Absorption of ephedrine onto sulphonic acid cation-exchange resins

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Detailed studies of the kinetics of absorption of ephedrine onto the sulphonic acid cation-exchange resins have been made and most of the results have been interpreted by the particle diffusion theory of Boyd, Adamson & Myers (1947). The rate constant has been found to be inversely proportional to the square of particle radius and also dependent on the solution concentration, the temperature and the cross-linking of the resin. Absorption of ephedrine onto the 9% cross-linked (C.L.) resin proceeds to its capacity from ephedrine solution and not from ephedrine hydrochloride solution when experiments are made in closed tubes; with 13·5% C.L. resin, absorption does not proceed to capacity even after 2 months. The rate constant of absorption of ephedrine onto the sodium form of the resin is low as compared with the hydrogen form. In most cases diffusion coefficients have been calculated.

MANY attempts have been made to clarify the rate-controlling mechanism of exchange of inorganic ions but much less attention has been paid to the exchange of organic ions. Kressman & Kitchener (1949) working on a phenolsulphonic acid resin reported that exchange of large organic ions was controlled by particle diffusion. Saunders & Srivastava (1950, 1955) made a detailed study of absorption of several organic bases on to carboxylic acid resins and concluded that diffusion of these molecules into the resin particle was rate controlling. They found that rate of absorption onto an exchanger was dependent on the concentration of solute, the solvent, the temperature, the particle size and degree of cross-linking of the resin, and the dissociation constant of the organic base and its molecular size. Their experimental results however did not obey the particle diffusion equation of Boyd, Adamson & Myers (1947) and they arrived at their own conclusions by deriving appropriate equations. Kawabe, Sugimoto & Yanagita (1954) have studied the absorption of nicotine onto sulphonic acid and carboxylic acid exchangers and conclude that, in both, the rate is controlled by particle diffusion. We have already reported (1956) that the elution of ephedrine from sulphonic acid resins obeys the particle diffusion equation of Boyd & others (1947) when experiments are made by the infinite bath method.

In the present work the kinetics of absorption of ephedrine onto the sulphonic acid ion-exchange resins from aqueous solutions of ephedrine and ephedrine hydrochloride have been studied and conditions have been worked out for the absorption of ephedrine to the full capacity of the resin.

Experimental

Materials. Preliminary conditioning of the resins have been described elsewhere (Chaudhry & Saunders, 1956). A description of the resin

fractions used is given in Table 1. Water absorptions are the quantities of water which are absorbed by the dry resins as determined by drying at 110°.

TABLE 1. DESCRIPTIONS OF RESIN FRACTIONS

Resin	a	b	c	d
Nominal divinyl-benzene content (%) i.e. degree of cross-linking (C.L.)	4·5	9*	9*	13·5
B.S.S. fraction of the air-dried hydrogen form ..	30–36	20–30	40–60	40–44
Moisture content (%) of the air-dried hydrogen form ..	28·0	26·4	26·2	24·7
Mean swollen particle diameter (mm)	0·70	0·71	0·45	0·45
Exchange capacity mg equiv/g dry resin (110°) ..	5·25	5·08	5·08	4·98
Water absorptions (mg)/mg equiv of dry resin (H) ..	342	169	—	124
Water absorption (mg)/mg equiv of dry resin (ephedrine)	153	55	—	—
Linear expansion (%) of swollen particle of hydrogen form of resin on absorption of ephedrine..	−1·4	+2·4	—	+3·4

* This is a usual degree of cross-linking in the commercial cation exchangers of this type.

ABSORPTION OF EPHEDRINE ONTO THE RESIN

Kinetic absorption studies were made with 50 ml portions of the aqueous solutions and 2·54 mg equiv of swollen particles of the resin. In all the experiments the amount of total ephedrine (ephedrine base and ephedrine hydrochloride) present in 50 ml of solution was more than the available capacity of the resin particles with which it was in contact.

The kinetic measurements were made by the closed tube method of Chaudhry & Saunders (1956). Four systems have been studied and the experimental details are described below.

A. *Absorption onto the hydrogen form of the resins from aqueous solutions of ephedrine.* In the first set of experiments, a comparison of rates of absorption (up to 6 hr) of ephedrine onto 2·54 mg equiv of the hydrogen form of resin b (Table 1) was made from two solutions. (i) 6 mg equiv of ephedrine in 50 ml water and (ii), 3 mg equiv of ephedrine base plus 3 mg equiv of ephedrine hydrochloride in 50 ml water. The results showed that the difference in uptake of the two was negligible.

