1040. *The Sorption of Oxytetracycline and Chlorotetracycline by Sulphonated Polystyrene Resins*

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The effect of the structure of the ion-exchange resin on the sorption of oxytetracycline and chlorotetracycline ions by sulphonated polystyrene resins has been investigated. Evidence has been obtained for the aggregation of these ions in the resin. The effect of variations in the degree of cross-linking of the resin structure and the concentration of the functional groups on the selective behaviour of the resin towards these antibiotics is described and discussed.

In investigations of the sorption of organic ions by ion-exchange resins it has been found that the affinities of large organic ions for ion-exchange resins are frequently very much higher than the affinities of small organic and inorganic ions. These high affinities shown by large organic ions cannot be attributed to an increased coulombic interaction between the organic ion and the ionic group in the resin and have generally been considered to be due to the effect of additional interactions between the sorbed ion and the resin matrix, *e.g.*, hydrogen bonding, dipole–dipole or dipole–induced dipole interactions, interactions due to dispersion forces or hydrophobic bonding.

The mechanism of the sorption of large organic ions, and especially antibiotics, by ion-exchange resins has been studied extensively by Samsonov and his co-workers.[1-3] These investigations have involved the study of the effect of resin structure on ion-exchange equilibria and the measurement of the heats and free energies of exchange. From the thermodynamic properties, the relative importance of enthalpy and entropy factors has been assessed and information obtained on the nature and magnitude of the ion-resin interactions.

In studies of the effect of resin structure on the sorption of organic ions the important resin parameters are (*a*) the nature and concentration of the functional groups and (*b*) the physical and chemical structure of the resin matrix. With aqueous systems, these parameters will determine both the water content of the swollen resin and its ion-exchange behaviour. The sulphonated polystyrene resins are very suitable for the study of the exchange of organic ions since these resins can be prepared with reproducible properties and reasonably well-defined structures. The concentration of the functional groups can be varied, without changing the structure of the polymer matrix, using the techniques of partial sulphonation and desulphonation.[4, 5] The structure of the cross-linked polymer network can be modified by varying the proportion of divinylbenzene used as the cross-linking agent or by polymerising the styrene–divinylbenzene mixture in the presence of a diluent. The latter procedure leads to polymers with an expanded network or a macroporous structure.[6]

In the present investigation the sorption of oxytetracycline and chlorotetracycline by two series of sulphonated polystyrene resins has been investigated. In the first series the polymers were fully sulphonated and cross-linked with from 0·5 to 6·6% of divinylbenzene (DVB). In the second series, the resins were cross-linked with 1% of divinylbenzene and the exchange capacity varied from approximately 2 to 5 mequiv./g.

EXPERIMENTAL

Materials.—The fully sulphonated resins cross-linked with 0·5, 1·0, and 6·6% of divinylbenzene were prepared from the corresponding cross-linked polystyrene bead polymers using a procedure essentially similar to that developed by Reichenberg for the controlled sulphonation of cross-linked polystyrene.[4] The resin beads were heated with a mixture of 90 parts by volume of AnalaR nitrobenzene and 10 parts by volume of AnalaR sulphuric acid (98%) at 60° until complete monosulphonation had been achieved. The resins cross-linked with 2 and 4·5% of divinylbenzene were chromatographic grade materials supplied by the Permutit Co. Ltd. (Zeo-Karb 225, SRC 7, and SRC 11). Details of the properties of these resins are in Table 1.

TABLE 1

% DVB in copolymer	Particle diameter of air-dry sulphonated resin (μ)	Ion-exchange capacity (mequiv./g. of dry H-form resin)	Swelling coefficient
0·5	150—250	5·2	22
1·0	124—152	5·17	9·2
2·0	76—104	5·33	3·7
4·5	76—104	5·24	2·8
6·6	76—89	5·1	1·8

The ion-exchange capacities were determined by converting a sample of each resin from the H into the Na form, titrating the H^+ ion liberated, and drying the sample to constant weight. The swelling coefficient, an approximate measure of the degree of swelling in water, is the volume of a bed of the swollen resin divided by the corresponding bed-volume of the dry resin.

The partially sulphonated resins were prepared from a polystyrene bead polymer cross-linked with 1% of divinylbenzene. By using the sulphonation conditions described above and

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[1] G. V. Samsonov, " Sorption and Chromatography of Antibiotics," Academy of Sciences, U.S.S.R., Moscow–Leningrad, 1960.

