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Ion Exchange Resins: An approach for the Development of Advanced Materials with Industrial, Pharmaceutical and Clinical Applications

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ABSTRACT

Ion exchange resins (IER) are cross-linked water insoluble polymers that contain ionisable acidic or basic functional groups and have the ability to exchange counter-ions from surrounding within aqueous solutions. On the basis of nature of the exchangeable ion of the resin as a cation or anion, classified into two main classes, cationic exchange resin, and anionic exchange resins, respectively. Due to versatile properties of IER, it has received considerable attention from worldwide pharmaceutical scientists. Research has shown that for the past few years, IER is equally suitable for drug delivery techniques, including controlled release, topical, transdermal, nasal and taste masking. The efficacy IER mainly depends upon their physical properties such as porosity, acid-base strength, the degree of cross linking, stability, purity, and particle size. Ion-exchange resins (Drug-Resin complex) of drugs can help in reducing the dose, fluctuations in blood and tissue concentrations, avoiding dose dumping, and maintenance of drug concentration below toxic level can be achieved. The major drawback of sustained release or extended release is dose dumping, resulting in increased risk of high dose toxicity. The utilization of IER has occupied an important place in the development of controlled or sustained release systems because of their better drug-retaining properties and prevention of dose dumping. Resins are polymers that contain appropriately substituted acidic groups, such as carboxylic and sulfonic for cation exchangers; or basic groups, such as quaternary ammonium group for anion exchangers. Drug resin complexation converts drug to amorphous form leading to improved drug dissolution. Many studies have reported the use of IER for drug delivery on the desired site of action. Sulfonated and carboxylic resins with a polystyrene backbone are mostly used in clinical medicine. This review will cover various types of ion exchange resin, their property, chemistry; The role of IER in controlled drug delivery systems, its Industrial, Pharmaceutical and clinical applications, methods of preparation of IER along with their resins.

Keywords: Ion Exchange Resins, Taste Masking, Resin Drug Complex, Controlled Release, Anion Exchange, Cation Exchange, Controlled Release, Resinates.

1. INTRODUCTION

Ion exchange resins are suitably insoluble high molecular weight polyelectrolyte, which has exchangeable mobile ions, which are exchanged reversibly and stoichiometrically with ions having similar charge present in surrounding medium. These exchanges take place without any physical change to the ion exchange material.

An ion-exchange resin is an insoluble matrix (support) normally in the form of small (0.5-1 mm diameter) beads, usually white or yellowish, fabricated from an organic polymer substrate. The beads are typically porous, which provides a high surface area. The trapping of ions occurs with concomitant releasing of other ions; thus the process is called ion-exchange.

