CHAPTER **10**

Ion Exchange

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Ion exchangers may be described as insoluble solids of complex structure which contain cations or anions capable of being exchanged for other cations or anions in stoichiometrically equivalent amounts. The process whereby such an exchange of ions occurs is referred to as *ion exchange*. The process is usually a reversible one.

The development of the technique of ion exchange has evolved over count-less centuries, although its serious study has been fairly recent. Historical references indicate that ion exchange was utilized as far back as Biblical times.[1] The current interest in this phenomenon, however, was initiated in 1850 by the work of Thompson and Way[2] in their study of soil samples. Their investigations showed that calcium in soil was exchanged for ammonium ions as a solution of ammonium sulfate or carbonate was added to soil. The

results of this study stimulated further experimentation regarding the ion exchange capabilities of various soils, clays, zeolites, and inorganic silicates. Applications of the inorganic ion exchangers, however, were somewhat hampered by their limited stability over a wide range of pH.

Hence, the synthesis of sulfonic acid resins and polyamine resins by Adams and Holmes,[3] in 1935, and the synthesis of styrene and acrylic resins by D'Alelio,[4] in 1944, greatly improved the possibility of utilizing ion exchange resins in various industrial and analytical procedures. Since then, organic exchangers have been prepared in a variety of structures so that specific purposes may be accomplished by their use.

10.1 TYPES OF EXCHANGERS

Although organic ion exchange resins are employed most commonly, this does not preclude the use of other materials capable of exchanging ions. Thus, many substances such as inorganic compounds, coals, and immiscible liquids find application in numerous instances.

In any case, the ion exchanger is depicted as a three-dimensional network of atoms carrying a positive or negative charge together with sufficient mobile ions of opposite charge to provide an electrically neutral system. For example, a cation exchanger is described as a macromolecular anion with mobile cations, whereas an anion exchanger is a macromolecular cation with mobile anions. It is these mobile, or counter, ions which are capable of being exchanged for other ions of the same sign when a solution of electrolyte is added to an exchanger. The mobile ions may be hydrogen, sodium, chloride hydroxyl, sulfate, and similar small ions.

Ion exchange resins are composed of irregular three-dimensional hydrocarbon networks to which various functional ionic groups are attached. Cation exchangers are usually prepared with either sulfonic, carboxylic, phenolic, phosphoric, or phosphonous acid groups. Anion exchangers possess primary, secondary, tertiary, or quaternary amine groups. A single ionic group or a combination of similarly charged groups may be present in the resin. In the case of the amphoteric ion exchangers both positively and negatively charged functional groups are included in the resin.

The hydrocarbon network results from the polymerization of appropriate compounds through condensation or addition reactions. Condensation of aromatic or aliphatic sulfonic acids with phenols and formaldehyde, of phenolic carboxylic or sulfonic acids with formaldehyde, and of phenoxyacetic acid and related compounds with formaldehyde, produce polymers which act as cation exchangers. Similar reactions between aromatic amines and formaldehyde; aliphatic amines, formaldehyde and phenol; or aliphatic amines and dichloroethane or epichlorhydrin result in the formation of polymers which exhibit anion exchange properties.
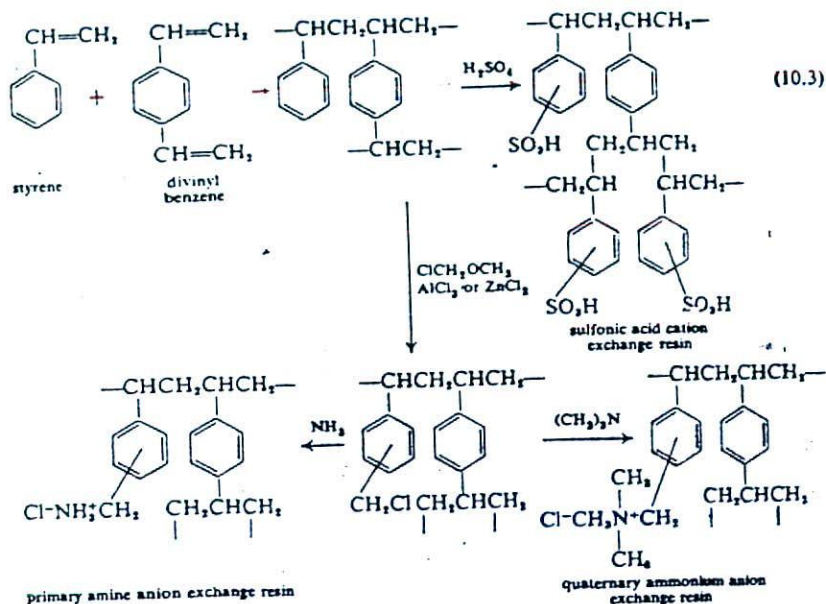
Reactions (10.1) and (10.2) illustrate the preparation of ion exchange resins by condensation polymerization.