[2] G. V. Samsonov, A. A. Selezneva, N. P. Kuznetsova, S. B. Tikhomirova, and L. P. Fleer, *Kolloid. Zhur.*, 1963, **25**, 222.

[3] G. V. Samsonov and V. A. Pasechnik, *Zhur. fiz. Khim.*, 1962, **36**, 2727.

[4] D. Reichenberg and D. V. Woodford, to be published.

[5] G. E. Boyd, B. A. Soldano, and O. D. Bonner, *J. Phys. Chem.*, 1954, **58**, 456; S. Lindenbaum, C. F. Jumper, and G. E. Boyd, *ibid.*, 1959, **63**, 1924.

[6] J. R. Millar, D. G. Smith, W. E. Marr, and T. R. E. Kressman, *J.*, 1963, 218, 2779; 1964, 2740.

varying the sulphonation time between 5 and 50 hr. a series of partially sulphonated resins was obtained. Details of these resins are in Table 2.

TABLE 2

Sulphonation time (hr.)	Particle diameter of air-dry sulphonated resin (μ)	Ion-exchange capacity (mequiv./g. of dry H-form resin)	Swelling coefficient
5	76—104	2·29	1·6
8	124—152	3·15	4·6
16	124—152	4·45	9·5
50·5	124—152	5·17	9·2

In each case, after sulphonation, samples of material with a particle diameter greater than 211 μ and less than 76 μ were separated from the product and the ion-exchange capacities of these two samples measured. In no case was the difference between the capacities of the two samples greater than 0·3 mequiv./g. indicating that, as judged by ordinary chemical analysis, approximately uniform partial sulphonation of the copolymer had been achieved. It should however be noted that the more highly cross-linked regions of the resin structure had probably not been sulphonated. The distribution of sulphonic acid groups in the more open regions of the polymer network would be expected to be random.

Oxytetracycline hydrochloride (Karpov Factory, Moscow) and chlorotetracycline hydrochloride (Lederle Laboratories) were used as received.

Sorption Experiments.—A solution of oxytetracycline in dilute hydrochloric acid of known concentration was shaken with a weighed amount of H form resin (of known water content) in a glass bottle fitted with a polyethylene stopper. The bottle was rotated (end over end) in an air thermostat at 23° ± 0·5° until equilibrium was attained. The concentration of the oxytetracycline in solution was then determined using a Unicam S.P. 500 spectrophotometer. The optical absorption at 360 mμ of the solution adjusted to pH 1 was measured and the concentration of the antibiotic calculated from a calibration curve. The pH of the equilibrated solution was also measured using a Doran pH meter and glass electrode. In experiments at pH 1·6 and below there was no significant change in pH on sorption of the antibiotic. The time needed to reach equilibrium was measured in preliminary experiments and was found to vary from 15 min. with the fully sulphonated 1% divinylbenzene resin to *ca.* 3 days with the partially sulphonated resin of lowest exchange capacity. In these preliminary experiments no difference in ion-exchange behaviour at equilibrium was observed between a resin sample with a particle diameter greater than 211 μ and a sample with a particle diameter less than 100 μ.

A similar procedure to that described above was used in the study of the sorption of chlorotetracycline. The changes in particle size on sorption of oxytetracycline were followed by microscopic examination. The diameters of more than 30 resin particles (immersed in the equilibrium solution) were measured and an average diameter calculated.

RESULTS AND DISCUSSION

Both oxytetracycline and chlorotetracycline are amphoteric substances each having one basic and two acidic groups. In this work the exchange of antibiotic and hydrogen ions was investigated. Under the conditions used (pH $\leqslant$2), the oxytetracycline and chlorotetracycline would be present in solution almost entirely in the form of univalent cations; the pK_a values [7] for oxytetracycline are 3·10, 7·26, and 9·11, and for chlorotetracycline 3·30, 7·44, and 9·27. It may therefore be assumed that the exchange process can be represented by the equation

$$\bar{H}^+ + A^+ \rightleftharpoons \bar{A}^+ + H^+$$

where A^+ and H^+ represent the organic and hydrogen ions in solution and the corresponding barred symbols represent ions in the resin phase. We may then define a selectivity coefficient by the equation

$$K_H{}^A = \frac{\bar{c}_A\, c_H}{\bar{c}_H\, c_A} = \frac{\bar{c}_A\, c_H}{(Q - \bar{c}_A)c_A} \qquad (1)$$