1.1 Classification of IER

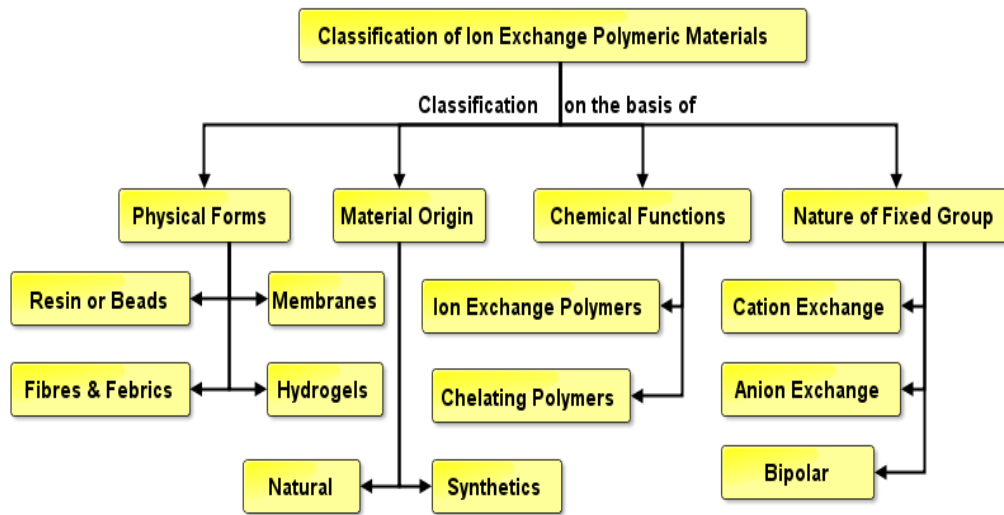


Figure 1: Classification of Ion-Exchangers

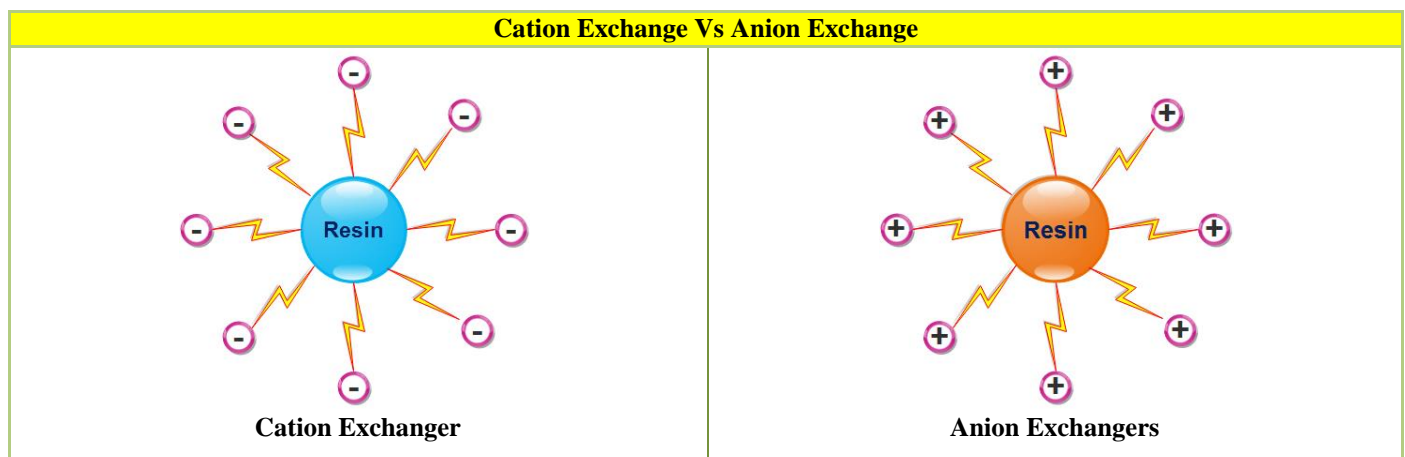
Table 1: Drug and Respective Resins Binding Nature

For binding of Basic Drug , to Cation Exchange Resin	For Binding Acidic Drug , to Anion Exchange Resin
(A) Resin (Na-Form) + Drug (Salt Form)	(A) Resin (Cl-Form) +Drug (Salt Form)
(B) Resin (Na-Form) +Drug (As Free Base)	(B) Resin (Cl-Form) +Drug (As Free Acid)
(C) Resin (H-Form) +Drug (Salt Form)	(C) Resin (As Free Base) +Drug (Salt Form)
(D) Resin (H-Form) +Drug (As Free Base)	(D) Resin (As Free Base) + Drug (As Free Acid)

2. ION EXCHANGE THEORY

2.1 Basic Theory

Ion exchange resins are cross linked polymers which have active functional groups in form of electrically charged (Positive or negative) sites. Ions with opposite charge attracted by the active site of polymer but may be replaced by another similarly charged ions depending upon their relative affinity to the active site and their concentration. The effectiveness of ion exchange resins mainly depends on two factors: favourability of any given ions and number of available active sites for exchange. Active sites may be maximized by providing significant surface area. Generally, Ion exchange resins are marketed in the form of porous beads.



- Cation Exchangers has Negative Charge to attract Cations.
- Anion Exchangers has Positive Charge to attract Anions.