$$(10.1)$$

$$(10.2)$$
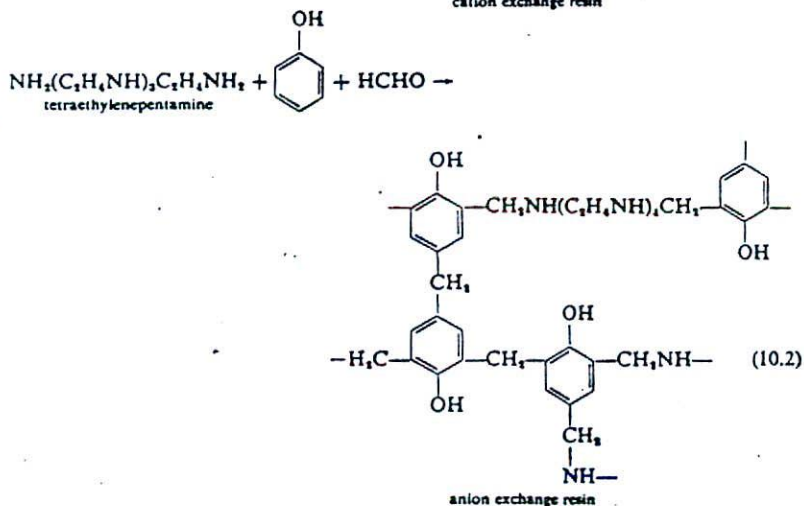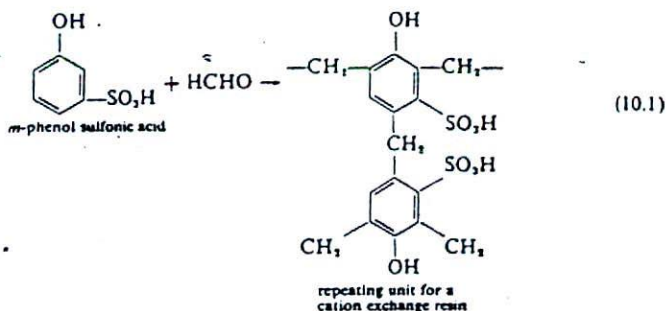
Ion exchangers in current use are usually prepared by addition polymerization reactions. These resins are more stable to heat and chemicals than the condensation polymers, there is greater flexibility in the particle size obtained, and the degree of cross-linking within the polymer can be regulated more easily.

(Cationic resins of this type are prepared by the interaction of divinylbenzene, butadiene, or isoprene with acrylic acid, methacrylic acid, or styrene, followed by treatment with sulfuric acid, chlorosulfonic acid, or phosphorus trichloride.) (With the anionic resins ammonia or primary-, secondary-, or tertiary-alkyl amines are reacted either directly with the polymer or after the polymer has undergone chloromethylation or nitration.)

Addition polymerization of styrene and divinylbenzene and the introduction of cationic and anionic groups is indicated in reaction (10.3).

CH=CH₂   CH=CH₂   —CHCH₂CHCH₂—   —CHCH₂CHCH₂—

(benzene rings)   (10.3)

H_2SO_4

CH=CH₂   —CHCH₂—   SO₃H   CH₂CHCH₂
styrene   divinyl   —CH₂CH   CHCH₂—
          benzene

SO₃H   SO₃H
sulfonic acid cation
exchange resin

$ClCH_2OCH_3$
$AlCl_3$ or $ZnCl_2$

—CHCH₂CHCH₂—   —CHCH₂CHCH₂—   —CHCH₂CHCH₂—

NH_3 $(CH_3)_3N$

Cl⁻NH₃⁺CH₂   CH₂CHCH₂   CH₂Cl CH₂CHCH₂   CH₃
                                         Cl⁻CH₂N⁺CH₃   CH₂CHCH₂
                                         CH₃

primary amine anion exchange resin   quaternary ammonium anion
                                          exchange resin

Since several different resin polymers could result from any one particular reaction, the formulas usually given merely represent a possible structure which might exist in the resin.

Other ion exchange resins for specific purposes have been synthesized, particularly those with chelating groups or optically active groups. Resins with a quinone structure can act as insoluble oxidizing or reducing agents, where an exchange or transfer of electrons rather than ions takes place.

The organic ion exchange resins, for the most part, exhibit insolubility in the common solvents, stability to heat, chemicals and mechanical action, and high ion exchange capacities. The fact that they can be prepared with various ionic groups present and with differing degrees of cross-linking in the resin structure provide additional advantages, in that the resin can be made to meet the needs of a particular situation.

The *inorganic ion exchangers* include certain minerals, synthetic zeolites, and metallic salts. The minerals which act as cation exchangers are the zeolites (analcite, natrolite, chabazite), clays (beidellite, montmorillonite), and glauconites. All are aluminosilicates with alkali or alkaline earth cations which can be exchanged for other cations. The minerals apatite and hydroxyapatite are the principal anion exchange substances.

The synthetic inorganic compounds used for ion exchange purposes usually resemble the natural zeolites. The early compounds had an irregular crystalline structure somewhat similar to that of the ion exchange resins. More recent products, the molecular sieves, possess a regular crystalline structure approximating the natural zeolites.

Hydrous oxides of tri- and tetravalent metals have been employed as cation

exchangers; however, they are not particularly stable in the presence of either acid or base. The tetravalent metals in the form of their phosphates, molybdates, tungstates, arsenates, and vanadates function more satisfactorily as cation exchangers. The latter, when compared to the organic resins, have high exchange capacities, greater stability to temperature changes, greater selectivity for simple inorganic ions, and greater resistance to the effects of radiation.

