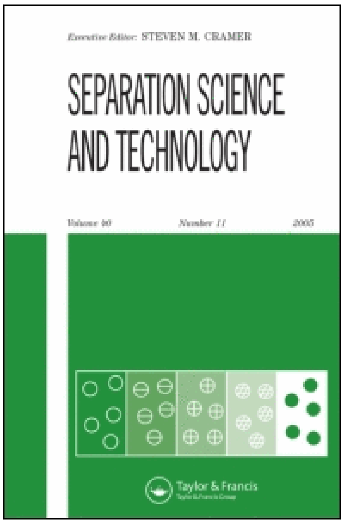

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Ion Exchangers for the Recovery of Penicillin from Its Waste

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Abstract

A large amount of penicillin is lost during the extraction and crystallization stages in the process of its manufacture. In the present work attempts were made to recover the penicillin by the use of three anion exchangers: Amberlite IRA-401, Dowex-1, and Tulsion A-27. In all, seven different elements were tried for the desorption of adsorbed penicillin. It was observed that with increasing DVB content of the resin, the adsorption capacity of the penicillin decreased. The extent of desorption with various eluents varied with the type of resin used. The effect of flow rate and penicillin content in the feed were also studied.

Substantial quantities of penicillin are lost during extraction and crystallization stages with raffinate and mother liquor, respectively, in the commercial manufacture of K penicillin G. The overall recovery of penicillin is only about 75 to 80% of that present in the fermentation broth. Considering the high cost of material, it is worthwhile investigating the possibilities of recovering penicillin from these wastes.

It has been recognized that ion exchange is a suitable method for the recovery of penicillin from its aqueous solution, especially when the concentration of penicillin in the aqueous phase is low. A considerable amount of work in this field has been done by Samsanov and co-workers (*1*, *2*). Penicillin sorption by high capacity anionite (EDE-10) was irreversible in presence of anions of sulfuric, phosphoric, and certain other acids. The exchange was equivalent with the chloride form, whereas in the case of sulfate and phosphate ions the exchange was not equivalent. Penicillin sorption was found to be selective, as well as reversible, in the case of low capacity acidic anionites such as ASM-4 and ASD-3. The desorption of penicillin from strongly basic anionite ASD-3 was almost quantitative with phosphate buffers. Vedeneeva and co-workers (*3*) studied the adsorption capacity and selectivity of the strong anion-exchange resins AV-18 and FAF, and concluded that though the adsorption of penicillin was almost quantitative, its elution was poor. It was reported (*4*) that "difficult-to-elute" substances, such as K penicillin G, could be rapidly eluted from Amberlite IRA-401 (Cl) strong base resin by a mixed solution containing at least 50% (vol) of an organic water-soluble compound, such as alcohol, ketone, or amide, and 0.1 to 15% of an ionizable salt. The elution was almost quantitative with 70% aqueous methanol containing 7.5% NH_4Cl. Elution of penicillin from activated carbon (*5*) was achieved using aqueous methyl alcohol and ethyl alcohol, with 70% alcohol concentration reported to be the best but still inferior to 85% aqueous acetone. An aqueous solution of sodium chloride or the buffer solution (*6*) was also used as the eluent for desorbing penicillin from quaternery ammonium anion-exchange resins based on styrene (99.5 to 98%) and polyvinylbenzene (0.5 to 2%) copolymer. Kunin and Myers (*7*) showed a sharp decrease in the ability to adsorb penicillin with an increase in the degree of cross-linking. The resin studied was modified Amberlite IRA-400 anion-exchange resin.

It is apparent from the foregoing information that the adsorption of penicillin on strongly acidic high capacity resin is almost quantitative. However, the desorption output from such resins is poor. Strongly basic resins or low capacity anionites might be more suitable because desorption with them is rapid and quantitative. Also, the selectivity for penicillin has been reported to be better with basic types or low capacity anionites.

EXPERIMENTAL

Three different ion-exchange resins, namely Amberlite IRA-401, Tulsion A-27, and Dowex-1, have been studied. Their characteristics are given in Table 1.

Ion Exchange with Aqueous K Penicillin Solution

In order to assess the feasibility of adsorption of K penicillin on an ion-exchange resin and its desorption, experiments were conducted using commercial Amberlite IRA-401 resin. The resin was converted to its acetate form. An aqueous solution of K penicillin containing 3500 mg/L of penicillin was passed over a resin bed containing about 1 g of resin in a 125 × 700 mm glass column at a flow rate of 2.045 mL/min cm^2. The total amount of penicillin adsorbed was 1019.1 mg in 125 min when the

