption amount at time t and equilibrium, respectively.[40,41]

The parameters, k_{p2} and q_e and the correlative coefficient R^2 from eq 4 are listed in Table 2. The values of q_e for all four alkaloids are close to the experimental equilibrium capacity values (Q_e), and the correlative coefficients for all four model compounds on all resins are greater than 0.99, suggesting that the pseudo-second-order rate equation fitted the experimental adsorption uptake data very well. In the pseudo-second-order equation, the initial adsorption rate, v_0, can be calculated as

$$v_0 = k_{p2}q_e^{\,2} \tag{5}$$

As shown in Table 2, the initial adsorption rates were quite different for different resins, It was observed that the low-polar resins showed higher initial adsorption rates for all four alkaloids studied in this work while the strong-polar resins exhibited the lowest initial adsorption rates, which was similar to the trend for adsorption capacities of different resins discussed above. The HPD300 resin showed the highest initial adsorption rate for ligustrazine hydrochloride, colchicine, and matrine, which might be due to its large average surface area and a similar polarity with these alkaloids. However, for berberine hydrochloride, the HPD100B and AB-8 resins

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Table 2. Q_e and Parameters in Pseudo-Second-Order Rate Equation for Berberine Hydrochloride, Ligustrazine Hydrochloride, Colchicine, And Matrine[a]

resins	Q_e / mg·g^{-1}	q_e / mg·g^{-1}	$k_{P2}\cdot10^{-2}$ / g·mg^{-1}·s^{-1}	v_0 / mg·g^{-1}·s^{-1}
		Berberine Hydrochloride		
HPD100B	120.0	123.5 ± 1.61	0.714 ± 0.004	108.7
HPD300	113.1	114.9 ± 1.59	0.762 ± 0.006	100.6
AB-8	117.2	119.0 ± 2.00	0.834 ± 0.005	118.1
HPD722	120.7	123.5 ± 1.84	0.738 ± 0.006	112.9
		Ligustrazine Hydrochloride		
HPD100B	153.4	153.8 ± 2.63	1.188 ± 0.240	281.2
HPD300	168.7	169.5 ± 1.69	1.662 ± 0.180	484.1
AB-8	148.1	144.9 ± 1.57	1.110 ± 0.060	233.6
HPD722	129.5	128.2 ± 3.46	2.016 ± 0.360	331.0
		Colchicine		
HPD100B	175.7	181.8 ± 1.88	0.732 ± 0.004	242.2
HPD300	210.8	212.8 ± 2.87	0.774 ± 0.004	350.9
AB-8	169.7	175.4 ± 1.51	0.798 ± 0.004	245.3
HPD722	171.4	175.4 ± 2.18	1.110 ± 0.060	341.7
		Matrine		
HPD100B	203.5	208.3 ± 2.08	0.864 ± 0.004	375.0
HPD300	204.2	204.1 ± 2.61	1.122 ± 0.005	468.4
AB-8	180.2	181.8 ± 2.68	1.098 ± 0.060	363.8
HPD722	204.1	208.3 ± 3.81	1.284 ± 0.120	556.6

[a] Q_e, experimental equilibrium adsorption capacity; q_e, calculated equilibrium adsorption capacity; k_{P2}, pseudo-second-order rate constant; v_0, initial adsorption rate. The standard uncertainty $u(T)$ is $u(T)$ = 1 K, the combined standard uncertainty $u_c(Q_e)$ is $u_c(Q_e)$ = 2.0 mg·g^{-1}, and the standard deviations of q_e and k_{P2} are given in the table.

exhibited even higher initial adsorption rates than those of HPD300 resin, which might be resulted from their larger average pore diameters.