Strong Vs. Weak Exchange Materials			
			
Strong Cation exchanger	Weak Cation exchanger	Strong Anion exchanger	Weak Anion exchanger
Strong Exchanger Stay Ionized as pH varies between 2 and 12. Weak exchanger can lose Ionization as a Function of pH.			

Figure 3: Schematics of Cation & Anion Exchange Resin

2.2 Chemistry of Ion-Exchange Resin

By far the most common chemistry for ion exchange polymers is based on styrene. The monomer and the polymer polystyrene are shown in the figure. Desired functional groups can be introduced after polymer formation, or styrene derivatives with the appropriate functional groups can be copolymerized with styrene. Very seldom is a simple linear polymer used because it is too oily and it changes dimensions markedly as an ion exchanges for another. Almost all ion exchange resins have some degree of cross-linking that comes from adding divinyl benzene to the reaction mixture. The vinyl groups participate in different chains and link them together as shown in the figure.

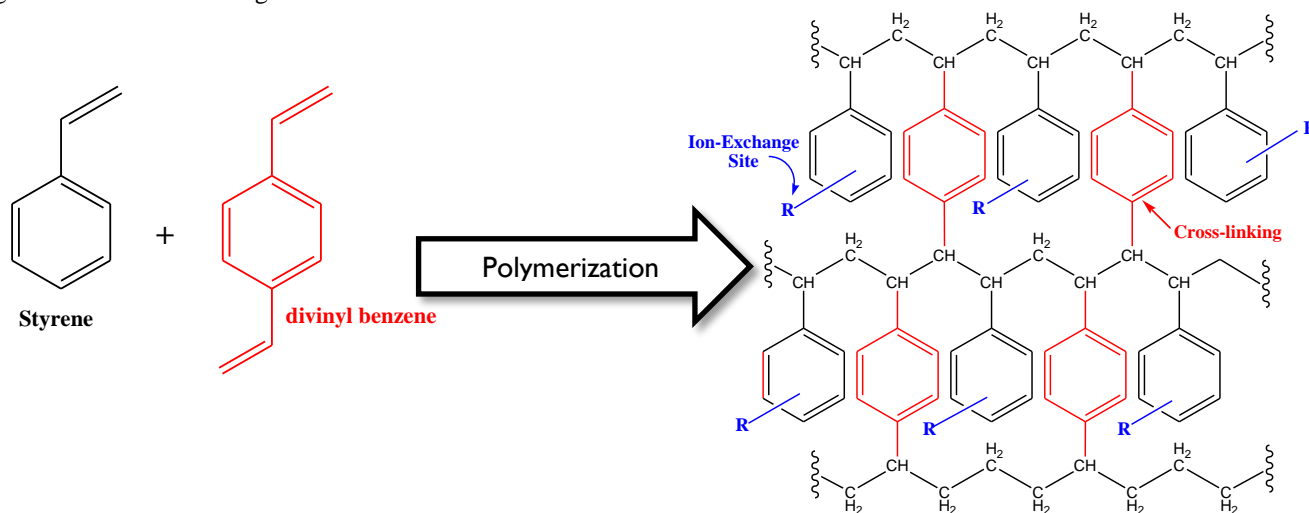


Figure 2: Structure of Styrene, Divinyl Benzene & Simple Chain Polymer Structure

Cross-linking, usually on the order of 0.5 to 15 percent, comes from adding divinyl benzene to their action mixture during the production of the resin. The particularly significant effects of cross-linking increases are a prolonged time for equilibration and an accompanying decrease in capacity. The size of the particles also plays a role in the utility of the resin. Smaller particles usually are more effective because of the increased surface area but cause large head losses that drive up pump equipment and energy costs. There are many permutations of charge, strength, particle size, cross-linking, temperature & pH that allow tailoring ion exchange to a particular task. Temperature and pH also affect the effectiveness of ion exchange, since pH is inherently tied to the number of ions available for exchange, and temperature governs the kinetics of the process. The rate limiting step is not always the same, and temperature's role is still not thoroughly understood.