TABLE 1

Characteristics of Cation-Exchange Resins Studied

Resin	Amberlite IRA-401	Tulsion A-27 (Indian)	Dowex-1
Resin base	Polystyrene	Cross-linked polystyrene	Cross-linked polystyrene
Active group	$N^+(CH_3)_3$	$CH_2N^+(CH_3)_3Cl^-$	$N^+(CH_3)_3$
DVB content, % wt	2.0	6.2	8.0
Total capacity, meq/g			
Dry basis	3.4	2.4	3.3
Wet basis	0.8	1.4	1.2
Particle size, mm	0.40–0.55	0.40	0.15–0.28
Maximum allowable temperature, °C	75	60	75
Bulk density, g/mL	0.65	0.75	0.70
State	Porous	Nonporous	Nonporous
Moisture content, %wt	45	46	39–45

effluent concentration reached the 3500 mg/L level. The elution with *N* KCl solution recovered 639.15 mg of penicillin in 70 min, after which there was no appreciable desorption. Complete desorption with KCl solution was not possible, as reported in published information (*1*). All the penicillin samples in the study were analyzed by the standard iodometric method (*8*). The average error in estimating the potency was 6.5%.

Preparation of Synthetic Crystallization Waste

The crystallization waste is usually a mixture of two solutions, one containing 240.9 mg/mL of penicillin K and another containing aqueous K acetate solution (saturated at 27°C) of 1.4 specific gravity in a volume ratio of 1 : 0.8. K penicillin content of a mixture was determined from its potency value, i.e., 400,000 IU/mL or 1660 IU/mg. The weight ratio of K penicillin to K acetate solution was 1 : 3.33, and hence the synthetic waste samples were prepared by mixing K penicillin crystals and a saturated solution of K acetate in that ratio.

Ion Exchange with Crystallization Waste

The experimental cycle consisted of the following steps.

(*a*) *Ion Exchange*. The waste solution was passed over the resin bed at the desired flow rate after the resin bed, exhausted from the previous cycle, was converted into the acetate form. After taking a sufficient number of samples for analysis at regular intervals, the exchange was stopped. The following reaction took place:

$$\overline{\mathrm{RCH_3COO}} + \mathrm{KP} \rightleftarrows \overline{\mathrm{RP}} + \mathrm{CH_3COOK}$$

where the bar indicates the resin phase, and P and R refer to exchangable ions of the penicillin and the resin matrix, respectively.

(*b*) *Backwash*. Here the adsorbed penicillin was eluted. The resin bed was converted to the respective forms according to

$$\overline{\mathrm{RP}} + \mathrm{R'A} \rightleftarrows \mathrm{R'P} + \mathrm{RA}$$

where R′ and A represent cations such as Na^+ or K^+ and anions such as Cl^-,SO^{2-},or PO^{3-}, respectively, R′A being an eluent.

(*c*) *Rinse*, The rinse ensured the removal of excess eluent from the resin bed by demineralized water.

(*d*) *Regeneration.* The resin bed was regenerated to its original acetate form by passing 125 to 150 mL of *N* sodium acetate solution at a flow rate of 1 to 2 mL/min cm^2. The reaction taking place during regeneration was

$$\overline{RA} + CH_3COONa \rightleftarrows \overline{RCH_3COO} + NaA$$

In order to achieve the above-mentioned steps satisfactorily, the following operating conditions were chosen:

Backwash flow rate	6–8 mL/min cm^2
Volume of backwash solution	1.5 L
Elution flow rate	2–4 mL/min cm^2
Elution contact time	70–140 min
Rinse volume	1.5L
Flow rate of crystallization waste	1–2.4 mL/min cm^2

Variables studied during the work were the concentration of pencillin K in the feed, the flow rate of the feed solution, the resin type, and the eluent type.

The feed concentration was varied from 1460 to 6341 mg/L, corresponding to 729 to 3109 mg of K pencillin fed. The experiments were carried out in the 1 to 2.3 mL/min cm^2 range of the feed flow rate.

Eluent systems used were 0.5 *N* KCl (E_1), 1 *N* KCl (E_2), 2 *N* KCl (E_3), [*M*/15 (KH_2PO_4 + Na_2HPO_4) + 1% sodium citrate] (E_4), [2.5% aqueous solution each of Na_2HPO_4 and Na_2SO_4] (E_5), [*M*/15 (KH_2PO_4 + Na_2HPO_4) + 1% sodium oxalate] (E_6), and [*M*/15 KH_2PO_4 + Na_2HPO_4) + 0.5 *M* urea] (E_7).

In each set of experiments, consisting of adsorption and elution, seven samples (20 mL each) of effluent were collected at regular intervals. They were analyzed for their penicillin content, and breakthrough and elution curves were plotted on a cumulative basis. The amounts adsorbed and desorbed were computed as areas under these curves. For this purpose penicillin solutions of different concentration were passed over the resin at different flow rates for different periods of time. All the data are not presented in this article.