TABLE 10.1: Commercially Available Ion Exchangers

Name	Type	Composition	Manufacturer
Duolite C-63	Cation	Polystyrene phosphonic acid resin	Chemical Process Co.
Duolite C-62	Cation	Polystyrene phosphonous acid resin	Chemical Process Co.
Amberlite IR-120	Cation	Polystyrene sulfonic acid resin	Rohm & Haas Co.
Amberlite IRC-50	Cation	Methacrylic carboxylic acid resin	Rohm & Haas Co.
Dowex 50	Cation	Polystyrene nuclear sulfonic acid resin	Dow Chemical Co.
Duolite A-30	Anion	Aliphatic amine resin, tertiary and quaternary	Chemical Process Co.
Amberlite IR-4B	Anion	Phenolic amine resin	Rohm & Haas Co.
Amberlite IR-45	Anion	Polystyrene amine resin	Rohm & Haas Co.
Dowex 1	Anion	Polystyrene trimethyl-benzyl ammonium resin	Dow Chemical Co.
Permutit SK	Anion	Quaternary amine resin, pyridinium groups	Permutit Co.
Zeo-Karb	Cation	Sulfonated coal	Permutit Co.
Zeo-Dur	Cation	Processed glauconite	Permutit Co.
Decalso	Cation	Sodium alumino-silicate	Permutit Co.
Molecular sieve 4A	Cation	Synthetic zeolite	Linde Co.
Bio-Rad ZP-1	Cation	Zirconium phosphate	Bio-Rad Labs.
DEAE-cellulose	Anion	Diethylaminoethyl cellulose	Brown Co.
CM-cellulose	Cation	Carboxymethyl-cellulose	Brown Co.
D2EHPA	Cation	Di-2-ethylhexyl phosphoric acid	Union Carbide Chemical Co.
Aliquat 336	Anion	Tricaprylmethyl-ammonium chloride	General Mills, Inc.
Duolite S-10	Redox	Amine resin containing copper	Chemical Process Co.
Retardion 11-A-8	Chelating	Dowex 1 containing polyacrylate anion	Dow Chemical Co.
Amberplex C-1	Cation	Resin membrane	Rohm & Haas Co.
Nepton AR-111-A	Anion	Resin membrane	Ionics, Inc.

Coal is used as an ion exchanger, especially in the sulfonated form, where sulfonic acid groups are added to the weak acid groups already present in the material. The sulfonated coals are similar in action to the organic resins, although they have a less uniform structure and are less resistant to the effect of chemicals and mechanical abuse.

Liquid ion exchangers are water immiscible long-chain aliphatic amines, which act as anion exchangers, or fatty-acid dialklyphosphates, which function as cation exchangers. Aside from the fact that these substances are liquids their ability to exchange ions is much the same as insoluble solids.

Some of the commercially available ion exchangers are given in Table 10.1.

10.2 MECHANISM OF ION EXCHANGE

A multiplicity of ideas has developed over a period of years to explain the phenomenon of ion exchange. Since the process involves many variables, the theory tends to be very complex, especially from a mathematical point of view. Some of the factors considered are the ions involved in the exchange (concentration, number of different kinds of ions, properties of individual ions), the ion exchanger employed (structure, exchange capacity, degree of crosslinking, swelling properties, sorption properties), temperature, solvent system, diffusion effects, and electrochemical properties. A comprehensive treatment of the theoretical aspects of ion exchange is given by Helfferich.[5] Much of the theory is related to ion exchange resins.

In most ion exchange operations it is preferable to work with dilute solutions to attain an effective transfer of ions. When an ion exchanger is placed in a solvent, varying quantities of solvent are sorbed, causing the exchanger to swell. The hydrocarbon network expands as much as the crosslinking of the molecule will permit, and solvent molecules enter the network. The swelling continues until the forces causing the expansion of the network by repulsion of similarly charged ions is counterbalanced by the forces causing the solvation of the ions of the network and dilution of the ionic concentration by the solvent through osmotic pressure differences.

The swelling is usually more pronounced in the presence of polar solvents than nonpolar ones, in that the presence of the fixed ionic groups tends to promote greater forces of solvation, repulsion, and osmotic effect. Exceptions are noted, however, with some resins. The more polar and more highly ionized these ionic groups in the resin become, the greater will be the tendency for swelling. With some nonpolar solvents, marked swelling may take place as a result of the attraction of the solvent for the nonpolar portions of the exchanger molecule.

The kind of ion in solution may also influence the swelling factor and exchange of ions from the resin. Ions which are readily solvated tend to aid the expansion of the resin network. That is, when a solvated ion replaces

another ion already within the resin, the solvated ion occupies a greater volume and the resin expands to make room for this new ion. With strong cationic exchangers in aqueous solutions the hydration of ions and swelling of the resin follow the same pattern, for example,

$$Li > Na > NH_4 > K > Rb > Cs \quad \text{and} \quad Mg > Ca > Sr > Ba$$

The reverse of these sequences is noted in the sorption of ions by the resin; that is, the ions which are hydrated most are bound to the resin least strongly and hence are more easily exchanged. When concentrated solutions of electrolytes are used or when weakly acidic cationic exchangers are involved, the order of exchange may be the reverse of that found with the strong sulfonic acid exchangers.

The valence of the ion in solution may affect the swelling of a resin considerably, particularly if the resin has a low percentage of cross-linking units. In this case, the lower the valence of the ion, the more it contributes to the swelling. As the ions within the resin become solvated, solvent is introduced into the resin and expansion results. Since there are a certain number of ionic sites within the resin that may be involved in the exchange of ions, it is apparent that if more ions are present, more solvent will be carried along with them. Thus, the swelling effect here depends on the numbers of ions present. If, for example, divalent ions, instead of univalent ions, are present in solution form, only half as many ions could be exchanged and proportionally less solvent introduced into the resin structure. The osmotic effect also depends on the number of particles present, and so this, too, would be decreased, and swelling would be diminished. With resins which are highly cross-linked, the opposite effect of valence may be observed.

In the exchange of ions it is usually noted that ions with higher valences are more strongly sorbed by a resin than ions of lower valence, for example,

$$Th > Al > Ca > Na$$

If a more highly concentrated solution is used, this order is often reversed.

