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PHYSICAL CHEMISTRY OF NANOCLUSTERS AND NANOMATERIALS

Sorption of Amphenicols on Magnetic Hypercrosslinked Polystyrene

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Abstract—A study is performed of the sorption of chloramphenicol, florfenicol, and thiamphenicol on magnetic hypercrosslinked polystyrene (HCPS/Fe_3O_4). Magnetic HCPS is obtained via the sorption of Fe_3O_4 nanoparticles on commercially available HCPS Diapak P-3. The specific surface areas and parameters of the porous structure of the magnetic HCPS are determined by means of low-temperature nitrogen adsorption. It is found that introducing Fe_3O_4 nanoparticles into the HCPS matrix slightly lowers the specific surface area of the sorbent (from 1132 to 1080 m^2/d) and the volume of pores, but these characteristics are strong enough to use the resulting composite as a sorbent. It is established that the HCPS-based magnetic sorbent exhibits superparamagnetic properties. The saturation magnetization is 1.7 emu/g, enough to extract the sorbent from the solution under the action of the magnetic field of a permanent magnet. It is shown that magnetic HCPS can be used for the group sorption concentration of amphenicols via magnetic solid-phase extraction.

Keywords: chloramphenicol, florfenicol, thiamphenicol, magnetic hypercrosslinked polystyrene, sorption

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INTRODUCTION

Amphenicols (chloramphenicol, florfenicol and thiamphenicol) are effective bacteriostatic antibiotics that find application in practical and veterinary medicine due to their wide range of pharmacological actions and low cost. There is considerable interest in studying the sorption of amphenicols, due to the need to assess the presence of these antibiotics in environmental objects [1, 2], the search for more effective means of sorption for purifying water of the residues of these drugs [3], and developing ways of isolating and concentrating them when determining the amounts of amphenicols in food [4].

A variety of carbon sorbents are mainly used to remove chloramphenicol from water. These include activated carbons [5–7], biochars [8, 9], mesoporous carbon materials [10], and magnetic mesoporous carbon [11]. Samples of food products are pretreated via solid-phase extraction (SPE) using hydrophobized silica gel modified with C18 groups [12, 13]; a polymeric sorbent based on polydivinylbenzene and N-vinylpyrrolidone Oasis HLB [14, 15]; its analog, the sorbent Strata-X [16]; carbon nanotubes [17]; and molecularly imprinted sorbents [18–20], the main advantage of which is high selectivity with respect to target compounds. Magnetic molecularly imprinted sorbents based on silica gel also have enhanced selectivity and effectiveness with respect to amphenicols [21–24]. They are used in magnetic SPE, but the synthesis of such materials is complex and multistage.

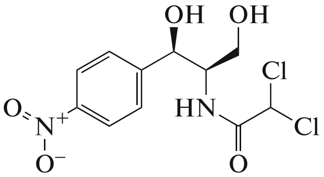
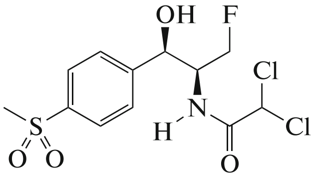
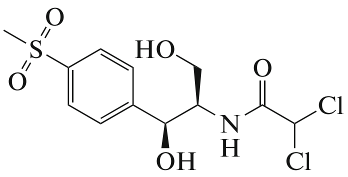
Of the polymeric sorbents that find application in the preparation of magnetic sorbents, highly crosslinked polystyrenes (HCPS) are of great interest. There are several ways of obtaining magnetic HCPS based on polymerization with Fe_3O_4 nanoparticles [25–27], the chemical deposition of magnetite in pores of HCPS [28, 29], and the sorption of preliminarily synthesized Fe_3O_4 nanoparticles on HCPS [30, 31]. Magnetic HCPS are used in the sorption isolation of such polar biologically active compounds as amphetamines [25], triazines, diethyl phthalate [26], nitrofurazone [27], tetracyclines [27, 30], and sulfonamides [31].