RESULTS AND DISCUSSIONS

The results of experiments on adsorption of penicillin by Amberlite IRA–401 resin are shown in Table 2. The total amount of penicillin adsorbed on the basis of penicillin fed has been calculated from the breakthrough curve.

The effect of penicillin fed is apparent from the results of the Experiments 1 and 5, in which the amount of penicillin adsorbed decreased from

68.85 to 60.55% for penicillin feeds of 1750 and 820 mg, respectively.

As for the elution studies (Table 3), eluent E_4 was the most effective with a maximum desorption of ~67%. The eluent was passed at a given flow rate until the concentration of penicillin in the eluate remained constant at a fairly low level. The total quantity of effluent collected was ~330 mL.

The exchange capacity of Amberlite IRA-401 was quite high even after 10 cycles. When used in the Cl^- form and fed with 1548 mg (3160 mg/L) of pure K penicillin at 1.93 mL/min cm², it adsorbed 936 mg of penicillin. The adsorbed penicillin could be effectively eluted with a system consisting of 250 mL of *N* KCl and 150 mL of [*M*/15 (KH_2PO_4 + Na_2HPO_4) + 0.5 *M* urea]. Elution was done at a flow rate of 2.11 mL/min cm², and the recovery was 68.6% of the amount adsorbed. This recovery was higher than for any of the eluents used previously, and there was no discontinuity in the desorption curve. This discrete run shows the possibility of using a mixed eluent system effectively.

TABLE 2

Adsorption of Penicillin on Amberlite IRA-401 (theoretical exchange capacity: 1150 mg/g dry resin)

Expt No.	Total penicillin fed (mg)	Flow rate (mL/min cm²)	Penicillin adsorbed on basis of exchange capacity	
			mg	%
1	1750.0	1.66	792.2	68.85
2	1715.0	2.20	811.2	70.53
3	1562.0	1.28	830.9	72.25
4	911.4	1.76	588.8	51.60
5	820.2	1.67	696.4	60.35
6	729.0	2.02	505.2	43.91
7	911.4	1.76	555.2	48.28

TABLE 3

Elution of Penicillin Adsorbed on Amberlite IRA-401

Expt No.	Penicillin adsorbed (mg)	Eluent	Eluent flow rate (mL/min cm²)	Penicillin desorbed	
				mg	% of adsorbed
1	792.2	E_1	1.44	387.9	48.9
2	811.2	E_2	1.47	426.1	52.5
3	830.9	E_3	1.42	396.6	47.7
4	588.8	E_4	1.43	397.8	67.6
5	696.4	E_5	1.36	195.4	28.1
6	505.2	E_6	1.59	308.1	61.0
7	555.2	E_7	1.72	274.9	49.5

In the case of Tulsion A-27 resin, five sets of experiments were conducted. The results are shown in Table 4. The data show that the amount of penicillin adsorbed increased sharply from 36.4 to 96.7% with an increase in the amount of penicillin fed (1541 to 2663.2 mg). This shows that the total amount of penicillin fed has a significant influence on the extent of adsorption. Experiments 3 and 4 also show an increase in the extent of adsorption with an increase in the flow rate of the penicillin solution. Eluents E_1 and E_3 were not used for desorption experiments because they had poor desorption outputs. However, E_5 was retained because this system is essentially free of KCl which has been reported to give incomplete desorption. The results of elution experiments with Tulsion A-27 resin are given in Table 5. The maximum desorption, ~69.3%, was achieved with E_2, while the desorption output was considerably lower for the other eluents as compared to Amberlite IRA-401. Hence the choice of desorbent is a strong function of the type of resin used for the adsorption of penicillin.

Similar experiments were conducted with Dowex-1 resin. The data are shown in Table 6. In this case the amount adsorbed was ~94%, which

TABLE 4

Adsorption of Penicillin on Tulsion A-27 (theoretical exchange capacity of resin: 750 mg/g dry resin)

Expt No.	Total penicillin fed (mg)	Flow rate (mL/min cm^2)	Penicillin adsorbed on basis of exchange capacity	
			mg	%
1	1541.0	2.30	273.0	36.4
2	1552.0	1.00	351.8	46.4
3	2663.2	2.23	727.3	96.7
4	2662.6	1.01	467.9	62.3
5	3107.1	2.06	708.3	94.4

TABLE 5

Elution of Penicillin Adsorbed on Tulsion A-27

Expt No.	Penicillin adsorbed (mg)	Eluent	Eluent flow rate (mL/min cm^2)	Penicillin desorbed	
				mg	% of adsorbed
1	273.0	E_2	1.63	189.3	69.30
2	351.8	E_4	1.15	144.2	41.40
3	727.3	E_5	1.62	127.0	17.17
4	467	E_6	1.60	165.2	35.30
5	708.3	E_7	2.01	111.9	15.80

