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THIOSEMICARBAZONE IMMOBILIZED ON CROSS-LINKED IONIC POLYMERS

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ABSTRACT: This work presents results of studies of thiosemicarbazone 5-NO2-salicylic aldehyde immobilization on the ionic cross-linked polymers: AV-17(Cl) (containing strongly basic groups), Amberlite IRC-50 (containing carboxylic groups) and composite AV-17(Cr) (containing chromium compounds). It is demonstrated that the rate of sorption of thiosemicarbazone on AV-17(Cl) and AV-17(Cr) is described with the pseudo-second kinetic model and is limited by the intra-particle diffusion. The sorption isotherm on these sorbents is approximated by the BET sorption model. Polymers loaded with thiosemicarbazone retain metal cations from the solution of $CuSO_4$, $Co(NO_3)_2$, $ZnSO_4$, $NiSO_4$, $FeSO_4$ and $Fe(NO_3)_3$ as a result of their coordination with the electrons donor atoms of the substrate. Thus the immobilized complexes of thiosemicarbazone on polymers were obtained. The reverse processes - the sorption of thiosemicarbazone on the Amberlite IRC-50 polymer which has been complexed with metal cations were also investigated.

KEYWORDS: thiosemicarbazone, immobilization, ionic cross-linked polymer, sorption kinetics, BET isotherm.

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1. INTRODUCTION

It is known that thiosemicarbazone and its derivatives exhibit biological activity. Thiosemicarbazones are chemical compounds have anti - tuberculosis properties [1,2] and are part of a group of tuberculostatic drugs. The thiosemicarbazone derivatives possess a various of antimicrobial (*Staphylococcus epidermidis, Bacillus cereus, Moraxella cattarhalis, Staph, Saprophyticus,*

Staphylococcus aureus, Enterococcus faecalis, Cryptococcus) and antifungal (*Candida albicans, Aspergillus flavans, Paracoccidioides brasiliensis*) activity [3,4]. An enhanced biological activity has complex combinations of thiosemicarbazones with metals. Antimicrobial activity possesses the complexes of Cu (II), Ni (II), Co (II) with thiosemicarbazone derivatives [5-9.] Some metal complexes with thiosemicarbazone derivatives possess not only antibacterial, but also anti-cancer and anti-HIV properties [10-12]. Only a few of the articles devoted to the biological properties of thiosemicarbazones and their complexes with metals have been cited here. In these articles, the biological activity of thiosemicarbazones and their complex compounds have been investigated under single-phase systems. But when local action of the drugs is required, it is necessary that thiosemicarbazone compounds be immobilized on an inert substrate. In this case the biological activity occurs slower than in single-phase systems. Upon using the Disc Diffusion Susceptibility Methods seems that the drug is immobilized on the support [13], but the act of biological activity takes place in a single phase, i.e. in solution. It is of interest to research the immobilization of thiosemicarbazone and its compounds with metals on the support which would not allow their diffusion in the liquid phase. In this paper we studied the processes of immobilization of thiosemicarbazone on cross-linked ionic polymers, on polymer containing metallic compounds and coordination of metallic cations with immobilized thiosemicarbazone on polymer. The following article will present the results of the biological activity research of the obtained samples.

2. MATERIALS AND METHODS

Materials: The commercial strongly basic AV-17(Cl) and weak acid Amberlite IRC-50(H) gel-type cross-linked polymers have been used. The AV-17(Cl), containing R_4N^+ functional groups, had full exchange capacity 3.5-4.2 mequiv/g, and Amberlite IRC-50, containing >CH–COOH functional groups, had exchange capacity 10.0 mequiv/g [14]. Also, the AV-17(Cr) composite [15] have been used. The composite AV-17 (Cr) was obtained according to Ref. [15]. Immobilized on polymers was thiosemicarbazone 5-NO_2-salicylic aldehyde. The corresponding solutions were prepared using the following substances: $CuSO_4$, $NiSO_4$, $ZnSO_4$, $FeSO_4$, $Fe(NO_3)_3$, $Co(NO_3)_2$; H_2SO_4 (1M), NaOH, NH2OH.HCl. Thiosemicarbazone 5-NO2-salicylic aldehyde was dissolved in 96% (vol) ethanol.