The aim of this work was to study the sorption of chloramphenicol, florfenicol, and thiamphenicol on magnetic HCPS and assess the possibility of using this sorbent for the group preconcentration of these compounds. So far, magnetic HCPS have not been used for this purpose.

EXPERIMENTAL

Samples of Diapak P-3 HCPS (Diapak P-3 cartridges, ZAO BioKhimMak ST) were used as the initial material for obtaining a magnetic sorbent. $FeCl_3 \cdot 6H_2O$ (analytically pure), Mohr's salt $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$ (analytically pure), and NH_3

Table 1. Physicochemical parameters of the studied amphenicols

Parameter	Chloramphenicol	Florfenicol	Thiamphenicol
			
$\log K_{ow}^*$	1.14	0.8	–0.3
pK_a^*	11.03	10.73	11.05
S_{mol}, nm^{2*}	0.75	0.60	0.82

Values pK_a marked with an asterisk were taken from [2]; values $\log K_{ow}$ for the neutral form were taken from [28]; and values S_{mol} (the maximum cross-section area of the optimum conformation of the molecule) were calculated using the ACD Labs 6.00 software package (Advanced Chemistry Development Inc., Canada).

(high purity) were used for the synthesis of Fe_3O_4. Magnetic hypercrosslinked polystyrene (HCPS/Fe_3O_4) was obtained in two stages, according to the procedure we developed in [30]. Nanosized particles of magnetite Fe_3O_4 were first obtained and then adsorbed on hypercrosslinked polystyrene. The magnetic HCPS was activated with methanol prior to use. The specific surface areas and characteristics of the porous structure of the samples were determined via low-temperature nitrogen adsorption on an ASAP 2010 N automatic sorbtometer (Micromeritics, United States). The magnetization curves of the samples were measured using a setup developed on the basis of a vibrating magnetometer to study the topochemical transformations of ferromagnet nanoparticles. Measurements were made at room temperature and a frequency of 73 Hz, in the range of up to 6.5 kOe. The setup was described in [32].

The objects of our sorption study were chloramphenicol (Acros Organics, 98%), florfenicol (Glentham, >99%), and thiamphenicol (Acros Organics, 98%). The structures and some physical and chemical properties of the studied substances are given in Table 1. Stock solutions of amphenicols (1×10^{-2} M) were prepared by dissolving their exact weights in ethanol and stored at 4°C. Working solutions of the compounds were prepared by diluting stock solutions with deionized water immediately before use.

The pH values of the solutions were monitored on an Expert 001 pH ionomer (Ekoniks-Expert, Russia). The magnetic sorbent was separated from the solution using an Nd-Fe-B magnet (20 × 20 × 20 mm). The absorption spectra and optical densities of solutions were recorded on an SF-104 spectrophotometer (Aquilon, Russia). Distilled water was additionally purified using a water purification system (Millipore, Germany).

A weighed portion of the magnetic sorbent (0.020 ± 0.001 g) was placed in a test tube with a screw cap to study sorption. The sorbent was activated with methanol and held for 5 min. Then 25 mL of the test substance solution was added and shaken on an electromechanical vibratory mixer until sorption equilibrium was established. Finally, the sorbent was separated from the solution magnetically, and the concentration of amphenicols in the equilibrium aqueous phase was determined spectrophotometrically according to their absorption in the UV region.