2.3 Working Mechanics of Ion Exchange Resins

Solution containing ions with similar charge passed down a resin bed can flow through the cross-linked polymer, bringing it into intimate contact with the exchange sites but exchange process depends upon various factors like relative affinity, Cross linkage of resin, particle size, pH, form of resin, Size of exchanging ions, selectivity of counter ions, mixing times etc.

Factors Affecting Loading of Drug into & Release from the Ion-Exchange Material

Table 3. Factors Affecting Loading of Drug into & Release from the Ion-Exchange Material

Factor	Mechanism of Effect
1. Ion-exchanger Dependent	
Ion-exchange capacity	Donnan potential, number of ionic binding sites.
Nature of fixed ionic groups	Ionisation, selectivity
Preloaded counter-ion	pH, selectivity
Particle size	Surface area, particle diffusion
Degree of cross linking	Pore size of ion exchanger, particle diffusion
2. Drug Dependent	
Lipophilicity	Binding affinity
pka	Ionisation
Stearical properties	Binding accessibility
Molecular size	Diffusion coefficient, binding affinity, binding accessibility
3. External Conditions	
Concentration of solution	Donnan potential
pH	Ionisation of drug and ion-exchanger
Temperature	Porosity of ion-exchanger, diffusion
Agitation	Film diffusion

Cross Linkage of Resin: Cross linkage of Resins affects the porosity and swelling properties of resins. Low cross linkage agents swell remarkably upon hydration. Higher grades have finer pore structure thus reducing loading efficiency with increase in cross linking. Low cross linkage increases the loading efficiency but also increases release rates.

Particle Size: Particle size does not have an effect on drug loading. It affects the only rate of exchange of ions species. The rate of exchange decreases with bead diameter due to a reduction in diffusive path lengths hence larger particle size affords a slow release pattern.

Ph: Protonated fractions of moderately weak acid or basic drug and weak functionality resin undergo change with pH changes thereby increasing/decreasing drug resin interaction and hence loading.

A form of Resin: It was found that resins of H⁺ form have high loading capacity, as it possesses lower pH value than Na⁺. It has been found that drugs loaded onto H⁺ form of resin degrades while that a Na⁺ form does not degrade.

Size of Exchanging Ions: larger the size of exchanging ions, slower will be the diffusion rates and release.

Selectivity of Counter Ions: The ions with low selectivity for resins such as H⁺ gets replaced easily resulting in higher drug loading.

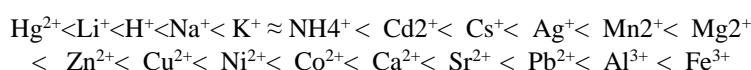
Mixing Time: Drug loading increases rapidly in the initial 9 h and further increases between 20-30 h. probably because of the surface absorptive phenomenon.

Relative Affinities of Various Ions: The affinity of an ion for a charged site on the resin depends on the hydrated radius of the ion. As this radius is smaller for ions with greater charge, the relative affinities depend on the charge or valence as shown:
Single-charged ion < ion with 2 charges < ion with 3 charges < multi-charged ion

This is ideal for most practical situations because we can prepare a resin in the form of a monovalent ion such as Na⁺ or H⁺ and exchange for an ion such as Ca⁺⁺, Mg⁺⁺, or Fe⁺⁺⁺ and have the relative affinity in our favour.

Although we might expect that an ion exchange resin that has a great affinity for a particular ion should be the best choice for a process, is probably not true because every strong binding means that the removal of that ion for regeneration of the resin will be much difficult. The concentration required for the regenerating ion and the cost will be less if a resin is selected which is adequate for the task but does not hold the ion too tightly.

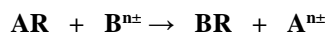
The affinity of sulphonic acid resins for cations varies with the ionic size and charge of the cation. Generally, the affinity is greatest for large ions with high valency. For dilute solutions the order of affinity for some common cations is approximate:



A corresponding list for amine based anion exchangers is:



Suppose a resin has a greater affinity for ion B than for ion A. If the resin contains ion A and ion B is dissolved in the water passing through it, then the following exchange takes place, the reaction proceeding to the right (R represents the resin):



When the resin exchange capacity nears exhaustion, it will mostly be in the BR form.