3.3. Adsorption Isotherms. As illustrated in Figure 5, the adsorption capacities for all four alkaloids on four different resins increased with the equilibrium concentration and level off when the equilibrium concentrations of berberine hydrochloride, ligustrazine hydrochloride, colchicine, and matrine reached ($1.08\cdot10^{-3}$, $1.74\cdot10^{-3}$, $5.01\cdot10^{-4}$, and $1.21\cdot10^{-3}$) mmol·kg^{-1}, respectively. The equilibrium adsorption capacity of matrine was 120 mg·g^{-1}, 150 mg·g^{-1}, 105 mg·g^{-1}, and 90 mg·g^{-1} on HPD100B, HPD300, HPD722, and AB-8, respectively, at the equilibrium concentration of 0.060 mg·cm^{-3} ($1.61\cdot10^{-4}$ mmol·kg^{-1}, $3.47\cdot10^{-4}$ mmol·kg^{-1}, $1.50\cdot10^{-4}$ mmol·kg^{-1}, and $2.42\cdot10^{-4}$ mmol·kg^{-1} respectively), which was larger than DF01 resin whose adsorption capacity for matrine was about 25 mg·g^{-1} at the same equilibrium concentration at 25 °C,[42] while the adsorption of berberine hydrochloride on the four resins was seen to be weaker than that on some commercial minerals such as bentonites and zeolites.[43,44]

Langmuir and Freundlich equations were used to fit the adsorption isotherms and to describe the adsorption behavior of the alkaloids on resins:

The linear form of Langmuir isotherms equation is given by

$$\frac{1}{Q_e} = \frac{1}{K_L\cdot C_e} + \frac{1}{Q_{max}} \quad (6)$$

and the linear form of Freundlich isotherms equation is

$$\log Q_e = \log K_F + \left(\frac{1}{n}\right)\log C_e \quad (7)$$

where Q_{max} (mg·g^{-1}) is the monlayer adsorption capacity; K_L (cm^3·g^{-1}) is the Langmuir constant, and K_F is the Freundlich constant. K_F (mg$^{1-1/n}$·cm$^{3\cdot1/n}$·g^{-1}) is an indicator of the equilibrium adsorption capacity, and n is an empirical constant related to the surface energy heterogeneity of the adsorbent.

The Langmuir and Freundlich parameters that were determined from the linear regression of the adsorption isotherms are summarized in Table 3 and Table 4, respectively. A comparison of the fitting results of a specific alkaloid on the resins shows that more dependable correlation coefficients are exhibited for berberine hydrochloride and ligustrazine hydrochloride by the Freundlich equation, while both the Langmuir and Freundlich equations fit well the adsorption of colchicine and matrine.

The n value for the Freundlich equation was a measure of the deviation from an infinite perfect plane homogeneous surface in contact with a well-mixed solution. Reductions in the $1/n$ value from 1 indicated greater spatial constraints on adsorption. This was a reflection of particle surface 3D morphology and the ability of the adsorbing molecule to access this surface.[45] Generally, the adsorption easily occurred when the $1/n$ value was between 0.1 and 0.5; it tended not to happen when the $1/n$ value was between 0.5 and 1.0, and it was almost unable to occur when the $1/n$ value exceeded 1.[46] Table 4 indicated that the values of $1/n$ for colchicine and ligustrazine hydrochloride on all the resins were between 0.1 and 0.5, which indicated that the adsorption of colchicine and ligustrazine hydrochloride on all the resins could take place easily. However, the adsorption of berberine hydrochloride could take place easily on HPD300, AB-8, HPD722, but not on HPD100B, and the adsorption of matrine tended not to happen on all the resins selected. Thus, the present experimental results might indicate that the surfaces of these resins are not ideal surfaces for the adsorption of berberine hydrochloride and matrine solutions.

3.4. Dynamic Adsorption Breakthrough Curves on HPD300 Resin. The HPD300 resin had lower values of $1/n$ for berberine hydrochloride, ligustrazine hydrochloride, and colchicine, and displayed better adsorption and desorption properties for all four alkaloid compounds. More important, the order of $1/n$ values of the four alkaloids on HPD300 have an order of: colchicine < ligustrazine hydrochloride < berberine hydrochloride < matrine, implying that the adsorption affinity of HPD300 toward matrine was the lowest while the adsorption affinity with colchicine was the highest among the four alkaloids, and HPD300 should show an excellent separation property between these four alkaloids. Therefore, the HPD300 resin was selected for a dynamic adsorption breakthrough (or leakage) test of separation of colchicine, ligustrazine hydrochloride, berberine hydrochloride, and matrine from their mixture solution.