RESULTS AND DISCUSSION

Preparation and Study of HCPS/Fe_3O_4 Magnetic Sorbent

Magnetic hyper-crosslinked polystyrene (HCPS/Fe_3O_4) was obtained via the absorption of preliminarily synthesized magnetite nanoparticles on HCPS. Nanosized Fe_3O_4 particles were obtained through chemical precipitation according to Massart [33]. A mixture of $FeCl_3{\cdot}6H_2O$ (1 mL 1 M solution in 2 M HCl) and $FeSO_4{\cdot}(NH_4)_2SO_4{\cdot}6H_2O$ (1 mL 0.5 M solution) solutions in deionized water was added gradually to an aqueous solution of ammonia (40 mL, 0.5 M), after which the resulting suspension was stirred for 30 min at room temperature. The concentration of Fe_3O_4 was 2.9 mg/mL. Transmission electron microscopy data showed the diameter of magnetite nanoparticles synthesized in this way was 10–20 nm. The surface area of a dry sample of the synthesized NPs was 70 m^2/g. Magnetic measurements showed that the synthesized Fe_3O_4 nanoparticles were superparamagnetic. There is no hysteresis loop on the magnetization curve of the samples, which is typical of magnetic particles in the nanosize state (<25 nm). The saturation magnetization of Fe_3O_4 nanoparticles falls to 72, 58, and 41.7 emu/g 7, 30, and 60 days later, respectively, when they are stored in air, apparently due to their oxidation.

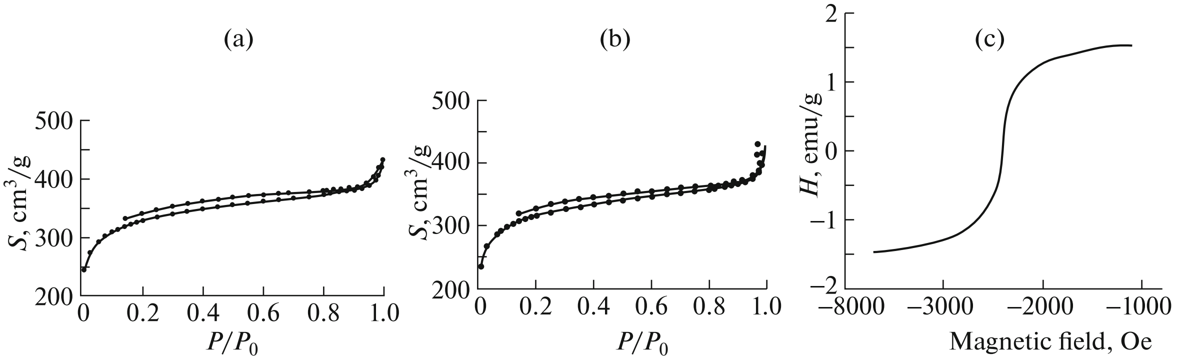


Fig. 1. Nitrogen sorption–desorption isotherms on (a) HCPS, (b) magnetic HCPS, and (c) magnetization curve of magnetic HCPS. P/P_0 is the relative pressure, S is adsorption, and H is magnetization.

Sorption was conducted from water, acetonitrile, acetone, isopropanol, and methanol in order to select a solvent that allows maximum recovery of Fe_3O_4 into the HCPS matrix. We used 0.4 mL of a suspension of freshly deposited Fe_3O_4 nanoparticles, dispersed in 5 mL of the chosen solvent and shaken for 40 min with 20 mg of HCPS. The content of Fe_3O_4 in the sorbent matrix was monitored via diffuse reflectance spectroscopy. It was found that HCPS quantitatively absorbed 96–97% of the particles of Fe_3O_4 from methanol on, while the rates of recovery from isopropanol, water, acetone, and acetonitrile were 83, 61, 14, and 12%, respectively. The sorption capacity of HCPS with respect to magnetite nanoparticles sorbed from methanol was 135 mg/g.

Isotherms of nitrogen sorption–desorption on HCPS and HCPS/Fe_3O_4 at 77 K were compared (Figs. 1a, 1b). The specific surface areas of the sorbents, the areas of micro- and mesopores, the volumes of micro- and mesopores, and the average pore diameter were calculated. The resulting values are given in Table 2. We can see the specific surface of the sorbent and the pore volume fell slightly when nanoparticles of Fe_3O_4 were introduced into the HCPS matrix. However, these volumes are high enough to use the resulting composite as a sorbent. The composition of the magnetic HCPS included macro-, meso-, and micropores, the proportions of which were 5, 43, and 52%, respectively.