Analysis: The content of Fe^{2+}, Fe^{3+}, Cr^{3+} ions and thiosemicarbazone 5-NO_2-salicylic aldehyde was determined photocolorimetrically [16]. The content of other cations was determined titrimetrically [17].

Obtaining of composite AV-17(Cr): A 5 g of the dried AV-17(Cl) was put in contact with 0.5 L of solution $KCr(SO_4)_2 \cdot 12H_2O$, containing 2 g Cr/L at 55 ºC for 10 h. The system "polymer-solution of Cr(III)" pH value was adjusted periodically to 4.2 using KOH solution. When contacting the AV-17(Cl) polymer with the $M_2(SO_4)_3$ solution in its phase, the jarosite mineral type compounds are formed: $R_4N[M_3(OH)_6(SO_4)_2$ where M can be Cr^{3+}, Fe^{3+} and others trivalent cations, and R_4N^+ is the functional group of the polymer [15]. The Cr^{3+} content in the polymer was 9.06 mg Cr/g.

3. RESULT AND DISCUSSION

Kinetics of thiosemicarbazone sorption on AV-17(Cl) and AV-17(Cr).

The thiosemicarbazone 5-NO_2-salicylic aldehyde with the formula
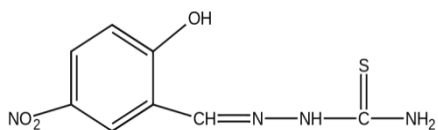
will be noted with HL.

On the AV-17 (Cl) polymer, HL may be retained only as a result of dispersion interactions, but on the AV-17 (Cr) sorbent, and as a result of coordinate bonds with the metal, replacing the SO_4^{2-} groups in the jarosite type compounds. The kinetic curve of HL absorption on AV-17 (Cl) or AV-17(Cr) was obtained at 20.5 °C. For this, 0.2 g of polymer was contacted with 50 ml of HL solution with concentration of $17 \cdot 10^{-3}$ mmol/L for 24 h. The HL sorption was calculated using Eq. (1):

$$S = \frac{(C_o - C_t)V}{m} \tag{1}$$

Where S is sorption value (mmol/g), Co and Ct is the initial concentration and respectively after contacting of the polymer with solution (mmol/L), V is the solution volume in contact with sorbent sample (mL), m is the mass of sorbent sample (g). The kinetic curve of HL sorption on AV-17(Cl) is shown in Fig.1 and on AV-17(Cr) in Fig.2. From Figures 1 and 2, it is seen that the sorption equilibrium takes place quite slowly. This occurs because in the ethanol solution of HL the degree of swelling of the polymer is much lower than in water [18] and the diffusion of the thiosemicarbazone molecules in the polymer phase is slow. To investigate the kinetics mechanism, which controls the sorption process of HL on AV-17(Cl) the nonlinear forms of the pseudo-first order (PFO) and pseudo-second-order (PSO) kinetic models [19, 20] were used. The nonlinear form of the integrated PFO kinetic model is described by Eq.(2):

$$St =$$
$$Se(1e^{-k_1 t}) \tag{2}$$

where St and Se are the amount of cations sorbed at a time t and at equilibrium (mg cation/g), respectively; k_1 is the rate constant in the PFO kinetic model (min^{-1}).