TABLE 6

Adsorption of Penicillin on Dowex-1 (theoretical exchange capacity: 1100 mg/g dry resin)

Expt No.	Total penicillin fed (mg)	Flow rate (mL/min cm^2)	Penicillin adsorbed on basis of exchange capacity	
			mg	%
1	3107.0	1.14	1039.0	94.5
2	3109.0	2.10	1036.4	94.2
3	1553.0	2.20	477.4	43.4
4	1553.3	2.30	495.7	45.0
5	1331.4	1.16	485.8	44.2

TABLE 7

Elution of Penicillin Adsorbed on Dowex-1

Expt No.	Penicillin adsorbed (mg)	Eluent	Eluent flow rate (mL/min cm^2)	Penicillin desorbed	
				mg	% of adsorbed
1	1039.0	E_2	1.84	314.8	30.3
2	1036.4	E_4	2.10	257.7	25.0
3	477.4	E_5	1.98	248.5	52.0
4	495.7	E_6	2.10	234.2	47.2
5	485.8	E_7	1.93	210.9	43.4

decreased sharply with a decrease in the amount of penicillin fed. The flow rate is seen to have practically no effect for the same amount of penicillin fed. The desorption outputs (Table 7) with the eluent systems studied for Dowex-1 resin were lower than those for Amberlite IRA-401 and Tulsion A-27, the maximum being 52% with E_5.

The major difference in the characteristics of the three resins is their degree of cross-linking. This is closely related to the DVB content of the resin. A low degree of cross-linking, i.e., a low DVB content, can cause the resin to swell considerably, facilitating a faster rate of ion exchange. Hence, the larger the amount of penicillin fed, the greater the degree of adsorption to be expected. However, such a resin has a low resistance to mechanical breakdown and low selectivity for particular ions. Differences in grain size and porosity are of little concern, and they have no practical relevance to the degree of cross-linking.

The effect of the DVB content of the resin on the amount of penicillin adsorbed at constant flow rate and penicillin fed is shown in Table 8. Resins with a low DVB content, and hence a low degree of cross-linking, show the maximum adsorption capacity. Data on the variation of desorp-

TABLE 8

Effect of DVB Content on Adsorption of Penicillin

Penicillin fed (mg)	Flow rate (mL/min cm²)	% DVB content of the resin	Penicillin adsorbed (% theoretical)
1553	1.1	2.0	72.25
		6.2	46.40
		8.0	44.15
1525	2.2	2.0	70.53
		6.2	36.40
		8.0	43.40

tion output with DVB content of the resin, shown in Table 9, indicate that the trend depends on the eluent type. However, considering the adsorption and desorption processes together, a resin with 2% DVB content would be quite adequate with all the eluents studied, except E_5. The data in Table 9 have been computed from Tables 3, 5, and 7.

CONCLUSIONS

(1) All three resins showed good adsorption capacity for penicillin from its synthetic crystallization waste.

(2) With an increase in the amount of penicillin fed, there was a considerable increase in the extent of adsorption. This effect was more pronounced for ion-exchange resins with higher DVB contents, i.e., Tulsion A-27 and Dowex-1. In the cases of Tulsion A-27 and Dowex-1, the extent of adsorption increased from 35 to 45% to more than 94% when the amount of penicillin fed was increased from 1550 mg to double that value for the same flow rate. This shows clearly that by having longer contact times or by having higher concentrations of penicillin in the feed, the near-theoretical exchange capacity of a resin can be utilized.

(3) The change in the flow rate of penicillin solution over the resin had a rather insignificant effect on its quantitative adsorption.

(4) The eluent system depended on the type of resin used. In the case of Amberlite IRA-401, the eluent consisting of a mixture of $M/15$ ($KH_2PO_4 + Na_2HPO_4$) and 1% sodium citrate was the most suitable, whereas for Tulsion A-27 and Dowex-1 resins, 1 N KCl and 2.5% aqueous solutions of Na_2HPO_4 and of Na_2SO_4 worked well as eluting agents.

(5) The adsorption capacity for penicillin decreased with an increase in the DVB content of the resin. However, different eluents showed

TABLE 9

Variation of Elution Characteristics with DVB Content of Resin

	Eluent														
	E_2			E_4			E_5			E_6			E_7		
% DVB content	2	6.2	8	2	6.2	8	2	6.2	8	2	6.2	8	2	6.2	8
% Penicillin adsorbed	52.5	69.3	30.3	67.6	41.4	25.0	28.0	17.2	52.0	61.0	35.3	47.2	49.5	15.8	43.4

different behaviors with respect to the DVB content of a resin or the degree of cross-linking. This supports the earlier conclusion reported in the literature (*1*) that the desorption output is related to resin–penicillin–eluent interaction.

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