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[7] A. Albert, *Nature*, 1953, **172**, 201: "Stability Constants of Metal-Ion Complexes," Special Publication No. 17, The Chemical Society, London, 1964, p. 726.

where c_A and c_H are the concentrations of the two ions in solution, $\bar{c}_A$ and $\bar{c}_H$ are the corresponding concentrations in the resin phase, and Q is the total concentration of counter-ions in the resin. For exchange processes involving univalent ions the value of the selectivity coefficient does not depend on the choice of concentration scale. In this Paper, it is assumed that concentrations both in the resin and in solution are expressed on a molar scale. From equation (1) the selectivity coefficient was calculated from the amount of organic ion sorbed at equilibrium, the total exchange capacity of the resin, and the ratio of the concentrations of the ions in solution.

The results obtained with oxytetracycline, hydrogen ion, and the series of fully sulphonated resins of different degrees of cross-linking are shown in Figure 1 where the selectivity coefficient K_H^O for the oxytetracycline–hydrogen ion system has been plotted against $\bar{X}_O$, the equivalent fraction of oxytetracycline in the resin phase. It will be apparent that the form of these curves is very different from that commonly observed with ion-exchange equilibria involving small univalent ions; usually, the selectivity coefficient K_B^A decreases as the equivalent fraction of A is increased. Each of the curves shown in Figure 1 can be divided into three parts: (*a*) an initial part at low values of $\bar{X}_O$, in which the selectivity coefficient is approximately constant (this part may be absent in the case of the curve for the 6·6% divinylbenzene resin); (*b*) a part in which K_H^O increases rapidly towards a maximum with increasing $\bar{X}_O$; and (*c*) a final part in which K_H^O falls rapidly towards zero. It will also be noted from the results with the 1% divinylbenzene resin that there are corresponding changes in the diameter of the resin particles.

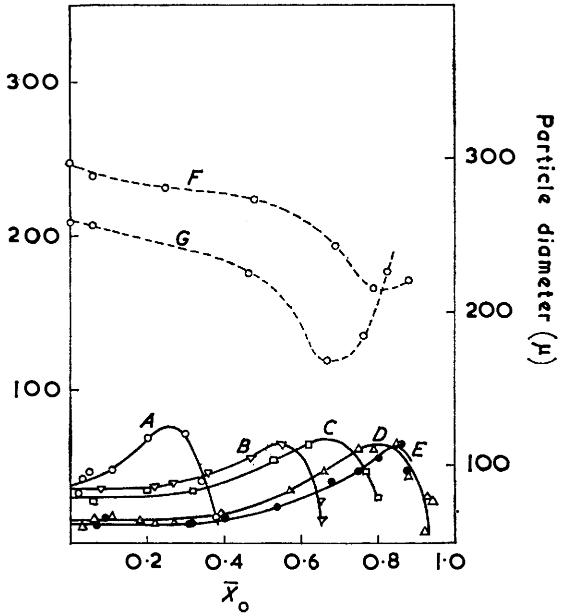

FIGURE 1. Exchange of oxytetracycline and hydrogen ions with fully sulphonated polystyrene resins

(*a*) Selectivity coefficients: *A*, 6·6% DVB resin (pH 1·6); *B*, 4·5% DVB resin (pH 1·6); *C*, 2% DVB resin (pH 1·6); *D*, 1% DVB resin (pH 2·0); *E*, 0·5% DVB resin (pH 1·6). (*b*) Particle diameter of fully sulphonated 1% DVB resin: *F*, at pH 2; *G*, at pH 1.

[DVB = divinylbenzene]

The final part of each curve almost certainly represents the approach to a limiting exchange capacity for oxytetracycline which is less than the exchange capacity of the resin for sodium ion. Values of $\bar{X}_O$ greater than this limiting value cannot be achieved and the limiting exchange capacity can be estimated by extrapolation. This type of behaviour is commonly observed with large organic ions such as antibiotics.[1] The low exchange capacity for the large organic ion may be explained in two ways. First, it may be assumed that there is a lack of space within the resin structure for the accommodation of the organic ion in a concentration equivalent to the total exchange capacity of the resin,[8] even if each of the exchange sites is accessible to the organic ion at low values of

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[8] D. K. Hale, D. I. Packham, and K. W. Pepper, *J.*, 1953, 844.