The value of the k_1 was determined using the linear form of the PFO kinetic model which is expressed by Eq.(3):

$$\ln(Se - St) = \ln Se - k_1 t \tag{3}$$

The nonlinear form of the PSO kinetic model is expressed by Eq.(4):

$$St = \frac{k_2 Se^2 t}{1 + k_2 \ Se \ t} \ , \tag{4}$$

where St and Se have the same meaning as in Eq.(2), and k_2 is the rate constant of PSO kinetic model (g $mmol^{-1}$ min^{-1}). The value of the k_2 and Se were determined using the linear form of the PSO kinetic

model which is expressed by Eq.(5):

$$\frac{t}{St} = \frac{1}{k_2 Se^2} + \frac{1}{Se} t \tag{5}$$

To explain the diffusion mechanism of the sorption process, intraparticle diffusion [21] is expressed by equation (6):

$$S_t = k_{id} * t^{0.5} + C_i \tag{6}$$

where k_{id} is the intraparticular constant (g mmol^{-1}min$^{-0.5}$), C_i is a constant providing information about the thickness effect of the boundary layer. In order to determine the sorption limiting step, the graph Eq.(7) [22] have been used:

$$-ln(1 - F) = f(t), \tag{7}$$

where: $F = St/Se$, t is time (min).

Two different error functions were used to determine the validity of kinetic models and isotherms, which were fitted by the non-linear regression method: coefficient of determination (R^2), and the nonlinear Chi-square (χ^2) test, estimated by Eq. (8).

$$\chi^2 = \sum \frac{(S_{,exp} - S_{calc})^2}{S_{calc}} \tag{8}$$

The high values of R^2 and the low values of χ^2, the best theoretical approach for describing the sorption data. Considering the k_1 and k_2 values in Table 1, the kinetic curves of HL sorption on the AV-17(Cl) and AV-17 (Cr) sorbents there were calculated   according to the PFO and PSO

Table 1: Values of parameters obtained by non-linear regression method for sorption o thiosemicarbazide on AV-17(Cl) and AV-17(Cr)

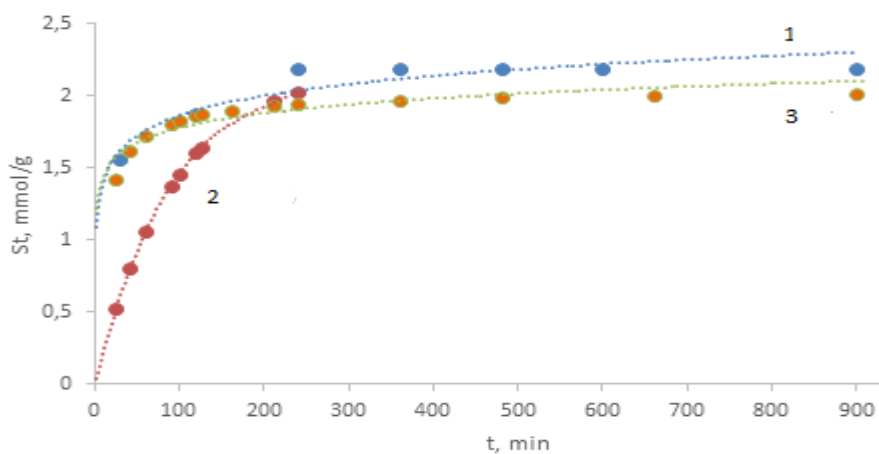| Kinetic model	Parameters	AV-17(Cl)	AV-17(Cr)
PFO	Se (calculated), mmol g^{-1}	2.19	2.06
	k_1, min^{-1}	0.011	0.0063
	R^2	0.8742	0.9623
	X^2	2.8800	8.1053
PSO	Se (calculated), mmol g^{-1}	2.03	1.93
	k_2, g mmol^{-1} min^{-1}	46.0	38.5
	R^2	0.8742	0.9623
	X^2	0.0016	0.0220

Fig. 1. The kinetic curves of the thiosemicarbazone sorption on AV-17 (Cl): obtained experimentally (1), calculated with PFO (2) and PSO (3) kinetic models.