The effects of swelling, sorption, and exchange with anionic resins follows much the same pattern as cationic resins, although they have not been studied quite so thoroughly. A typical order for increasing exchange ability of anions is

sulfate < chromate < citrate < tartrate < nitrate < arsenate < phosphate < molybdate < acetate, iodide, bromide < chloride < fluoride

The hydroxyl ion would be found at the end of the series when strong basic resins are used and at the beginning of the series with weak basic resins. Deviations within the sequence may be noted as the concentration of the ions in solution is increased, the pH is varied or the degree of cross-linking in the resin is modified.

Exchangers tend to become more selective for ions as the degree of cross-linking is increased.

Nonelectrolytes and weak electrolytes are usually sorbed by ion exchangers much more strongly than electrolytes. Sorption is enhanced by the formation of complexes between the ionic portions of the exchanger and the nonelectrolyte solute. Sorption is decreased when the solute molecule becomes too large to enter the exchanger network; the exchanger then acts as a filter or sieve. Sorption is also decreased by a salting-out effect when there is not sufficient free solvent available to keep the solute in solution. Highly cross-linked resins and highly solvated counter ions contribute to the latter condition.

The behavior of ion exchangers to the effects of the various factors influencing the process is sometimes depicted by visualizing the exchanger either in the form of a crystalline lattice structure or a membrane or a two-layer structure or a combination of these.

In the *crystal lattice* approach[6,7] the exchanger is pictured as a completely dissociated solid in which each ion is surrounded by a fixed number of ions of opposite charge. Since the ions on the surface are less influenced by attractive forces than the underlying layers of ions, the surface ions are readily exchanged for other ions, especially when the exchanger is placed in a highly polar solvent such as water. The crystalline structure is rather rigid and is limited in its ability to swell and to accommodate ions and molecules of various sizes. If the counter ions are too large, a sieve effect rather than exchange will take place. The ion selectivity will depend on how strongly the surface ion is held by attractive forces within the crystal.

Since a crystalline structure is found primarily with the inorganic ion exchangers, these are the materials most affected by this approach of ion exchange action. This view has been applied to ion exchange resins even though the resins are not crystalline in nature. This explanation might be used to illustrate the sieve action of both the inorganic and resin exchangers. Sieve action with ion exchange resins is most evident when the degree of cross-linking is high and the counter ions are very large.

When the action of ion exchange is compared to that of a semipermeable *membrane*,[8] the large, somewhat flexible, polymeric portion of the exchanger containing the exchangeable ion is considered a nondiffusible ion, and the junction between the solid and liquid phases is considered to be the membrane. In such a system there is an unequal distribution of diffusible and nondiffusible ions on either side of a membrane. This, then, is an application of the Donnan membrane equilibrium and is used to determine the ability of ions to penetrate or be excluded by the exchanger. The Donnan and swelling effects are also used to explain ion exchange equilibria.

If a cation exchanger is placed in a dilute solution of a strong electrolyte such as sodium chloride, there is very little sorption of electrolyte by the exchanger. As ions migrate from the solution to the exchanger and from the exchanger to the solution, an electrical potential difference is developed which tends to retain the cations in the exchanger and anions in solution. At equilibrium

the concentration of sodium chloride must be the same on both sides of the membrane.

$$(Na^+)_s(Cl^-)_s = (Na^+)_r(Cl^-)_r \tag{10.4}$$

Since an electrically neutral system must be maintained, the concentrations of sodium and chloride ions on the solution side of the membrane must be equal:

$$(Na^+)_s = (Cl^-)_s \tag{10.5}$$

and that of sodium on the resin side of the membrane must equal that of the chloride and resin anions:

$$(Na^+)_r = (Cl^-)_r + (A^-)_r \tag{10.6}$$

The amount of sodium ions is thus greater in the resin phase. Since the concentrations of sodium and chloride ions on the solution side are equal, we have

$$(Cl^-)_s^2 = (Na^+)_r(Cl^-)_r \tag{10.7}$$

which indicates that the concentration of chloride, and likewise sodium chloride, is greater in the solution than in the resin.

In rigorous treatment of the equilibrium concentration, terms are expressed as activities, and consideration is made for the swelling pressure of the exchanger, temperature, and molal volume of the electrolyte. The equilibrium may be established with anion exchangers as well.

When an exchanger is placed in a more concentrated solution of electrolyte, increased sorption of ions will be found.

The exclusion of ions by an exchanger is increased through the use of dilute solutions of strong electrolytes, exchangers with high capacities and high degrees of cross-linking, counter ions with a low valence, and co-ions (ions of the same electrical charge as the exchanger network) with a high valence.

Advantage is taken of the Donnan equilibrium effects in the process known as *ion exclusion*. By this method it is possible to separate strong electrolytes from weak electrolytes and nonelectrolytes, since the latter are more strongly sorbed. Similar separations are also brought about by ion retardation, where electrolytes are more strongly sorbed by the exchanger than nonelectrolytes.

When an exchanger is depicted as a structure composed of *two layers*, it was first compared to an electrically charged double-layered colloidal particle. This viewpoint represented an ion exchanger as a structure with a fixed inner layer and a diffuse mobile outer layer of charges. In the ion-exchange process, ions migrate between the diffuse ion layer and a solution in contact with this diffuse layer until an equilibrium is reached. When other ions are added to the exchanger-solution mixture, equilibrium is upset, and it is re-established, only through the exchange of ions from the solution into the diffuse layer. The degree of exchange depends upon the concentration and pH of the external solution.

In more recent concepts of the kinetics of ion exchange, the process is described in terms of particle diffusion and film diffusion.* Either type of diffusion, or both, may be the rate-determining step.