$\bar{X}_{\rm O}$. The second explanation is that some regions of the resin gel are completely inaccessible to the organic ions even at low values of $\bar{X}_{\rm O}$ and small ions situated at exchange sites in these regions cannot be replaced by the large organic ions.[1] The first explanation can account satisfactorily for the limiting capacities observed in the sorption of organic ions of moderate size, *e.g.*, tetraethylammonium ions from neutral solutions by resins of moderate cross-linking. With larger organic ions such as antibiotics, however, the second explanation is more satisfactory. In the present series of results, for example, a limiting value for $\bar{X}_{\rm O}$ less than unity is observed even with resins containing 1 and 2% divinylbenzene. The weight swelling in water of the H^+ form of the 2% divinylbenzene resin corresponds to the presence of approximately 40 water molecules per sulphonate group so that with these two resins there should, *a priori*, be sufficient space within the extended resin structure for the accommodation of the organic ions. It will be noted from Figure 1 that the limiting value for $\bar{X}_{\rm O}$ decreases with increasing cross-linking and that with the resin containing 6·6% divinylbenzene values of $\bar{X}_{\rm O}$ greater than 0·4 were not achieved. It appears likely that the inaccessible sites are in regions of relatively high cross-linking and that the proportion of these sites increases with increase in the divinylbenzene content of the polymer.

If it is assumed that some of the exchange sites are inaccessible to the large organic ions and that the hydrogen ions in the neighbourhood of these sites do not play any effective part in the exchange process then we may redefine a selectivity coefficient for the exchange process by the equation

$$\boldsymbol{K}_{\rm H}^{\rm A} = \frac{\bar{c}_{\rm A}}{(Q_{\rm A} - \bar{c}_{\rm A})}\,\frac{c_{\rm H}}{c_{\rm A}} \qquad (2)$$

where $Q_{\rm A}$ is the total concentration of counter ions at accessible exchange sites and $(Q_{\rm A} - \bar{c}_{\rm A})$ represents the concentration of hydrogen ions in the resin which can be replaced by organic ions.

When the selectivity coefficients are recalculated using equation (2) then curves of the form shown in Figure 2 are obtained. Here, $\boldsymbol{K}_{\rm H}^{\rm O}$, the redefined selectivity coefficient for the oxytetracycline–hydrogen ion system has been plotted against $\bar{\mathbf{X}}_{\rm O}$ the fraction of accessible sites at which exchange has occurred. $\bar{\mathbf{X}}_{\rm O}$ is given by $\bar{\mathbf{X}}_{\rm O} = \bar{c}_{\rm O}/Q_{\rm O}$ where $\bar{c}_{\rm O}$ is the concentration of oxytetracycline ions in the resin and $Q_{\rm O}$ is the total concentration of oxytetracycline and exchangeable hydrogen ions. When $\bar{c}_{\rm O}$ approaches $Q_{\rm O}$ small experimental errors can lead to large errors in the value of $\boldsymbol{K}_{\rm H}^{\rm O}$. Values of $\boldsymbol{K}_{\rm H}^{\rm O}$ corresponding to values of $\bar{\mathbf{X}}_{\rm O} > 0{\cdot}90$ have therefore been omitted from Figure 2. From the results shown in Figure 2 it will be seen that, with a resin of given cross-linking, the value of $\boldsymbol{K}_{\rm H}^{\rm O}$ is comparatively low at low values of $\bar{\mathbf{X}}_{\rm O}$ but increases rapidly at higher values of $\bar{\mathbf{X}}_{\rm O}$. This rapid increase in $\boldsymbol{K}_{\rm H}^{\rm O}$ suggests that some form of co-operative sorption process is taking place since the oxytetracycline ions are apparently more and more strongly sorbed as the equivalent fraction of oxytetracycline in the resin increases. An effect of this type does not appear to have been observed previously with large organic ions and ion-exchange resins. Gregor, Belle, and Marcus[9] have, however, reported similar behaviour in anion-exchange systems involving ClO_4^-, SCN^-, and $CCl_3{\cdot}CO_2^-$ ions with Cl^- ion as a reference ion. They attributed the increase in selectivity with increasing equivalent fraction of the preferred ion to the formation of clusters or aggregates of counter-ions in the resin phase. The formation of aggregates in the adsorption of various dyes by silver halides, in the sorption of acid dyes by wool and in the sorption of basic dyes by films of oxidised cellulose, alginic acid, and gelatin has previously been described.[10] In these systems, aggregate formation could be detected by changes in the absorption spectrum of the dye. Other related systems include the dye–polymer complexes formed by cationic dyes such