kinetic models (Figures 1 and 2). The data of Table 1 and the curves of Figures 1 and 2 clearly demonstrate that the kinetics of HL sorption on AV-17 (Cl) and AV-17 (Cr)   corresponds to the PSO kinetic model which better consistent with the experimental data.
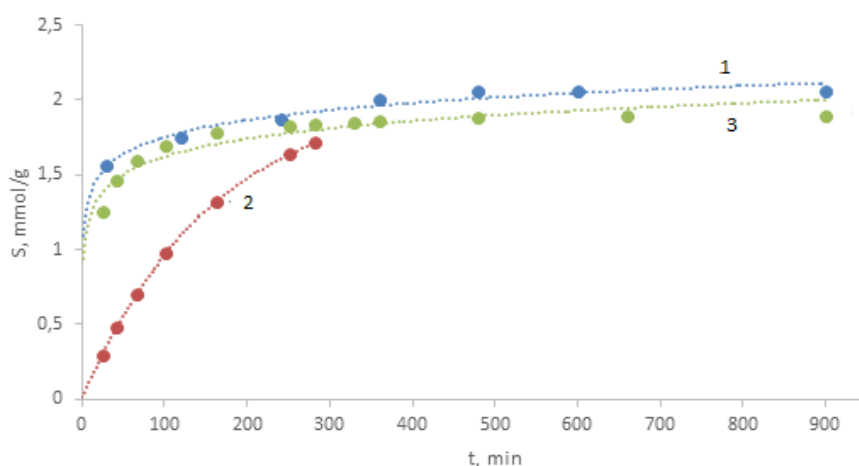

Fig.2. The kinetic curves of the thiosemicarbazone sorption on AV-17(Cr): obtained experimentally (1), calculated with PFO (2) and PSO (3) kinetic models.
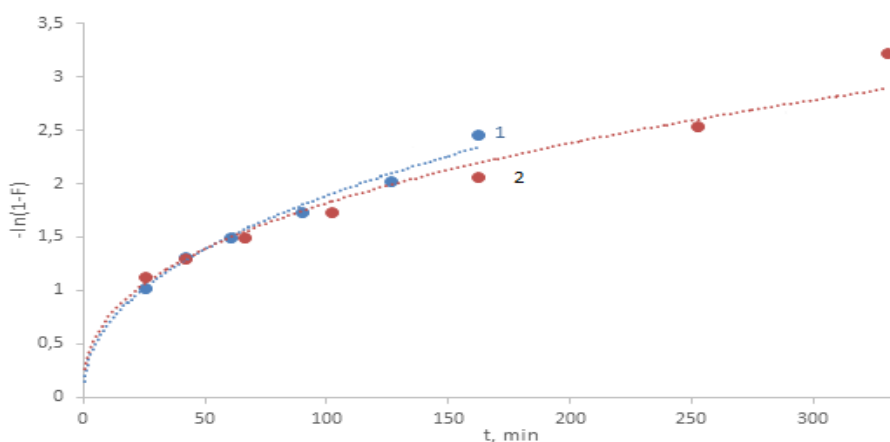

Fig.3. The graph $-ln(1-F) = f(t)$ for the sorption of 5-NO$_2$-salicylic aldehyde thiosemicarbazone   on the AV-17(Cl) -1 and AV-17(Cr) -2.