Particle diffusion refers to the diffusion of counter ions within the ion exchanger. It is most commonly encountered when exchangers are used in a column operation. This type of diffusion is increased through the use of dilute solutions; exchangers with a low degree of cross-linking, high exchange capacity, and small particle size; counter ions of low valence; and increasing temperature.

Film diffusion is the diffusion of counter ions through a surface film which surrounds the exchanger. This film is extremely thin but is thicker with unagitated exchangers than agitated ones. Diffusion of this nature is increased by the same factors as particle diffusion except that the solution should be very dilute and the counter ions smaller.

In an exchange reaction the over-all process may then be depicted as

$$A^+R^- + B^+ \rightleftharpoons B^+R^- + A^+ \qquad (10.8)$$
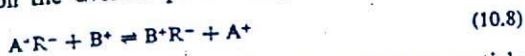
where B^+ ions diffuse through the film surrounding the exchanger particle with the concurrent diffusion of A^+ ions from the exchanger surface (film diffusion), or where B^+ ions diffuse through the exchanger structure and A^+ ions diffuse in the opposite direction to the solution (particle diffusion).

In the diffusion process both A^+ and B^+ ions must migrate at the same rate for electroneutrality to be maintained. If A^+ happens to be a faster-diffusing ion, an electrical potential will develop which will retard A^+ and accelerate B^+ so that the two will move at the same rate.

10.3 COLUMN OPERATION

Most of the analytical procedures involving ion exchange utilize the exchanger, usually a resin, in the form of a column. By this method ions may be replaced, concentrated, or separated, depending on the results desired.

In this type of operation a suitable glass tube is filled with a slurry of the exchanger. Solutions to be analyzed or treated are added to the top of the column and allowed to pass through the bed of exchanger. As ions from the solution come in contact with the exchanger, they are replaced by ions already within the exchanger. The process is repeated as successive new layers of solution reach the exchanger. Finally, when all ions of the exchanger have been replaced, solution ions will be detected in the fluid emerging from the column. At this stage the exchanger is said to be *exhausted*, and the detection of solution ions represents the *breakthrough point* for those ions. If more than one kind of ion were present in the solution originally added to the column of exchanger, each would have a different breakthrough point and thus could be separated from each other.

The solution added to the exchanger column is called the *influent* or *eluant;* the liquid coming out of the column is the *effluent* or *eluate.*

For the exchanger to be used again, a solution, which will provide ions that were originally present in the exchanger and remove all other ions, must be passed through the column. The return of the exchanger to the original state is known as *regeneration.* The removal of the other ions represents their *recovery.*

The success of column operation lies not only in the selection of the proper ion exchanger but also in the conditions under which the column is used.

In ion exchange chromatography several methods may be employed in column operation to separate a mixture of ions. These procedures, which are common to all forms of chromatography, are frontal analysis, displacement, and elution.

With *frontal analysis* an incomplete separation of ions is obtained. As the mixture of ions passes down the column, the ion which has the least affinity for the exchanger appears in the effluent first and is followed at different intervals by those which have a greater affinity for the exchanger. For example, in a mixture of ions A, B, and C, where A ion has the least attraction for the exchanger and C ion the most, A ions would be removed from the column first. After a period of time, B ions would also appear in the effluent, as well as A ions. In a similar manner C ions would be detected in the effluent along with A and B ions. The removal of the ions by frontal analysis is illustrated in Fig. 10.1(*a*). This type of column operation indicates the number of compounds present in a mixture by the number of fronts appearing when the concentration and volume of effluent are plotted. Only the first ion, A, can be obtained in pure form.