Figure 6 indicated that the HPD300 resin can separate these four alkaloids successfully. Matrine leaked out directly from the effluent after HPD300 made contact with the mixture solution, followed by berberine hydrochloride with the effluent volume, V, of 120 cm^3 ($C\cdot C_0^{-1}$ = 0.05), and then ligustrazine hydrochloride leaked out at the effluent volume of 300 cm^3; the breakthrough point of colchicine was up to 750 cm^3, and it leaked out at the last. In addition, it is interesting to see that the concentrations of ligustrazine hydrochloride, berberine hydrochloride, and matrine from the effluent solution increased as

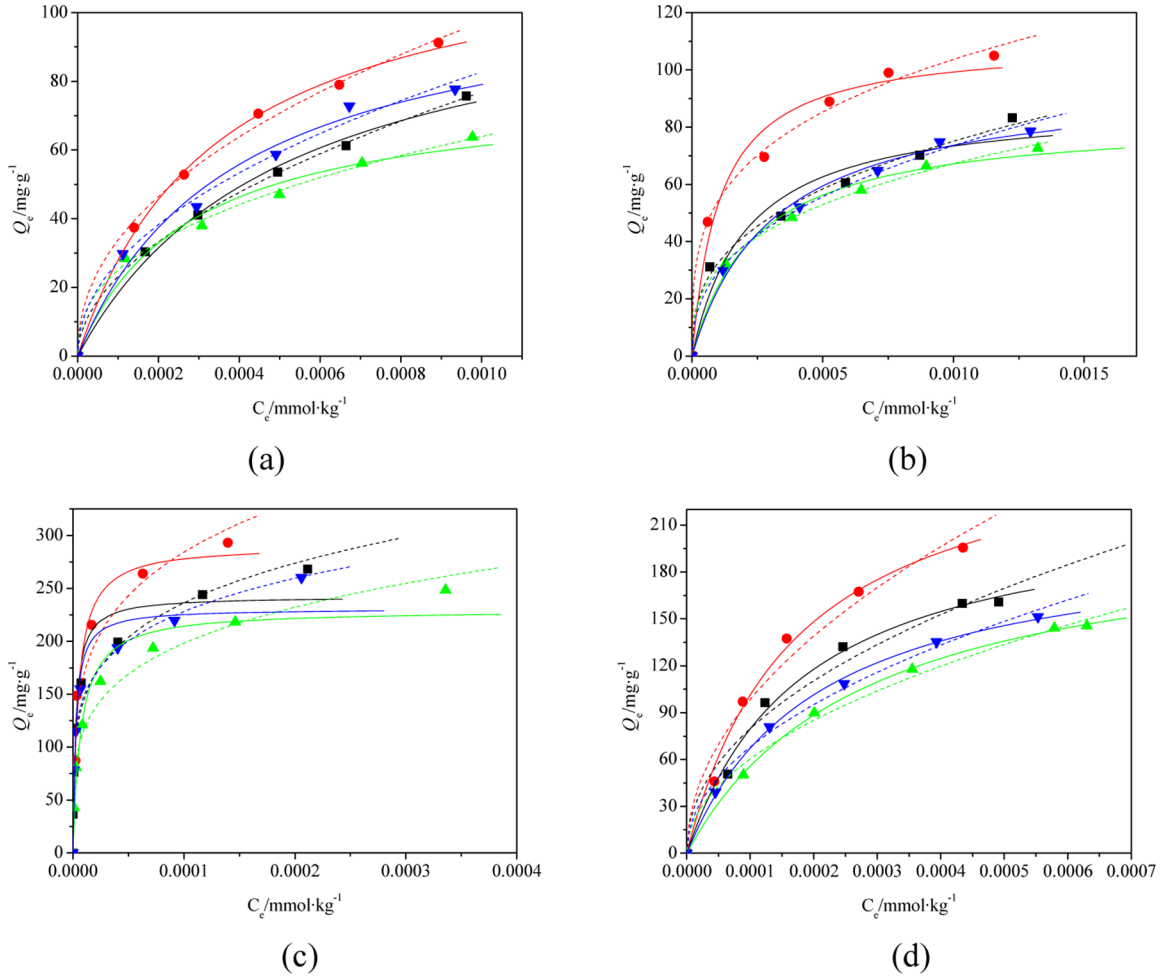

Figure 5. Adsorption isotherms for berberine hydrochloride (a), ligustrazine hydrochloride (b), colchicine (c), and matrine (d) on different resins at 30 °C: ■, HPD100B; ●, HPD300; ▲, AB-8; ▼, HPD722; —, Langmuire; ---, Freundlich.

the volume increased and reached the maximum values, then decreased to the same concentrations as the initial solution except for colchicine, and the peak concentrations were much higher than the initial concentrations. Similar results were also documented in earlier literature.[47,48] The possible explanation was the competitive adsorption between these four alkaloids in the mixture solution. All the alkaloids were adsorbed at the initial stage, but the ever adsorbed matrine was released from the active sites because of the higher affinity of HPD300 toward the other alkaloids over matrine. The desorption behavior resulted in a peak concentration of matrine in the effluent solution which was even higher than the initial concentration, and the displacement phenomenon promoted desorption of the unfavorable component. A similar displacement phenomenon happened to berberine hydrochloride and ligustrazine hydrochloride.

In the equilibrium experiment, it was observed that adsorption of matrine on the HPD300 resin is quite effective, and the equilibrium adsorption capacity of matrine is shown to be higher than those of berberine hydrochloride and ligustrazine hydrochloride. It is surprising to observe that matrine leaked out directly from the effluent mixture, which may occur because, on one hand, the $1/n$ value of matrine was much higher than the other three alkaloids, but, on the other hand, the matrine molecule should have a three-dimensional structure, which makes it hard to diffuse in the pores and easy to be displaced