It is known [22], that the linear dependence of $-ln(1-F) = f(t)$ (Eq.7) denotes that the sorption rate is limited by the external diffusion (through the liquid film on the sorbent granule), and the nonlinear dependence on the internal diffusion (in the sorbent granule). As can be seen from Figure 3, the dependence *-ln(1-F) = f (t)* is non-linear.Therefore we can consider that the rate of HL sorption to AV-17 (CI) and AV-17 (Cr) is limited by intra-particle diffusion. The fact that the rate of HL sorption on AV-17 (Cl) and AV-17 (Cr) is limited by   internal diffusion, more convincingly is demonstrated by the linear dependence of $S_t = f(t^{0.5})$ (Fig.4) [21].
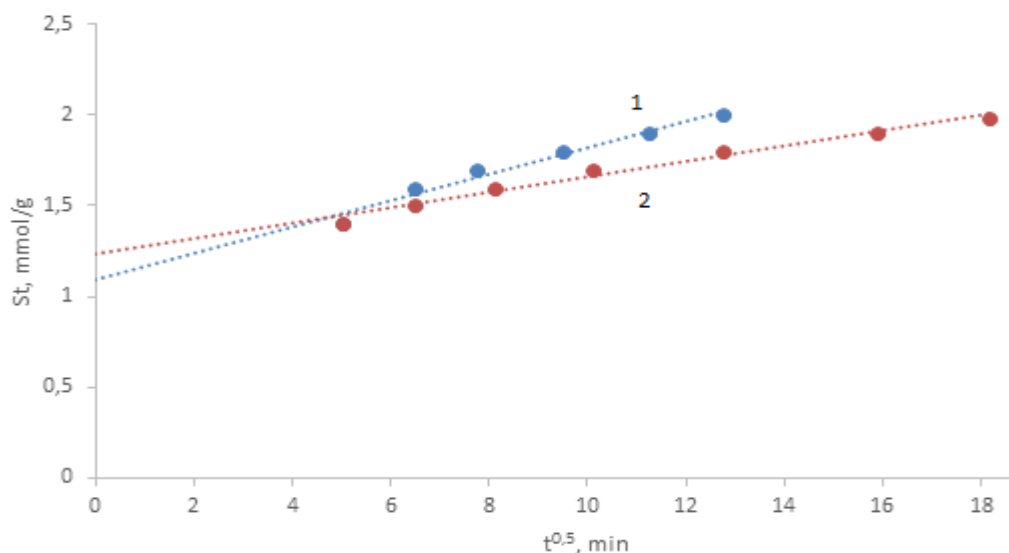

Fig.4. The *St = f (t^{0,5})* graph for the sorption of 5-NO$_2$-salicylic aldehyde thiosemicarbazone on the AV-17 (Cl) -1 and AV-17 (Cr)

The analysis of the experimental and calculated data shows that both the sorption value and the sorption rate of HL on the composite AV-17(Cr) are slightly lower than on the   AV = 17(Cl). This can be explained by the fact that the particles of jarosite compounds block some of the pores of the sorbent. On the other hand, as it is known, exchanging ligands in the Cr^{3+} compounds occurs very slowly.

Sorption isoterms of thiosemicarbazone sorption on AV-17(Cl) and AV-17(Cr)

In order to determine the sorption capacity of HL on the AV-17 (Cl) polymer and   AV-17 (Cr) composite, sorption isotherms were obtained. The experiment was carried out as follows: 0.2 g of sorbent was contacted   with 50 ml HL solution of   different concentrations at 25 °C for 24 hours. The results obtained are shown in Figures 5 and 6. As can be seen from these figures, the form of the experimentally obtained isotherms does not correspond to the Freundlich, Langmuir or Sips sorption models. We have approximated the isotherms with the BET sorption model. Although the BET sorption model has been developed for gas or vapor sorption, it can be used with some approximation and in some sorption processes in solutions [23, 24]. In this case, in the BET isotherm equation instead of P/Ps is introduced Ce/Cs, where P and Ps corresponds to the pressure and pressure of saturated vapors, and Ce and Cs - the equilibrium concentration   and the concentration of the saturated

solution.Thus the integrale BET equation used by us has the following form (Eq.9):