Table 2. Structural characteristics of hypercrosslinked polystyrene Diapak P-3 and magnetic hypercrosslinked polystyrene (HCPS/Fe_3O_4)

Sorbent	S_{BET}	S_{mic}	S_{mes}	V_t	V_{mic}	V_{mes}	D_h
HCPS	1132	707	219	0.6	0.32	0.25	2.11
HCPS/Fe_3O_4	1080	685	202	0.58	0.30	0.25	2.14

S_{BET} is the specific surface, m^2/g; S_{mic} is the micropore area, m^2/g; S_{mes} is the mesopore area, m^2/g; V_t is the pore volume, cm^3/g; V_{mic} is the micropore volume, cm^3/g; V_{mes} is the mesopore volume, cm^3/g; and D_h is the average pore diameter, nm.

There was no magnetic hysteresis loop on the magnetization curve of magnetic HCPS (Fig. 1c), indicating that the sorbent exhibited superparamagnetic properties. The saturation magnetization was 1.69 emu/g and the residual magnetization was 0.05 emu/g. The drop in the specific magnetization of magnetic HCPS relative to Fe_3O_4 was a natural consequence of diamagnetic HCPS being in the composition of the sorbent. The low residual magnetization allows us to use this sorbent in magnetic SPE. The sorbent exhibits magnetic properties only when an external magnetic field is applied. Without one, it can be uniformly dispersed in a solution.

Sorption of Amphenicols

The sorption of chloramphenicol, florfenicol, and thiamphenicol, depending on the period of contact between the phases, the pH of the solution, and the concentration of the extracted compounds, was studied on magnetic HCPS, and their sorption behaviors were compared. It was established that the time needed to reach sorption equilibrium was no more than 10 min for all of the studied amphenicols (Fig. 2a). The pK_a values of the amphenicols (Table 1) indicate they were present in the solutions in uncharged form when pH <9, and deprotonation of the amide group began when pH >9. The sorption of these compounds therefore depends weakly on pH (Fig. 2b). The maximum sorption of chloramphenicol is observed at pH 4.5–5.5, while that of florfenicol and thiamphenicol is observed at pH 4.5–9. The slight drop in sorption in acidic and alkaline media was possibly due to the formation of a positive charge on the surface of the magnetic HCPS in an acidic environment and a negative charge in an alkaline one [34]. In subsequent experiments, sorption was conducted using neutral solutions of amphenicols (pH ~5). Sorp-

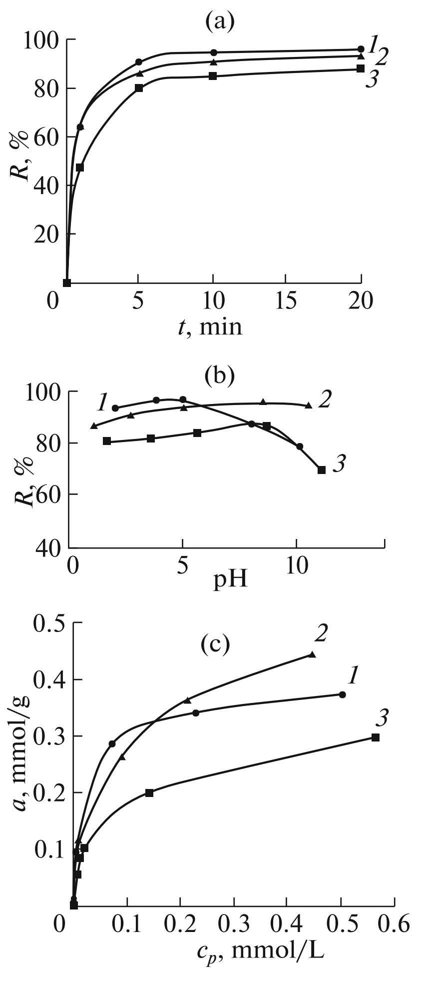


Fig. 2. Dependences of the degrees of extraction of (*1*) chloramphenicol, (*2*) florfenicol, and (*3*) thiamphenicol on magnetic HCPS on (a) the period of contact between the phases, (b) the pH of the solution, and (c) the concentration of amphenicols. $C_{\text{amphenicol}} = 5 \times 10^{-5}$ M, $V = 25$ mL, $m_{\text{sorb}} = 0.020 \pm 0.001$ g, (a, c) pH ~5, (b, c) $t = 10$ min.