A mass action relationship applies where the bracketed entities represent concentrations:

$$\frac{[\text{BR}][\text{A}]}{[\text{AR}][\text{B}]} = Q$$

Q is the equilibrium quotient and is a constant specific for the pair of ions and type of resin. This expression indicates that if a concentrated solution containing ion A is now passed through the exhausted bed, the resin will regenerate into the AR form ready for re-use, whilst ion B will be eluted into the water. All large scale applications for ion exchange resins involved such exhaustion and regeneration cycles.

Regeneration of the resin is also a feature of ion exchange. The resin is flushed free of the newly exchanged ions and contacted with a solution of the ions to replace them. Regeneration is initiated after most of the active sites have been used and the ion exchange is no longer effective. With regeneration, the same resin beads can be used over and over again, and the ions that we are looking to get out of the system can be concentrated in the backwash effluent, which is just a term for the spent fluid used to regenerate the ion exchanger.

Ion exchange technology encompasses the sciences of thermodynamics, kinetics, ion chemistry, fluid mechanics, and economics. Understanding the finer points of ion exchange helps to determine whether or not ion exchange will be useful for a particular application. Furthermore, new computer modelling capabilities are used to find new ion exchange substances with more specificity. The word specificity is a key word in ion exchange, as we generally want to create exchangers with one unique (specific) ion in mind, which will maximize efficiency, quality, and cost effectiveness.

Ion Exchange Capacity

Due to the equivalent character of ion exchange and the defined number of functional groups in the ion exchanger, an ion exchange reaction can be considered as a competition between counter ions for functional groups of the material. This competition can be written as

$$[\text{A}] + [\text{B}] + \dots = Q$$

Where the concentration of ions is expressed in the equivalent concentration scale as well as the total amount of ions inside the exchanger, Q , so called *capacity*. Equation defines the primary difference between the exchanger phase and conventional solutions where the total concentration is limited by only the solubility of constituents.

Ion Exchange Capacity is a major characteristic of ion exchange materials. From a practical point of view, an ion exchanger can be considered as a “reservoir” containing exchangeable counter ions. The counter ion content in a given amount of material is defined essentially by the number of fixed charges which must be compensated by the counter ions and thus is essentially constant. According to this fact, ion exchangers are quantitatively characterised by their capacity which is defined as the number of counter ion equivalents in a specified amount of the material.

Selection of Suitable IER: The selection of IER mainly based on the following factors:

- Ion exchanging Capacity of the IER i.e. the concentration of the exchangeable group in the resin usually expressed in meq/g of dry resin.
- Degree of cross linking in the resin matrix
- Nature of drug and site of drug delivery
- Swelling ratio
- Particle size of resin
- Biocompatibility and biodegradability
- Regulatory status of the IER

Mechanism of Ion Exchange Process

The interactions between the IER and drug, although primarily chemical in nature, are also partially a result of physical adsorption. These interactions are commonly referred to as ‘adsorption on IER’, rather than Complexation on most occasions. The IE process, therefore, is generally regarded as a double-decomposition process, in which the IER used is able to provide the type of ion required to replace the one that is adsorbed from the solution.