$$S = \frac{S_\infty B(C_e/C_s)}{(1-C_e/C_s)[1+(B-1)C_e/C_s]} \qquad (9)$$

Where, S is sorption value, mmol HL/g; S_∞ is first layer capacity, mmol HL/g; B is a constant, Ce – equilibrium HL concentration, mmol HL/L; Cs – pseudo saturated solution, mmol HL/L. At 22 ° C the Cs (HL) in 96 % (vol) ethanol is 28.5 mmol L^{-1}.
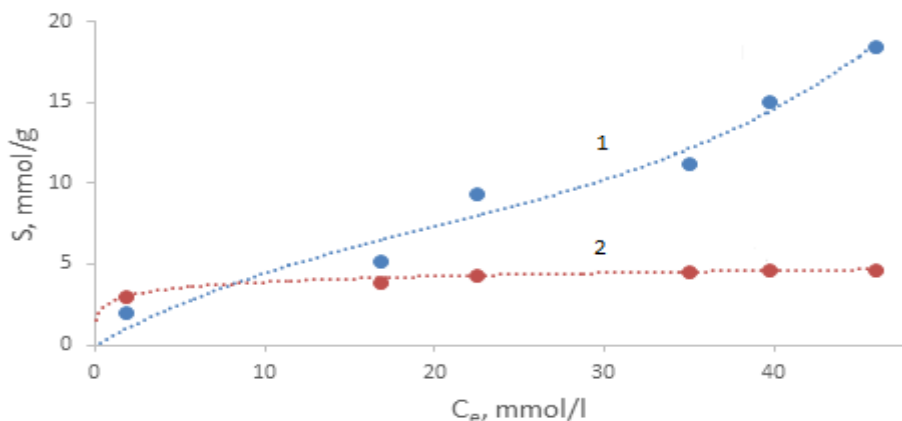

Fig.5. The 5-NO$_2$-salicylic aldehyde thiosemicarbazone sorption isotherm on AV-17 (Cl): 1- obtained experimentally, 2-   calculated according to the BET sorption model.

The isotherms of HL sorption on AV-17 (Cl) and AV-17 (Cr), obtained experimentally, are shown in Figures 5 and 6. Experimentally obtained isotherms data confirms that under similar conditions the HL sorption on AV-17(Cl) is slightly higher than on AV-17(Cr). For example, AV-17 (Cl) retains 18.5 mmol HL/ g (Ce = 46 mmol/L), and AV-17 (Cr) retains 17.5 10^{-3} mmol HL/g   (Ce = 50 mmol/L.

 Calculation of isotherm constants (Table 2) has been made using the linear form of the BET sorption model (Eq.10):

$$\frac{C_e/C_s)}{S(1-C_e/C_s)} = \frac{1}{S_\infty\ B} + \frac{(B-1)C_e/C_s}{S_\infty\ B} \qquad (10)$$

Using the constants value in Table 2, the isotherms of HL sorption on AV-17 (Cl) and AV-17 (Cr) were calculated (Figs. 5 and 6).
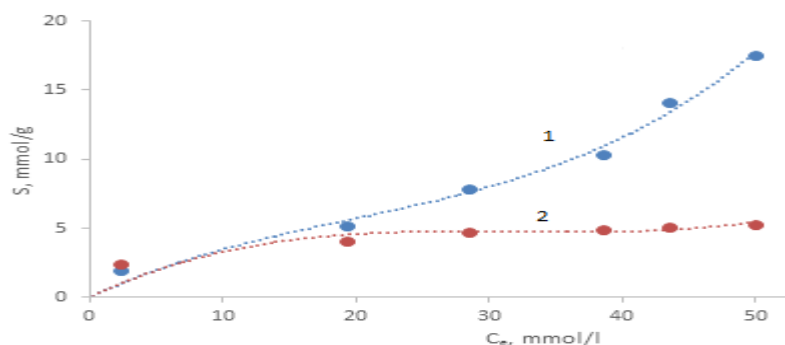

Figure 6. The 5-NO$_2$-salicylic aldehyde thiosemicarbazone sorption isotherm on AV-17 (Cr): 1- obtained experimentally, 2- calculated according to the BET sorption model.

Table 2. The values of the constants of BET sorption isotherm of   HL on AV-17(Cl) and AV-17(Cr)

Sorbent	$S\infty$, mmol g^{-1}	B, g mmol^{-1}	R^2	X^2
AV-17(Cl)	$5.43 \cdot 10^{-3}$	6572	0.9686	79.6379
AV-17(Cr)	$6.25 \cdot 10^{-3}$	3201	0.9874	52.7524

Although HL sorption on AV-17(Cl) is higher than on AV-17(Cr), the monolayer capacity on AV-17(Cl) is lower.