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[9] H. P. Gregor, J. Belle, and R. A. Marcus, *J. Amer. Chem. Soc.*, 1955, **77**, 2713.

[10] D. S. E. Campbell, D. Cathcart, C. H. Giles, and S. M. K. Rahman, *Trans. Faraday Soc.*, 1959, **55**, 1631.

as Acridine Orange and nucleic acids.[11] In these complexes evidence for aggregation has also been obtained from the study of optical properties.

A modified adsorption isotherm in which allowance was made for interactions between molecules adsorbed on a surface was derived many years ago by Frumkin;[12] a more recent derivation is that given by Fowler and Guggenheim.[13] Statistical treatments of the aggregation of dye molecules bound to a linear array of sites as in the dye–polymer complexes have been given by Geisser and Bradley.[14] In the systems now described, however, there is no evidence to indicate that aggregation can be considered to take place on an internal surface or that aggregation is confined to molecules bound to neighbouring sites on the same polymer chain.

For the interpretation of the results obtained with the anion-exchange systems mentioned previously, Gregor, Belle, and Marcus [9] used a model in which the chloride ions formed ion-pairs at random with the exchange groups in the resin but clustering interactions took place between neighbouring ClO_4^-, SCN^-, or $CCl_3{\cdot}CO_2^-$ ion-pairs. These interactions were assumed to lead to the formation of what was essentially a clustered or separate phase. The mass-action law for a heterogeneous system was then applied and theoretical curves calculated for the variation of the ion-concentration ratio in the resin with solution composition. Since, however, in the case of the antibiotic ions there is, at present, no direct evidence for the formation of a separate phase, an alternative theoretical approach is the application of the mass-action law for a homogeneous system. If, in the exchange process

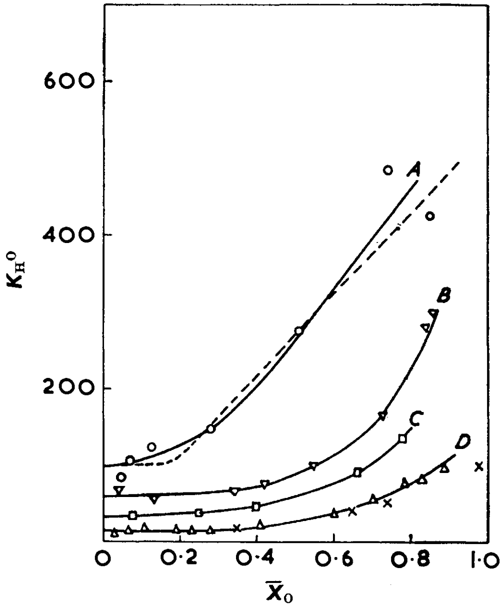

FIGURE 2. Exchange of oxytetracycline and hydrogen ions with fully sulphonated resins. Corrected selectivity coefficients: *A*, 6·6% DVB resin (theoretical variation - - - -); *B*, 4·5% DVB resin; *C*, 2% DVB resin; *D*, 1% DVB resin (theoretical values ×).

$$A^+ + \bar{B}^+ \rightleftharpoons \bar{A}^+ + B^+$$

the A^+ ions form aggregates in the resin phase, then it may be assumed that there is an equilibrium between A^+ ions and aggregates which can be represented by the equation

$$n\bar{A}^+ \rightleftharpoons (\bar{A}_n^{\,n+})$$

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[11] D. F. Bradley, *Trans. N.Y. Acad. Sci.*, Ser. II, 1961, **24**, 64; A. L. Stone and D. F. Bradley, *J. Amer. Chem. Soc.*, 1961, **83**, 3627.