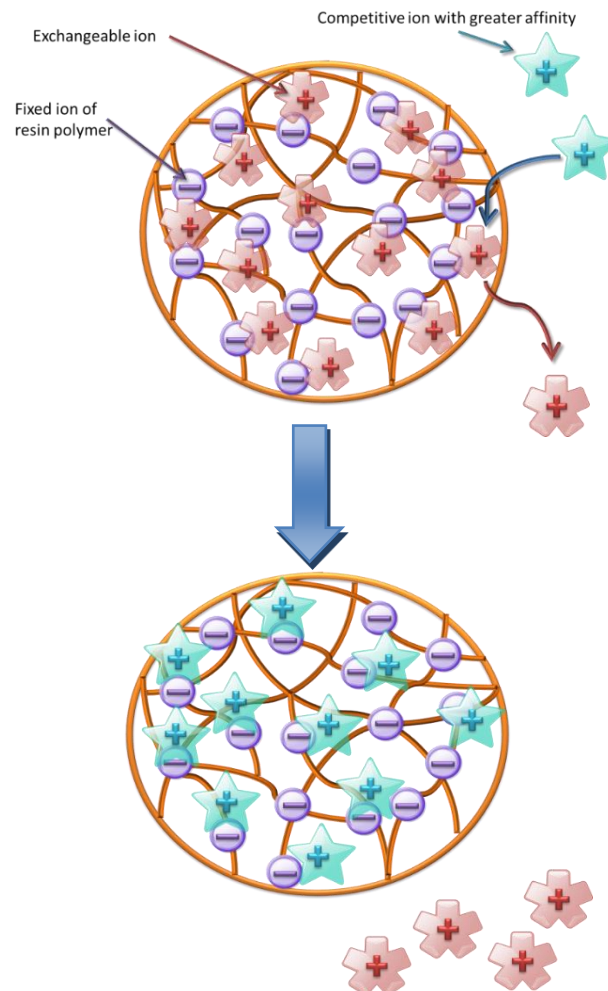


Figure 5: Schematic Diagram of Ion Exchange Process

3. APPLICATIONS OF ION EXCHANGE PROCESSES

The applications for ion exchange processes are numerous and cover a wide range of industries and house appliances. The purpose of separation dictates the selection of the type of the ion exchange materials, their physical form, and system configuration for practical application and thus forms the basis of a large number of ion exchange processes, which can be functionally divided into three main categories:

a. Substitution: A valuable ion (e.g., copper and silver) can be recovered from solution and replaced by worthless one. Toxic ion such as cyanide can be similarly removed from the solution and replaced by nontoxic one.

b. Separation: A solution containing a number of different ions passes through a column containing beads of an ion exchange resin. The ions are separated and emerge following the order of their increasing affinity for the resin.

c. Removal: By using a combination of a cation-exchange resin (in the H^+ form) and an anion-exchange resin (in the OH^- form) or bipolar resins, all ions are removed and replaced by water (H^+OH^-). The solution is thus demineralized.

Despite the diversity of ion exchange processes, their chief application of today is still the treatment of water with the principle offering of unlimited possibilities in other fields. Commercial ion exchange installations are serving in water and water treatment, food, and chemical industries include processes such as purification of sugar solutions, separation and purification of drugs and fine chemicals, purification of waste effluents, and the recovery of valuable wastes, for example, in the metallurgical industries, the extraction, and quantitative separation of elements and metallic complexes. The diverse applications of ion exchange processes can be classified into the following categories:

Water Production, For example

- Desalination of seawater
- Desalination of brackish water
- Production of pure and ultrapure water
- Water softening

Wastewater Treatment, for example

- Removal of heavy metals from industrial streams
- Removal of dyes and colours
- Removal of nitrate and ammonia
- Removal of fluoride
- Dealkalization.

Radioactive Waste Treatment, for example

- Waste decontamination
- Storage of radioactive waste

Isotopes separation and radioactive industry, for example

- Separation of uranium isotopes
- Separation of lithium isotopes
- Separation of boron isotopes

Recovery of metals, for example

- Recovery of precious metals such as silver, gold, and platinum
- Recovery of rare earth metals
- Recovery of transition metals

Purification and Separation in Chemical Industries, for example

- Production of caustic soda in chlor-alkali industry
- Production of sulfuric acid
- Recovery of chromic acid
- Synthesis of ethylbenzene
- Production of table salt
- Dehydration of solvents
- Removal of inorganic salts from waste streams in pulp and paper industry
- Electrolysis of water
- Catalysis in petroleum refineries (zeolites)