during the competitive adsorption process. In conclusion, HPD300 had an excellent potential for separating different kinds of alkaloids. It is necessary to consider the competitive adsorption of coexisting alkaloids on macroporous resins for the effective operation of adsorption processes for the separation and purification of different kinds of alkaloids from plant materials.

4. CONCLUSIONS

In this study, the adsorption and desorption properties of berberine hydrochloride, ligustrazine hydrochloride, colchicine, and matrine on nine different macroporous resins were investigated in batch adsorption/desorption equilibrium and kinetic experiments as well as the adsorption breakthrough column dynamic experiment of an alkaloid mixture on HPD300 resin. The pseudo-second-order adsorption rate equation correlates well the adsorption uptake curves of four alkaloids on four resins, and the initial adsorption rates from the pseudo-second-order rate equation were compared and discussed. Both Langmuir and Freundlich equations fit well the adsorption equilibrium data of four alkaloids on four resins at 303 K. On the basis of the adsorption equilibrium and kinetic results, the HPD300 resin was identified as the most promising adsorbent for alkaloids separation and purification because of its excellent adsorption and desorption properties for all four alkaloid compounds. The adsorption breakthrough experiment on the

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Table 3. Parameters in the Langmuir Isotherm Equation Together with R^2 for Berberine Hydrochloride, Ligustrazine Hydrochloride, Colchicine, and Matrine[a]

resins	Q_{max}/mg·g^{-1}	K_L/cm^3·g^{-1}	R^2
	Berberine Hydrochloride		
HPD100B	97.1 ± 8.67	689.7 ± 53.26	0.988
HPD300	117.8 ± 4.41	1041.7 ± 52.89	0.996
AB-8	65.5 ± 7.76	1087.0 ± 152.02	0.931
HPD722	89.8 ± 11.46	1030.9 ± 119.20	0.953
	Ligustrazine Hydrochloride		
HPD100B	74.0 ± 10.61	4347.8 ± 857.41	0.930
HPD300	101.4 ± 6.83	8333.3 ± 1475.68	0.944
AB-8	76.9 ± 4.23	2439.0 ± 269.98	0.979
HPD722	88.8 ± 4.92	2127.7 ± 207.39	0.990
	Colchicine		
HPD100B	177.6 ± 13.35	454752.2 ± 58965.18	0.959
HPD300	304.9 ± 12.69	138983.5 ± 25474.08	0.921
AB-8	177.6 ± 10.69	140524.4 ± 16283.10	0.972
HPD722	192.3 ± 16.46	384438.9 ± 62015.02	0.962
	Matrine		
HPD100B	225.5 ± 13.14	4954.0 ± 483.11	0.994
HPD300	274.9 ± 15.56	6466.0 ± 552.25	0.995
AB-8	216.5 ± 3.56	2941.2 ± 78.33	0.999
HPD722	193.1 ± 6.40	4347.8 ± 200.34	0.999