[12] A. N. Frumkin, *Z. phys. Chem.*, 1925, **116**, 466; *Z. Physik*, 1926, **35**, 792.

[13] R. Fowler and E. A. Guggenheim, " Statistical Mechanics," Cambridge University Press, 1956.

[14] S. Geisser and D. F. Bradley, *Bull. Inst. International de Statistique*, 1962, **39**, (4), 269.

where n is the number of ions in each aggregate. The association constant K_a will be given by

$$K_a = \bar{c}_{A_n}/(\bar{c}_A)^n \tag{3}$$

where $\bar{c}_{A_n}$ and $\bar{c}_A$ represent the concentrations of the associated and non-associated ions in the resin phase. It may also be assumed that the distribution of non-associated ions between resin and solution can be represented by the relationship

$$K_{\mathbf{B}}{}^{A} = \frac{\bar{c}_A}{\bar{c}_{\mathbf{B}}}\frac{c_{\mathbf{B}}}{c_A}$$

If the total concentration of A^+ ions in the resin phase is represented by $\bar{c}_{\bar{A}}$ then

$$\bar{c}_{\bar{A}} = \bar{c}_A + n\bar{c}_{A_n}$$

and if

$$K_{B}{}^{\bar{A}} = \frac{\bar{c}_{\bar{A}}}{\bar{c}_{\mathbf{B}}} \cdot \frac{c_{\mathbf{B}}}{c_A} \tag{4}$$

then it can be shown that

$$\log\,(K_{\mathbf{B}}{}^{\bar{A}} - K_{\mathbf{B}}{}^{A}) = \log nK_aK_{\mathbf{B}}{}^{A} + (n-1)\log \bar{c}_A \tag{5}$$

$$= \log nK_aK_{\mathbf{B}}{}^{A} + (n-1)\log\,(\bar{c}_{\bar{A}}K_{\mathbf{B}}{}^{A}/K_{\mathbf{B}}{}^{\bar{A}})$$

$$= \log nK_aK_{\mathbf{B}}{}^{A} + (n-1)\log\,(\bar{X}_{\bar{A}}Q_XK_B{}^{A}/K_{\mathbf{B}}{}^{\bar{A}}) \tag{6}$$

where $\bar{X}_{\bar{A}}$ is the equivalent fraction of A ions (associated and non-associated) in the resin phase and Q_X is the molar concentration of exchange groups in the resin. With a given resin, Q_X will depend on the degree of volume swelling of the resin and may therefore vary significantly with $\bar{X}_{\bar{A}}$. If a certain fraction of the exchange sites are inaccessible then it can similarly be shown that

$$\log\,(\boldsymbol{K}_{\mathbf{B}}{}^{\bar{A}} - \boldsymbol{K}_{B}{}^{A}) = \log nK_a\boldsymbol{K}_{B}{}^{A} + (n-1)\log\,(\bar{\boldsymbol{X}}_{\bar{A}}\;\boldsymbol{Q}_X\boldsymbol{K}_{\mathbf{B}}{}^{A}/\boldsymbol{K}_{\mathbf{B}}{}^{\bar{A}}) \tag{7}$$

where $\boldsymbol{K}_{\mathbf{B}}{}^{\bar{A}}$ and $\boldsymbol{K}_{\mathbf{B}}{}^{A}$ are selectivity coefficients defined as in equation (2), $\bar{\boldsymbol{X}}_{\bar{A}}$ is the equivalent fraction of accessible sites at which exchange has occurred and $\boldsymbol{Q}_X$ is the total concentration of counter-ions at accessible exchange sites.