Displacement development of the column is accomplished by means of a substance which has a very strong affinity for the exchanger. In effect, the displacer pushes out other ions for which the exchanger has less affinity. For example, a mixture of ions A, B, C, and D is placed on a column of exchanger. A ions have the least affinity for the exchanger and will appear in the effluent first, whereas D ions exhibit the greatest affinity for the exchanger and are found last in the effluent. As D ions displace C ions, the latter in turn displace B ions, which in turn displace A ions. The successive bands of ions are adjacent to each other and have sharp fronts. Figure 10.1(*b*) shows the results obtained by this method of column operation. A separation of ions is achieved by this procedure, the number of components in a mixture can readily be determined, and each is obtained in pure form. An overlapping of zones occurs to a greater or lesser extent, and this impairs the efficiency of the separation. However, the individual fractions may be rechromatographed to eliminate the overlapping to a considerable extent. This method is useful in preparative procedures.
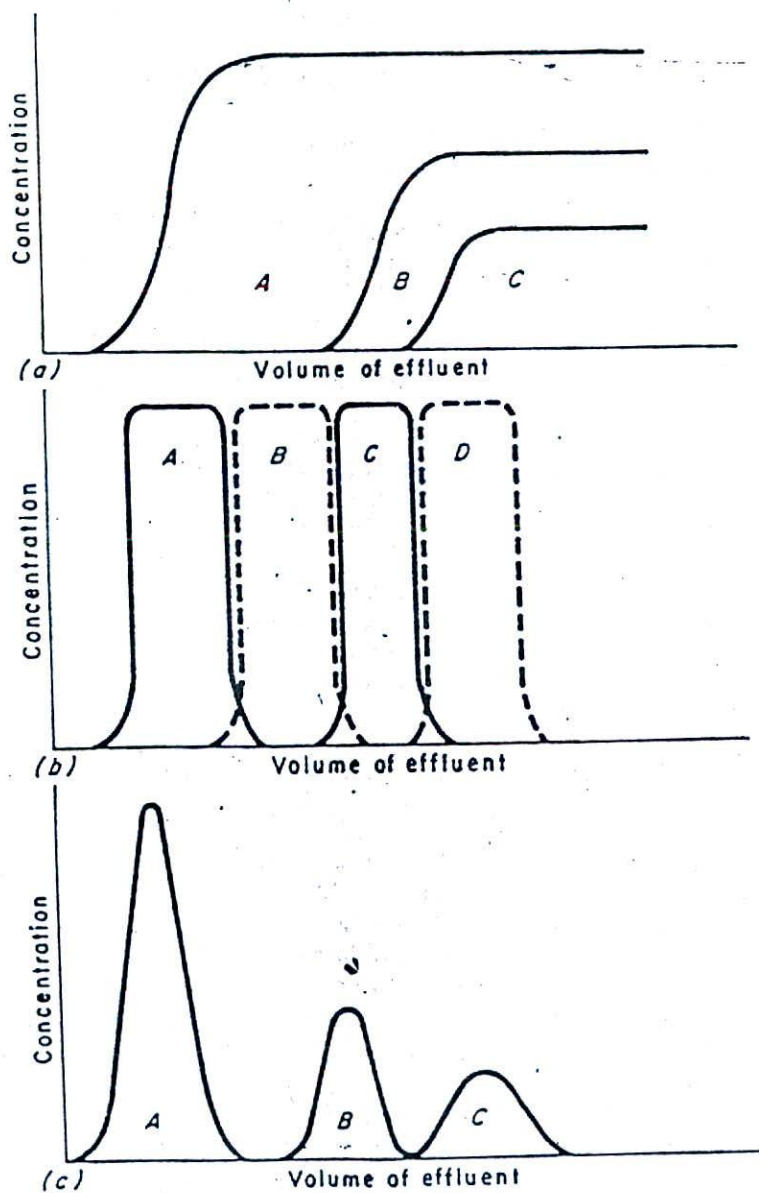
FIGURE 10.1: Ion exchange column methods: (a) frontal analysis; (b) displacement; (c) elution.

When *elution development* is performed, the components of a mixture separate and move down the column individually at different rates depending on the affinity of the ion for the exchanger. The ion with the least attraction for the exchanger will move most rapidly. In the mixture of A, B, and C ions, each moves in a band with A first and C last. As the movement downwards continues, the distance between A and B increases. Similarly, the distance between B and C becomes greater. Such a separation is shown in Fig. 10.1(c). The fronts are not as sharp as those found in the displacement method, and they tend to become more diffuse or flatter as they proceed down the column. Some overlapping of bands may occur as they become flatter and closer together. Elution is the preferred method for quantitative analysis. Efficient separations occur when small sample sizes, highly selective exchangers of small particle size, sufficiently long column lengths, and low flow rates are maintained.

Column operation of ion exchangers introduces additional factors to consider for theoretical treatment. Complete mathematical solutions to the theory are exceedingly involved. In less rigorous approaches many simplifications are introduced and many assumptions are made. In doing this only approximate results are obtained, yet these are useful provided it is remembered that misinterpretations may arise through these simplifications.

The many theories concerned with column performance are usually designated as equilibrium theories or rate theories.

The *equilibrium* or *plate theories*[10-12] compare the ion exchange column to a distillation column composed of a certain number of segments or plates. An equilibrium is assumed to be attained between the solution and the exchanger in each theoretical plate, Equilibrium is established in one plate before the solution travels to the next plate. This is viewed as being a continuous process as the solution flows down the column or as a discontinuous or isolated process. The efficiency of the column is based on the number of theoretical plates or on the height equivalent to a theoretical plate present in the column.

The number of plates in a column can be determined experimentally by plotting the elution curve [such as in Fig. 10.1(c)]. The curves are bell-shaped (gaussian) and move down the column at a constant speed. The concentration of the solute at peak maximum is given by

$$C_{max} = \frac{m}{V_{max}} \left(\frac{N}{2\pi} \right)^{1/2} \tag{10.9}$$

where C_{max} is the concentration of solute at peak maximum, V_{max} is the effluent volume at concentration maximum, N is the number of theoretical plates, and m is the total amount of solute in the band which is equal to the area under the curve. By rearranging the equation and solving for N, the

number of theoretical plates may be found.:

$$N = 2\pi\left(\frac{C_{max}V_{max}}{m}\right)^2 \tag{10.10}$$

N may also be calculated from the width of the curve by Eq. (10.11) where β

$$N = 8\left(\frac{V_{max}}{\beta}\right)^2. \tag{10.11}$$

is the width of the curve ($\beta = C_{max}$/void fraction or interstitial volume of the column $= 0.368C_{max}$).

The height equivalent to a theoretical plate can be calculated by

$$HETP = L/N \tag{10.12}$$

where L is the length of the column.

The equilibrium theories are convenient in that the equations are simple and easy to use. However, the number of plates and plate heights must be determined experimentally, which may lead to errors unless optimum column operation is attained. It has also been found that plate heights may vary for each solute present in the solution passed through the column.

Rate theories do not depend upon the establishment of equilibrium conditions in each theoretical plate, but rather are concerned with the flow of solution through a column and factors which may influence this flow and the exchange of ions. Plate height is determined from data based on diffusion, particle size, flow rates, and concentration.[13]

In the rate theories the *HETP* is found by

$$HETP = 1.64r + \frac{D_v}{(D_v + E)^2}\frac{0.142r^2F}{D_s}$$
$$+ \left(\frac{D_v}{D_s + E}\right)^2\frac{0.266r^2F}{D_L(1 + 70rF)} + \frac{D_LE2^{1/2}}{F} \tag{10.13}$$

where D_L is the diffusion coefficient in the interstitial liquid, D_s is the diffusion coefficient in the ion exchanger, D_v is the column distribution coefficient, E is the interstitial volume, F is the linear flow rate, and r is the radius of the particle.