[a] Q_{max}, monlayer adsorption capacity; K_L, Langmuir constant. The standard uncertainty $u(T)$ is $u(T)$ = 1 K, and the standard deviations of Q_{max} and K_L are given in the table.

Table 4. Parameters in the Freundlich Isotherm Equation Together with R^2 for Berberine Hydrochloride, Ligustrazine Hydrochloride, Colchicine, And Matrine[a]

resins	K_F/mg$^{1-1/n}$·cm$^{3\cdot1/n}$·g^{-1}	$1/n$	R^2
	Berberine Hydrochloride		
HPD100B	128.0 ± 1.61	0.5179 ± 0.00802	0.999
HPD300	158.7 ± 6.38	0.4801 ± 0.02498	0.992
AB-8	92.5 ± 3.47	0.3870 ± 0.02245	0.997
HPD722	133.8 ± 8.62	0.4802 ± 0.04058	0.992
	Ligustrazine Hydrochloride		
HPD100B	132.8 ± 7.86	0.3340 ± 0.02533	0.988
HPD300	171.3 ± 8.26	0.2849 ± 0.02030	0.991
AB-8	125.8 ± 3.92	0.3547 ± 0.01486	0.997
HPD722	155.1 ± 8.66	0.4209 ± 0.02835	0.993
	Colchicine		
HPD100B	597.0 ± 41.81	0.2668 ± 0.02167	0.974
HPD300	689.4 ± 95.22	0.2632 ± 0.03860	0.962
AB-8	513.8 ± 35.24	0.2853 ± 0.02347	0.974
HPD722	445.1 ± 25.55	0.2022 ± 0.01469	0.989
	Matrine		
HPD100B	552.9 ± 75.45	0.5459 ± 0.06534	0.979
HPD300	871.5 ± 118.76	0.6135 ± 0.06810	0.975
AB-8	415.6 ± 33.32	0.5385 ± 0.03947	0.993
HPD722	472.4 ± 35.91	0.5402 ± 0.03492	0.994

[a] K_F, Freundlich constant; $1/n$, empirical constant. The standard uncertainty $u(T)$ is $u(T)$ = 1 K, and the standard deviations of K_F and $1/n$ are given in the table.

HPD300 resin using a mixture solution further confirmed that it is possible to achieve an effective separation of the four alkaloids on the HPD300 resin. These experimental results obtained in this study could be applied to the separation and purification of different kinds of alkaloids in plant materials.

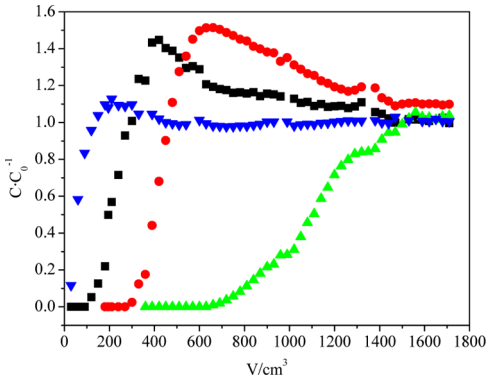

Figure 6. Dynamic adsorption breakthrough curves for an alkaloid mixture solution on HPD300 resin: ■, berberine hydrochloride; ●, ligustrazine hydrochloride; ▲, colchicine; ▼, matrine.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Tables S1 to S3 as described in the text. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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