The internal indicator method for initial stages of absorption. This method was used to study the initial stages of absorption. The hydrogen form of the resin was shaken with a solution of ephedrine hydrochloride and ephedrine, the amount of the latter being less than the available capacity of the resin. The solution, initially alkaline, became acidic when absorption of ephedrine onto the resin just exceeded the amount of ephedrine (free base) originally present in the solution. This change was shown by the indicator (methyl orange) present in the solution. The time elapsing between the addition of the solution to the resin and the colour transition of the indicator, was measured with a stop clock. Experiments for a number of stages of fractional absorption (F) at a particular solution concentration were made by varying the relative amounts of the free base and the hydrochloride, keeping the total ephedrine concentration constant.

F is defined by the equation:

$$F = Q_t/Q_c$$

Q_t is the amount in mg equiv of ephedrine absorbed onto the resin in time t, and Q_c is the total exchange capacity, in mg equiv, of the resin sample used in the measurement. The results have been interpreted by the particle diffusion theory of Boyd & others (1947). The values of rate constant, B, and the effective diffusion coefficient, D, have all been calculated in terms of F, as defined above.

$$\text{According to this theory } F = 1 - \frac{6}{\pi^2} \sum_{n=1}^{n=\infty} \frac{\exp(-n^2Bt)}{n^2} \text{ and } B = \pi^2D/r^2$$

where r is the mean radius of the swollen resin particles. Numerical values of F for given values of B have been computed by Boyd, Adamson & Myers and are given in the reference quoted above. The table of functions has been extended by Reichenberg (1953).

The hydrogen form of the resin fraction (swollen particles) and the solution under study were put into tubes, one for each fractional stage of the absorption. The tubes were stoppered and rotated in the thermostat bath, and the time was noted when the colour of the indicator solution changed from yellow to orange-red. The results by this method were compared with the results obtained by the method for subsequent stages of absorption; good agreement was found.

Method for subsequent stages of absorption. The method consisted of rotating in closed tubes, swollen particles of the hydrogen form of the resin with 50 ml of a solution containing 3 mg equiv of ephedrine buffered with ephedrine hydrochloride to give an appropriate concentration as total ephedrine. After each time interval, a tube was removed from the thermostat bath and its contents analysed for ephedrine (base) by titrating aliquot portions with 0·05N hydrochloric acid using methyl orange as indicator.

B. *Absorption onto the hydrogen form of resin from aqueous solutions of ephedrine hydrochloride.*

Closed tube method. The technique was the same as for the subsequent stages of absorption, described above, except that 50 ml portions of solutions of ephedrine hydrochloride were used and the contents of the tubes were analysed for free hydrochloric acid by titration with carbonate free 0·05N sodium hydroxide solution using methyl red as indicator. The absorption does not proceed to capacity and an equilibrium is set up.

Column method. 0·12N ephedrine hydrochloride solution was slowly passed through a column (20 cm × 1 cm) containing 2·54 mg equiv of hydrogen form of resin b, for seven days until the pH of the overnight effluent was the same as that of the influent. The amount of *free* hydrochloric acid found in the combined effluents was taken as equivalent to the amount of ephedrine absorbed onto the resin. The absorption in this case proceeds to the capacity of the resin sample because hydrochloric acid formed is removed by the downwards flow of the solution in the column.

C. *Absorption onto the sodium form of the resin from aqueous solutions of ephedrine hydrochloride.* A series of 2·54 mg equiv portions of hydrogen form of resin *b* were converted to the sodium form by shaking with 50 ml portions of a mixed solution of 0·2N sodium hydroxide and 0·8N sodium chloride. Each resin portion was washed and transferred to a closed tube to which was added 50 ml of 0·12N solution of ephedrine hydrochloride. The tubes were rotated in thermostat bath and their contents analysed for ephedrine by a modification of the colorimetric method of Allport & Jones (1942).

D. *Absorption of ephedrine onto the sodium form of the resin from aqueous solution of ephedrine.* The method was identical with that used for the preceding system, except that instead of 0·12N ephedrine hydrochloride solution, 0·12N ephedrine (free base) solution was used.

The amount of ephedrine absorbed onto the resin after three days was found to be 0·18 mg equiv, that is the F value was 0·07, showing that only a small amount of ephedrine was taken up by the sodium form of the resin, probably by a physical solution rather than by an exchange process.

Results and discussion

Absorption of ephedrine onto the hydrogen form of resin from ephedrine solutions. The Bt–t plots (Chaudhry & Saunders, 1956) for the initial stages of absorption (internal indicator method) were linear passing through the origin and it was possible to calculate the rate constant, B, in sec^{-1} and also the effective diffusion coefficient, D.