The four terms account for the nonequilibrium conditions which exist in column operation. The first term takes into consideration particle size and the fact that irregular flow and packing may produce channeling of the solution in the column. The number of plates will be increased when the particle size is decreased.

The second term is due to the effects of particle diffusion. The value of the term is directly proportional to flow rate and the square of the particle radius

and inversely proportional to the column distribution coefficient (the quantity of solute sorbed per cubic centimeter column volume per quantity of solute per cubic centimeter of solution). When particle diffusion predominates, the plate heights become larger and the number of theoretical plates will vary for different solutes in the solution.

The third term is concerned with film diffusion. This type of diffusion is of less importance than particle diffusion in most instances of ion exchange chromatography. The values will increase with high flow rates, high distribution coefficients, and low diffusion coefficients in the liquid phase.

The fourth term, longitudinal diffusion, is of little significance in ion exchange unless the flow rates are reduced considerably. The term is often neglected in calculations for *HETP*.

With the rate theory equation for *HETP*, optimum column operation is usually achieved when the first three terms are equal. The equation pertains primarily to elution development. When displacement development is used, alterations in the equation are necessary to account for nonlinear conditions and sharp fronts.

The rate theories usually permit a more satisfactory explanation of column operation because more information is included. This, however, makes the mathematical treatment more complex than the equilibrium theories, even when assumptions are introduced. The rate approach is instrumental in selecting optimum conditions for ion exchange operations and in anticipating column behavior.

10.4 APPLICATIONS

The applications of ion exchange are far too numerous to describe in detail. The process has been used in the purification and recovery of antibiotics, alkaloids, vitamins, hormones, and other chemicals of pharmaceutical importance during their manufacture. Successful separations and analyses have been obtained for amino acids, radioisotopes, peptides, carbohydrates, metals, inorganic anions, amines, organic acids, dyes, local anesthetics, and many other groups and types of organic and inorganic substances. The deionization of water, sugar refining, catalysis, treatment of foods and beverages, blood processing and fractionation and hydroponics are additional areas in which the use of ion exchangers have proved advantageous. Anionic resins have been introduced as a means of treating peptic ulcers. Cationic resins have been used to remove sodium from the body during the treatment of hypertension and edema and as diagnostic aids in gastric acidity tests. The resins have been incorporated with medicinal agents to achieve delayed action dosage. Suspensions or dispersions of ion exchange resins in ointments and lotions have been suggested for use in the treatment of various dermatological conditions.

10.5 EXPERIMENTS

A. ACID-BASE CHARACTERISTICS

Materials. Anion exchange resins, pH meter, cation exchange resins, Erlenmeyer flasks, 1 N HCl, 0.5 N NaCl, 1 N NaOH.

Procedure. Regenerate about 15 to 20 g of each type of resin with about 50 ml of 1 N HCl (for cationic resins) or 50 ml of 1 N NaOH (for anionic resins) to remove soluble components of the resin and displace any cations or anions present. Rinse free of acid or base with distilled water. Air-dry the regenerated resins. Add 0.5 g of dry cationic resin to a flask containing 100 ml 0.5 N NaCl (NaCl forces the reaction to completion). Add 0.5 g of dry anionic resin to a flask containing 50 ml distilled water. Prepare 11 such flasks for each resin type. Add 0.5 N NaOH to each flask containing cationic resin and 0.5 N HCl to each flask of anionic resin, using in each case 0, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, and 5.0 ml of the respective base or acid. Stopper the flasks and shake them intermittently during a 24- to 48-hr period until equilibrium is established. Filter the solutions and measure the pH of the equilibrium solutions by means of a pH meter. Plot pH against milli-equivalents of NaOH or HCl consumed per gram of dry resin.

Remarks. Owing to the functional groups on the ion exchangers, resins may resemble either strong or weak acids or strong or weak bases. Thus the titration curves should be typical of such acids or base. The titration curves provide useful information about the behavior of ion exchangers and the selection of a resin for a particular application.

Regenerant solutions for cation exchangers are usually HCl or H_2SO_4 for both weakly and strongly acidic resins. If the sodium form of the resin is desired, NaCl is used for strongly acidic resins and NaOH for weakly acidic resins. Strongly basic resins are regenerated with NaOH for the hydroxide form of the resin, with NaCl or HCl for the chloride form and with Na_2SO_4 or H_2SO_4 for the sulfate form. Weakly basic resins require NaOH, NH_4OH or Na_2CO_3 for the free base form, HCl for the chloride form, and H_2SO_4 for the sulfate form. The concentration of these regenerating solutions is generally 1 N or approximately 4 to 10%.

B. CAPACITY OF A CATIONIC RESIN

Materials. Cation exchange resins, Buchner funnel, 5% HCl, 50-ml burette, 0.1 N HCl, pH meter, 0.1 N NaOH, phenolphthalein test solution.