Using the above equation we calculated theoretical values for $\boldsymbol{K}_H{}^{O}$ corresponding to different values of $\bar{\boldsymbol{X}}_O$ for the fully sulphonated 1 and 6·6% DVB resins. In the case of the 6·6% DVB resin, $\boldsymbol{Q}_X$ was assumed to be constant and equal to $\boldsymbol{Q}_H$, the concentration of replaceable H^+ ions in the H form resin. The latter was estimated using the swelling data of Kressman and Millar.[15] It was also assumed that $\boldsymbol{K}_B{}^{A} = 100$, $n = 50$, and $\log nK_a = 32{\cdot}4$. The theoretical variation of $\boldsymbol{K}_H{}^{O}$ with $\bar{\boldsymbol{X}}_O$ is represented by the discontinuous line in Figure 2. With the 1% divinylbenzene resin, there were relatively large changes in resin volume as $\bar{\boldsymbol{X}}_O$ increased (see Figure 1) and a correction was therefore applied for variations in $\boldsymbol{Q}_X$. It was also assumed that $\boldsymbol{K}_{\mathbf{B}}{}^{A} = 15$, $n = 15$, and $\log nK_a = 11{\cdot}0$. Theoretical values of $\boldsymbol{K}_H{}^{O}$ for different values of $\bar{\boldsymbol{X}}_O$ with the 1% divinylbenzene resin are also shown in Figure 2. In these calculations, a value for $\boldsymbol{K}_B{}^{A}$ has been assumed and K_a and n have been adjusted to give the required variation in $\boldsymbol{K}_H{}^{O}$ with $\bar{\boldsymbol{X}}_O$ so that the approximate agreement between the calculated and experimental results is not very significant. Nevertheless, the values chosen for K_a and n are plausible, and the approximate agreement of the calculated and experimental results lends support to an interpretation of the results in terms of aggregate formation.

If the process of cluster or aggregate formation can be described by equation (7) then it can be seen that as $\bar{\boldsymbol{X}}_{\bar{A}}$ approaches zero, $\boldsymbol{K}_B{}^{\bar{A}}$ approaches $\boldsymbol{K}_{\mathbf{B}}{}^{A}$ and we may therefore assume that at low values of $\bar{\boldsymbol{X}}_{\bar{A}}$ the concentration of aggregates will be negligible and the

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[15] T. R. E. Kressman and J. R. Millar, *Chem. and Ind.*, **1961**, 1833.

observed selectivity coefficient will correspond to that for the individual ions. In Figure 2, it will be observed that, with the exception of the 6·6% divinylbenzene resin, there is, at low values of $\bar{X}_{\rm O}$ relatively little variation in $K_{\rm H}^{\rm O}$ with $\bar{X}_{\rm O}$ and the value of $K_{\rm H}^{\rm O}$ at $\bar{X}_{\rm O} = 0$ may be taken as that corresponding to the exchange of oxytetracycline ions in the absence of aggregate formation in the resin phase. For the different resins, the value of $K_{\rm H}^{\rm O}$ at $\bar{X}_{\rm O} = 0$ increases with increase in cross-linking. This effect can be attributed to an increase in the concentration of the organic polymer matrix in the swollen resin leading to an increased probability of interactions between the organic ions and the polymer matrix. A similar effect on increasing the degree of cross-linking of the resin has been observed in, for example, the sorption of amino-acids by sulphonated polystyrene resins.[16]

The results obtained in the study of the sorption of oxytetracycline by the series of partially sulphonated resins are shown in Figure 3. It will be seen that with all three resins there is a rapid fall in $K_{\rm H}^{\rm O}$ at high values of $\bar{X}_{\rm O}$ indicating a maximum exchange capacity for oxytetracycline which is less than that for sodium ion. In the case of the resin with an ion-exchange capacity of 4·45 mequiv./g. of dry H-form resin, the variation in $K_{\rm H}^{\rm O}$ with $\bar{X}_{\rm O}$ is very similar to that observed with the fully sulphonated resin (see Figure 1) and there is again an increase in the value of $K_{\rm H}^{\rm O}$ at intermediate values of $\bar{X}_{\rm O}$ indicating aggregate formation. When the ion-exchange capacity of the resin is reduced to 2·29 mequiv./g. (curve *A*) there is a very large increase in the value of $K_{\rm H}^{\rm O}$ at low values of $\bar{X}_{\rm O}$ and the selectivity coefficient falls continuously as $\bar{X}_{\rm O}$ increases. The form of the curve suggests that this resin contains a small proportion of exchange sites at which oxytetracycline is very strongly bound. It is most unlikely that this very great increase in the selectivity coefficient is due merely to an overall increase in the concentration of the organic matrix since there is no indication of an effect of this kind with the fully sulphonated 6·6% divinylbenzene resin. As will be seen from Figure 3, the partially sulphonated resin with an exchange capacity of 3·15 mequiv./g. shows a behaviour intermediate between that of the fully sulphonated resin and the resin of lower exchange capacity. The high values of $K_{\rm H}^{\rm O}$ at low values of $\bar{X}_{\rm O}$ observed with the two resins of