TABLE 2. EFFECT OF SOLUTION CONCENTRATION WITH RESIN *b* AT 25°, FOR THE INITIAL STAGES OF ABSORPTION

Concentration of ephedrine solution (N)	Rate constant, B $sec^{-1} \times 10^5$	Effective diffusion coefficient D $cm^2/sec^{-1} \times 10^8$
0·06	8·56	1·09
0·09	9·09	1·16
0·12	9·72	1·24
0·20	11·20	1·43
0·30	12·70	1·62
0·40	13·90	1·77
0·50	14·75	1·88
0·60	15·52	1·98
0·70	16·20	2·06
0·80	16·65	2·12

Effect of change in solution concentration. The values of the rate constant B, and also effective diffusion coefficient D (Table 2), increase with increase in solution concentration. The graph of D against solution concentration (C in g equiv/litre) could be fitted by an equation:

$$10^8D = 0.942 + 2.47C - 1.24C^2$$

The plots of F (combined for both initial and subsequent stages of absorption) against time (t) show that though the rate of absorption onto the resin *b* is higher with 0·66N solution than with 0·12N solution for

the initial stages of absorption (ratio of B for 0·66N/0·12N = 1·58) the two curves join after 6 hr and absorption to capacity proceeds in six days with both the solutions.   It can therefore be concluded that (i) the rate of absorption of ephedrine is affected by the solution concentration at the initial stages of absorption but not at the subsequent stages of absorption, (ii) the rate of absorption depends on the amount of ephedrine already absorbed onto the resin and (iii) the rate controlling mechanism is the diffusion of ephedrine into the resin particles which is a slow process particularly in the later stages when ephedrine is entering the innermost channels.

TABLE 3.   EFFECT OF RESIN PARTICLE ON ABSORPTION (INITIAL STAGES) OF EPHEDRINE AT 25°

Resin sample	Observed swollen diameter, mm	0·12N ephedrine concentration		0·66N ephedrine concentration	
		B sec^{-1} × 10^6	D cm^2 sec^{-1} × 10^8	B sec^{-1} × 10^6	D cm^2 sec^{-1} × 10^8
a	0·71	9·86	1·26	15·65	1·99
c	0·45	23·60	1·48	35·78	1·85

Effect of resin particle size (Table 3).   The rate constant, B, increases with the decrease in the resin particle size but the effective diffusion coefficient, D, remains almost constant at a particular solution concentration.

The value of B should be inversely proportional to the square of the particle radius, therefore the square root of the ratio of the values of B for a given ephedrine solution concentration should equal the inverse ratio of the mean particle diameters.   This inverse ratio of diameters of resin fractions *b* and *c* is 1·57; with 0·12N ephedrine solution concentration, the square root of the ratio of B values is 1·7; with 0·66N solution concentration it is 1·52.   This represents a reasonable agreement with the theory (Boyd & others, 1947; Reichenberg, 1953; Chaudhry & Saunders, 1956) considering the uncertainty in the mean particle diameter estimates. The ratio of values of D is 0·94 for the 0·66N solution and 1·18 for the 0·12N solution; this ratio should be equal to one in an ideal case.

Effect of degree of cross-linking.   Keeping the particle size constant, the rate constant is found to increase with decrease in percentage cross-linking (C.L.) (Table 4).   The effective diffusion coefficients D cm^2 sec^{-1} (× 10^9) are 636, 13·7 and 3·4 for the 4·5, 9 and 13·5% C.L. resins respectively;

TABLE 4.   EFFECT OF DEGREE OF CROSS-LINKING OF THE RESIN ON ABSORPTION (INITIAL STAGES) OF EPHEDRINE FROM 0·12N SOLUTION CONCENTRATION AT 25°

Resin	a	b	c	d
Cross-linking (%) D.V.B.	4·5	9	9	13·5
Swollen particle diameter (mm)	0·70	0·71	0·45	0·45
Water absorptions (mg/mg equiv of dry resin H)	342	169	—	124
B sec^{-1} × 10^6	512	9·86	28·60	6·62
D cm^2 sec^{-1} × 10^9	636	12·56	14·82	3·43

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the value of 13·7 for the 9% C.L. resin has been taken as the mean of 12·56 and 14·82 found with resins *b* and *c*. The water absorptions per mg equiv of the dry resins (hydrogen form) have been found to be 342, 169 and 124 mg for the 4·5, 9 and 13·5% C.L. resins, respectively. The rate of absorption of ephedrine, the value of D, and the water absorptions of the dry resins are all found to decrease with increase in the percentage of cross-linking of the resins.