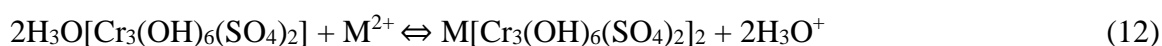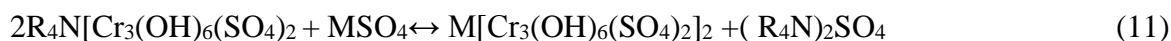**Sorption of 3d metals on sorbents containing thiosemicarbazone**

Biological activity possesses both thiosemicarbazones and their coordinative compounds with the cations of 3d metals. The formation of thiosemicarbazone coordinate compounds in the sorbent phase can be performed by two methods. 1. The sorbents are first loaded with thiosemicarbazone then with metal cations. 2. Sorbents are first loaded with metal cations, then with thiosemicarbazone. In this section we present the results of the research on the formation of the coordinative compounds of some 3d cations with thiosemicarbazone incorporated in the sorbent phase. The sorbents (AV-17(Cl+HL), AV-17(Cr+HL))   were previously obtained by contacting 5 g of   the AV-17(Cl) and AV-17(Cr) for 24 h   with 0.5 L solution of 5-NO$_2$ -salicylic aldehyde thiosemicarbazone containing 5 mmol/L. The HL content in AV-17(Cl+HL) sorbent constituted 0.182 mmol/g or 43.66 mg/g, and in AV-17(Cr+HL) - 0.167 mmol/g or 40.01 mg/g. Samples of 0.4 g of sorbent were contacted with 100mL of CuSO$_4$, Co(NO$_3$)$_2$, ZnSO$_4$, NiSO$_4$, FeSO$_4$ and Fe(NO$_3$)$_3$ solutions for 24 h at room temperature. After that the sorption of the metal cations on the sorbents was determined. The choice of salts has been carried out in such a way as to exclude the formation of jarosite mineral compounds in the sorbent phase. As is known [25], bivalent cations as well as trivalent cations in the absence of sulfate anions, do not form jarosite mineral compounds in the polymer phase containing strongly basic groups. So, the cations examined can be retained by AV-17(Cl+HL) sorbent only as a result of their coordination with electron donor atoms (N, S, OH) of HL. The results of the metal cation sorption on AV-17(Cl+HL) and AV-17(Cr+HL are presented in Table 3. These results seem very interesting. First, we can state with certainty that the metal cations in phase of AV-17 (Ci + HL) coordinate with the electron donor atoms of thiosemicarbazone. That is, in the polymer phase we have the immobilized coordinating compounds of thiosemicarbazone. Most likely, metal cations coordinate with N and S atoms of thiosemicarbazone, forming chelatocycles [26], but some cations such as Fe^{3+} could also coordinate with the oxygen of the phenolic groups. This can explain the fact that Fe^{3+} cations are retained on polymers containing HL, much more than other cations (Table 3). Regretfully, IR spectroscopy is less informative for investigated objects, and other spectroscopic methods are inapplicable.

Table.3. The data of metal cations sorption on AV-17(Cl+HL) or AV-17(Cr+HL

Solution	Sorbent	pHe	Co^*, mol/L	S,mmol/g	S, mg/g
ZnSO$_4$	AV-17(Cl+HL)	5.98	10.55	0.056	3.72
	AV-17(Cr+HL)	4.54		0.190	12.61
NiSO$_4$	AV-17(Cl+HL)	6.16	5.67	0.081	4.75
	AV-17(Cr+HL)	4.67		0.096	5.64
CuSO$_4$	AV-17(Cl+HL)	4.72	9.90	0.018	1.14
	AV-17(Cr+HL)	4.06		0.072	4.58
Co(NO$_3$)$_2$	AV-17(Cl+HL)	5.02	6.17	0.205	12.08
	AV-17(Crl+HL)	4.70		0.214	12.61
FeSO$_4$	AV-17(Cl+HL)	3.85	2.50	0.038	2.12
	AV-17(Crl+HL)	3.52		0.038	2.12
Fe(NO$_3$)$_3$	AV-17(Cl+HL)	2.30	2.65	0.331	18.49
	AV-17(Crl+HL)	1.95		0.369	20.61