Procedure. Place about 25 ml of wet resin in a 50-ml burette which has a small pleget of glass wool at the lower end. Regenerate the resin with about 250 ml of 5% HCl and wash free of acid with distilled water (about 250 ml

water, 1 hr). Transfer the resin from the column to a Buchner funnel to remove excess moisture. Vacuum should be applied for 5 to 10 min. Accurately weigh a 3- to 5-g sample of the drained resin, dry at 110°C for 8 hr, cool in a desiccator, and reweigh. From the loss in weight, calculate the moisture content.

$$\% \text{ moisture } = \text{loss of weight} \times 100/\text{weight wet resin}$$

Accurately weigh 1 g of the drained resin and place in a 250-ml Erlenmeyer flask. Add 200 ml of 5% $NaCl$ and titrate the liberated acid with 0.1 N NaOH, agitating vigorously. Use phenolphthalein test solution as the indicator or employ a pH meter to detect the end point. Calculate the total capacity.

$$\text{dry weight total capacity in meq/g} = \text{ml NaOH} \times N \text{ NaOH/g dry resin}$$
$$\text{wet weight total capacity in meq/g} = \text{ml NaOH} \times N \text{ NaOH/g wet resin}$$
$$\text{wet volume total capacity in meq/ml} = \text{ml NaOH} \times N \text{ NaOH/ml wet resin}$$

Remarks. The capacity provides information concerning changes in some of the chemical and physical properties as a resin is used over a period of time. Total capacity indicates the number of exchange sites available. When exchange sites become inactive or lost, the value decreases. If the cross-linking in the resin is destroyed, total capacity becomes less and moisture content greater. Total capacity for anionic resins may be determined in a somewhat similar manner.

C. QUANTITATIVE ESTIMATION OF EPHEDRINE SULFATE

Materials. Amberlite IR-45, 4% Na_2CO_3, isotonic ephedrine sulfate solution, 0.01 N HCl, methyl red test solution, 75% ethyl alcohol, pH meter.

Procedure. Regenerate the resin by passing 50 ml of 4% sodium carbonate solution through a column containing 10 g of the resin. Rinse free of sodium carbonate with distilled water. Use litmus paper to test for completeness of rinsing. Add 10 ml of ephedrine sulfate solution to the column. After the sample has passed into the resin bed, rinse the column with 100 ml of distilled water to remove sodium chloride. Then remove the ephedrine from the column by means of 100 ml of 75% ethyl alcohol. Titrate the alcoholic eluant with 0.01 N HCl using methyl red test solution as the indicator or a pH meter.[14] Calculate the amount of ephedrine sulfate present in the sample:

$$\text{g ephedrine sulfate} = \text{ml HCl} \times N \text{ HCl} \times \text{meq}$$

D. ANALYSIS OF DIPHENYLHYDANTOIN SODIUM CAPSULES

Materials. Amberlite IRC-50, azo violet, dimethylformamide, 1 N HCl, 0.1 sodium methoxide, 50-ml burette.

Procedure.   Regenerate the resin by passing 50 ml of 1 N HCl through a 50-ml burette containing 10 g of the resin. Rinse free of HCl with distilled water. Test for completeness of rinsing by means of litmus paper. Drain the water from the column, add dimethylformamide, and allow to stand 24 hr. Prior to use of the column, rinse with about 25 ml of dimethylformamide.

Dissolve the contents of 10 capsules in about 75 ml of dimethylformamide. Rinse the empty capsules with additional dimethylformamide to ensure complete solution of capsule contents. Filter the resulting solution into a 100-ml volumetric flask and wash the filter with sufficient dimethylformamide to bring the volume to 100 ml. Transfer a 10-ml aliquot to the resin column. Add dimethylformamide to the column until 50 ml of effluent is collected. Add 3 drops of a saturated solution of azo violet in benzene to the effluent and titrate to a blue end point with 0.1 N sodium methoxide. Calculate the amount of diphenylhydantoin sodium present per capsule:

g diphenylhydantoin sodium
$$= \text{ml sodium methoxide} \times N \text{ sodium methoxide} \times \text{meq}$$

Remarks.   The method may also be applied to barbiturate salts and many of their dosage forms.[15]

E. SEPARATION OF AMINO ACIDS

Materials.   Strong cation exchange resin, histidine, 0.15 M phosphate buffer, pH 7.2 (0.24 g NaH_2PO_4, 0.66 g Na_2HPO_4 per liter distilled water), leucine, tyrosine, 1 N HCl, 50-ml burette, ninhydrin solution (n-butanol saturated with water containing 0.2% ninhydrin).

Procedure.   Regenerate about 10 g of a strongly acidic cation exchange resin in a 50-ml burette with about 50 ml of 1 N HCl. Rinse free of acid with distilled water, testing for completeness of rinsing with litmus paper. Prepare a solution of 100 mg each of histidine, leucine, and tyrosine in sufficient distilled water to make 100 ml. Place 2 ml of the amino acid solution on the column. Elute the amino acids with 0.1 M phosphate buffer, pH 7.2, collecting about 35 1-ml fractions of eluate. Detect the presence of amino acids in each fraction with ninhydrin solution. Indicate the order of elution of the three compounds.[16]

Remarks.   The effective separation of more complex mixtures of amino acids may be performed following the procedures of Moore and Stein.[17] The retention or elution of various amino acids depends on the charge on the ion, attractive forces between the exchanger and solute, and variations in the degree of ionization of the acids as they pass through the column. Alterations in temperature, resin particle size, and degree of cross-linking of the resin may markedly enhance or detract from the efficiency of the separation. The pH of the eluting solution may be changed during an analysis to take advantage of

the fact that amino acids having isoelectric points higher than the pH of the resin will be retained on the exchanger. In general, when an eluting solution of a particular pH is used, the order of displacement of the amino acids follows the pK values. With cation exchange resins those of lower pK values are eluted first. Both cationic and anionic resins have been employed for the separation of amino acids in synthetic mixtures or biological products.

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