tion isotherms of amphenicols (Fig. 2c) from aqueous solutions on magnetic HCPS are described by the Langmuir equation. Physicochemical parameters were calculated using equations of linear dependences constructed in coordinates $1/a$–$1/c$. They include the values of limiting sorption (a_{m}), sorption constants (K), and changes in the Gibbs energy (ΔG°), which are given in Table 3.

The values of the limiting sorption of amphenicols are inversely proportional to the ones calculated for the maximum cross-section area of the optimum conformation of the molecules (S_{mol}, nm^2) indicated in Table 1: $a_{\text{m}} = 2721/S_{\text{mol}}$ (the coefficient of correlation squared, $R^2 = 0.93$). This could indicate dense filling of the surface's accessible sorbent pores by amphenicol molecules. An estimate of the limit value of the specific surface they occupy gives a value of (160 ± 20) m^2/g. This corresponds approximately to the surface area of mesopores (Table 2), and we may assume these structural elements make the main contribution to sorption. This indirectly substantiates the fast kinetics of sorption, which depend weakly on the size of the molecules (Fig. 2a). Relatively large mesopores are more accessible than micropores, whose penetration by the sorbate is associated with substantial limits on diffusion.

A comparison of the coefficients of distribution and degrees of extraction of amphenicols (Table 4) indicates that sorption grows along with the hydrophobicity of these compounds (Table 1) in the series thiamphenicol < florfenicol < chloramphenicol, testifying to the presence of hydrophobic interactions. A linear dependence is observed between the logarithm of the coefficient of distribution ($\log D$) and the parameter of hydrophobicity ($\log K_{\text{ow}}$) of the sorbed amphenicol, (coefficient of correlation R^2 is given in parentheses):

$$\log D = 0.3433 \log K_{\text{ow}} + 4.056 \quad (R^2 = 0.982).$$

Table 4 shows the rates of recovery and logarithms of the coefficients of distribution of amphenicols on magnetic HCPS, obtained under the selected optimum conditions. As can be seen, amphenicols are sorbed by 88–96%, showing that the sorbent is suitable for the group sorption preconcentration of these compounds.

Table 3. Values of limit sorption, constants of sorption, and changes in the standard Gibbs energy for amphenicols on magnetic HCPS

Compound	a_{m}, μmol/g	$K \times 10^{-3}$, L/mol	$-\Delta G^\circ_{298}$, kJ/mol
Chloramphenicol	381.2	56.05	27.07
Florfenicol	449.7	38.41	26.14
Thiamphenicol	314.8	21.85	24.74

Table 4. Logarithms of the coefficients of distribution ($\log D$) and degree of extraction (R, %) of amphenicols on magnetic hypercrosslinked polystyrene: $C_{\text{amphenicol}} = 5 \times 10^{-5}$ M, pH ~5, $V = 25$ mL, $m_{\text{sorb}} = 0.020 \pm 0.001$ g, $t = 10$ min ($n = 3$, $P = 0.95$)

Compound	$\log D$	R, %
Chloramphenicol	4.48	96 ± 2
Florfenicol	4.29	95 ± 3
Thiamphenicol	3.96	88 ± 4

CONCLUSIONS

Magnetic hypercrosslinked polystyrene exhibits high affinity toward amphenicol molecules and can be used for the group sorption preconcentration of compounds of this class from aqueous solutions.

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