TABLE 5. EFFECT OF SOLUTION CONCENTRATION, PARTICLE SIZE AND CROSS-LINKING OF THE RESIN ON PERCENTAGE ABSORPTION OF EPHEDRINE, i.e. F $\times$ 100 AT 25°

Time	0·12N solution concentration				0·66N solution concentration resin *b*
	Resin *a*	Resin *b*	Resin *c*	Resin *d*	
0·5 hr	100·1	38·0	67·6	33·2	47·2
1 hr	—	50·0	68·3	40·8	58·6
2 ,,	—	62·4	78·3	48·6	67·9
3 ,,	—	70·2	82·9	—	73·7
4 ,,	—	74·5	85·7	54·8	77·6
5 ,,	—	78·8	88·0	—	80·3
6 ,,	—	81·8	89·3	57·7	81·8
24 ,,	—	93·5	96·8	65·8	93·4
48 ,,	—	96·5	99·1	—	96·6
72 ,,	—	98·4	99·7	—	98·4
96 ,,	—	99·2	100·2	—	99·3
120 ,,	—	99·5	100·1	—	99·7
144 ,,	—	99·8	—	80·6	99·9
2 weeks	—	—	—	83·3	—
1 month	—	—	—	86·8	—
2 months	—	—	—	87·2	—

It is seen from Table 5 that although absorption proceeds to capacity with 4·5% C.L. resin in less than 30 min, it takes nearly seven days to do so in the case of 9% C.L. resin (same particle size). This difference is accentuated with the 13·5% C.L. resin where after two months the absorption proceeded to 87·2% of the capacity (F = 0·872).

TABLE 6. EFFECT OF TEMPERATURE ON ABSORPTION (INITIAL STAGES) OF EPHEDRINE; RESIN *b*; SOLUTION CONC. 0·12N

Temperature	25°	30°	35°	40°
Initial rate constant	9·86	12·77	16·61	21·10
Effective diffusion coefficient, D cm^2 sec^{-1} $\times$ 10^8	1·26	1·63	2·11	2·69

Effect of temperature. Increasing the temperature (Table 6) results in an increase of the rate constant and the effective diffusion coefficient. The plot of $\log_{10}$ B sec^{-1} against 1000/T, was linear and a heat of activation calculated from the slope of this plot, was found to be 9 ($\pm$1) kcal mole^{-1}. This value is rather high for a diffusion process, which may be partly due to hindrances experienced by ephedrine in its movements through the pores of the resin. In addition, the fact that the entering ephedrine has to displace nearly its own volume of water from the resin againt the influence of the water attracting sulphonic acid groups, will increase the activation energy for absorption.

Rate controlling mechanism. The fact that plots of Bt-time are linear and pass through the origin, as expected by the particle diffusion theory of Boyd & others (1947), establishes that the rate controlling mechanism is primarily diffusion of ephedrine in the resin particles. Also Kressman & Kitchener's test (1949) for particle diffusion was applied to these results by plotting F values against the square root of time (in min). Linear curves passing through the origin were obtained, as was to be expected if the particle mechanism was operative. Further support for particle mechanism is given by the study of different resin particle sizes.

Absorption of ephedrine onto the hydrogen form of the resin, from aqueous solutions of ephedrine hydrochloride. Absorption of ephedrine, when carried out by the closed tube method, does not proceed to the capacity of the resin, as after 24 hr an equilibrium is set up in which the sulphonic acid groups in the resin and the free hydrochloric acid liberated in the solution compete for the available ephedrine. The Bt-time plots are not linear due to the presence of free hydrochloric acid which tends to elute ephedrine from the resin. The plots of Bt calculated from the values of F' ($F' = Q_t/Q_\infty$) against the experimental value of time were also non-linear.

Absorption of ephedrine onto the sodium form of the resin from aqueous solution of ephedrine hydrochloride. The absorption does not proceed to the capacity of the resin as after about a week, an equilibrium is set up in which the liberated sodium ions and the ephedrine ions present in the solution compete for the sulphonic acid groups of the resin. The Bt-time plots are linear passing through the origin, the values being as follows:

$$B \text{ sec}^{-1} \times 10^5 = 1{\cdot}48; D \text{ cm}^2/\text{sec} \times 10^9 = 1{\cdot}88$$

It is seen that the rate constant and the effective diffusion coefficient are very low (about one-seventh of that of absorption on to the hydrogen form of the resin—Table 3) which is probably due to relatively greater work required to be done by the diffusing ephedrine ions to drive out the sodium ions. There was hardly any change in the resin particle size to account for this slow rate.

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