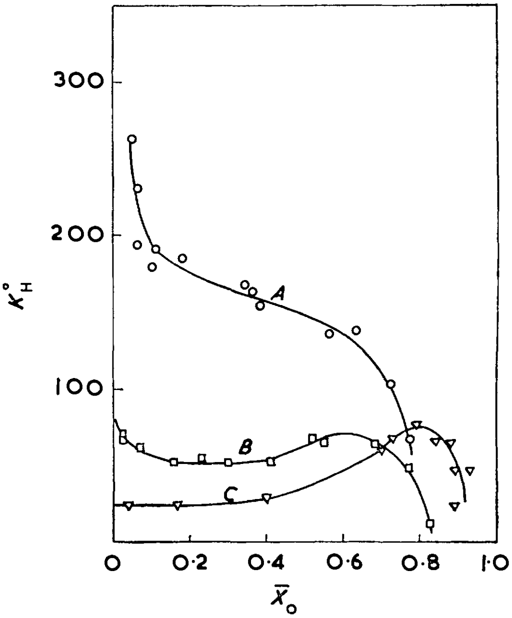

FIGURE 3. Exchange of oxytetracycline and hydrogen ions. Effect of degree of sulphonation of 1% DVB resin. Resin capacities: *A*, 2·29; *B*, 3·15; and *C*, 4·45 mequiv./g. of dry H form resin.

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[16] J. Feitelson, *J. Phys. Chem.*, **1963**, **67**, 2544.

lowest capacity suggest that in these resins there are exchange sites, possibly in the neighbourhood of highly cross-linked regions, where conditions are especially favourable for interactions with the resin matrix. The rapid fall in $K_H{}^O$ indicates that the proportion of these sites may be small.

The results obtained in the study of the exchange of chlorotetracycline and hydrogen ions with two fully sulphonated resins are shown in Figure 4 where $K_H{}^C$ has been plotted against $\bar{X}_C$. With the 0·5% divinylbenzene resin the results are very similar to those obtained with oxytetracycline and the rise in $K_H{}^C$ with increasing $\bar{X}_C$ again indicates aggregate formation. With the 6·6% divinylbenzene resin the results are very different: a low limiting exchange capacity for chlorotetracycline is observed but the selectivity coefficient reaches very high values at low values of $\bar{X}_C$. The form of this curve, which is similar to that observed with the low-capacity resins and oxytetracycline indicates that this resin contains a small proportion of sites at which chlorotetracycline is bound very much more strongly than oxytetracyline.

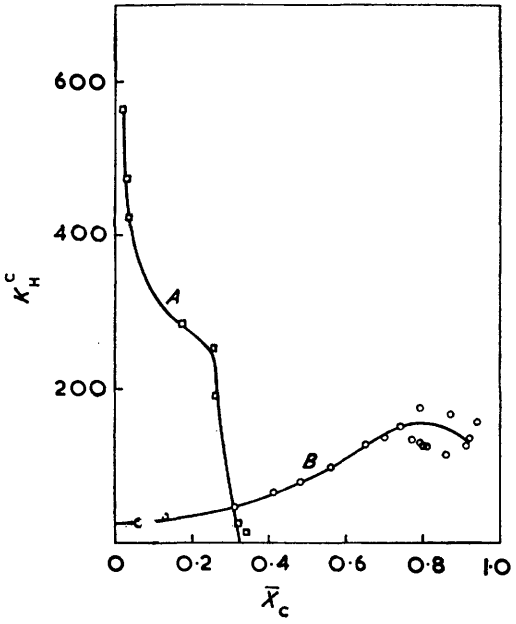

FIGURE 4. Exchange of chlorotetracycline and hydrogen ions with fully sulphonated resins. *A*, 6·6% DVB resin; *B*, 0·5% DVB resin.

The results of this study of the sorption of oxytetracycline and chlorotetracycline by sulphonated polystyrene resins show that the factors which determine the selectivity coefficient are complex. Evidence has been obtained for aggregate formation in the resin phase and, in general, an increase in cross-linking or a reduction in exchange capacity leads to an increase in selectivity but it appears likely that other structural factors can also lead to very large changes in the value of the selectivity coefficients.

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