*Co is initial concentration

On the other hand, although the contentof thiosemicarbazone in the AV-17(Cr+HL) phase is lower than in AV-17(Cl+HL), the sorption of metallic cations on AV-17(Cr+HL) is higher. So the existence of HL in the sorbent phase contributes to the retention of metal cations. Probably some of the metal cations are retained on AV-17(Cr + HL) as a result of their coordination with thiosemicarbazone, and other as a result of the cation exchange according to Eqs.11 and 12.

$$2R_4N[Cr_3(OH)_6(SO_4)_2] + MSO_4 \leftrightarrow M[Cr_3(OH)_6(SO_4)_2]_2 +(R_4N)_2SO_4 \qquad (11)$$

$$2H_3O[Cr_3(OH)_6(SO_4)_2] + M^{2+} \Leftrightarrow M[Cr_3(OH)_6(SO_4)_2]_2 + 2H_3O^+ \qquad (12)$$

Sorption thiosemicarbazone on Amberlite IRC-50 polimer louded with 3d cations

For the study, a cross-linked ionic Amberlite IRC-50 polymer containing carboxylic groups was used. On the first stage, the polymer was charged with metal cations upon contacting of 0.4 g with 100 mL solution of   CuSO$_4$, Co(NO$_3$)$_2$, ZnSO$_4$, NiSO$_4$, FeSO$_4$ and   Fe(NO$_3$)$_3$ with

Table 4. Data on the sorption of metal cations on Amberlite IRC-50 and the sorption of the thiosemicarbazone on Amberlite IRC-50 loaded with metal cations

Solution	CUSO$_4$	CuSO$_4$	Co(NO$_3$)$_2$	NISO$_4$	ZnSO$_4$	FeSO$_4$	Fe$_2$(SO$_4$)$_3$
Equilibrium pHe	3.40	3.90	5.14	4.96	4.45	3.73	2.42
Metal content in polymer, mg g^{-1}	4.45	19.28	12.69	12.44	17.44	22.69	20.24
Equilibrium Ce$_{(HL)}$, mmol L^{-1}	2.828	2.929	2.929	3.080	2.029	3.080	3.080
S$_{(HL)}$, mmol g^{-1}	0.088	0.063	0.063	0.025	0.063	0.025	0.025
S$_{(HL)}$, mg g^{-1}	21.25	15.15	15.15	6.06	15.15	6.06	6.06

respectively concentration 9.90; 9.80; 10.70; 5.67; 2.50 and 2.65 mmol/L at room temperature for 7 days. The metal content into the polymer samples is shown in Table 4. The samples of 0.2 g of polymer loaded with metal cations were contacted with 50 ml of thiosemicarbazone solution with the concentration 3.182 mmol/L at a room temperature for 7 days. The data of Table 4 shows that the sorption of thiosemicarbazone on the Amberlite IRC-50 polymer is the lower the higher the metal content in the polymer. So we can assume that thiosemicarbazone does not coordinate with the metal cations in the polymer phase. The decrease of thiosemicarbazone sorption with the increase in the metal content can be explained by the fact that the metal cations coordinating with the carboxylic groups lead to the additional crosslinking of the polymer chains. And this leads to a drastic decrease in the polymer pore size and, consequently, to a decrease in the diffusion of the thiosemicarbazone in the polymer phase. Previous results have shown [18], that the swelling in water of cross-linked carboxylic polymers containing Cu^{2+}, Cd^{2+} and Zn^{2+} cations is about 3 times lower than those containing Na^+. The effect of reducing the polymer swelling caused by the metal cation complexation is much higher than that caused by ethanol [18]. It should be noted that depending on the amount of divinylbenzene and the nature of the metal, the cations may be coordinated with a single or two (more frequently) carboxylic groups belonging to one or two polymeric chains. That is why there is no strict correlation between the metal content in the polymer phase and the sorption of thiosemicarbazone.

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