Separation and Purification in Food Industry, for example

- Purification of sugars
- Inversion of sugar
- Removal of tastes and odours
- Recovery of glutamic acid
- Deacidification of fruit juice
- Extraction of lactoperoxidase and purification of casein in dairy industries

Biotechnological applications, for example

- Production of organic acids such as citric, L-glutamic, and amino acids
- Separation of lactic acid from fermentative broth
- Recovery of proteins
- Enzyme immobilization
- Recovery of enzymes
- Production of biodiesel

Biomedical and pharmaceutical applications, for example

- Production of antibiotics
- Extraction of vitamins
- Drug delivery systems
- Gene and hormone delivery systems
- Ultrapure water for dilution of medicine

Soil remedy and improvement, for example

- Artificial soil
- Soil decontamination
- Improve water retention in sandy soil
- Determination of nitrogen content in soil

Chemical analysis, for example

- Ion chromatography

Energy conversion and solid state applications

- Battery separators
- Solid polymer electrolyte in fuel cells
- Sensors and actuators

Details of potential and fast-growing applications and their basic principles of operation together with the latest progress in the materials and accommodating process are discussed in the next chapters of this book.

Advantages of Ion Exchange Processes

The widespread applications of ion exchange processes in various industrial aspects are supported by a combination of various advantages including the following:

- Proven ability to remove a variety of impurities from various volumes with the availability of a wide number of resins.
- Tolerance for fluctuating feed flow rates.
- Low energy consumption.
- The accumulated experience that provides technically effective solutions that meet all system's design specifications.
- Large varieties of specific resins are available from suppliers. Each resin is effective in removing specific contaminants.
- Fast reaction and simple process operation.
- Can be operated at a high flow rate.
- The discharged effluents can achieve regulator acceptance.
- Cost-effectiveness which can be further improved by technical innovation including introducing cheap and highly tolerant ion exchange materials.
- The regenerate chemicals are cheap, and if well maintained, resin beds can last for many years before replacement is needed.

4. LIMITATIONS OF ION EXCHANGE PROCESS

Despite the extendable and diverse uses of the ion exchange process applications, there are a number of limitations which must be taken into consideration very carefully during the design stages. They include:

- High levels of suspended solids (greater than 10 ppm) and oil together with grease in wastewater may cause clogging of nonselective resins.
- Waste brine from regeneration step requires treatment and disposal, though waste volume can be reduced.
- Spent nonselective resins require frequent replacement and careful disposal.
- Competitive uptake by other ions may limit the effectiveness of nonselective exchange resins.
- The effectiveness of treatment is strongly influenced by water chemistry of the site (e.g., the presence of competing ions and pH of the water source).
- Oxidants present in the ground water may damage the ion exchange resin.
- Usually not feasible with high levels of total dissolved solids (TDS).
- Pre-treatment required for most surface water treatments.
- Wastewater is generated during the regeneration step, and it requires additional treatment and disposal.

5. APPLICATIONS OF ION EXCHANGE RESINS

5.1. Applications in Various Formulation-Related Problems [Aboule-Enein et al., 2007]

5.1.1. Taste Masking

The excessive bitterness of the active principal ingredients (APIs) in oral formulations is the major taste problem faced by the pharmaceutical industry. The bitterness of formulations can influence selection by physicians and markedly affect patient compliance [Sohi H. et al., 2004]. Masking of the unpleasant taste of a drug improves compliance and product value. Amongst the numerous available taste-masking methods, ion exchange resins are inexpensive and can be used to develop a simple, rapid and cost-effective method of taste masking [Roy G., 1997]. As shown in Table 4, a number of ion exchange resins have been researched for their ability to mask the unpleasant taste of drugs.

Many therapeutically useful drugs have quite a bitter taste, which limits their utility in oral formulations. The fact is that drug release from ion-exchange materials is highly dependent on the physiological pH and electrolyte concentration within the GI tract can be applied for taste masking of drugs [Borodkin and Sundberg, 1971; Lu et al., 1991; Agarwal et al., 2000; Pisal et al., 2004]. Typically, the ionised drug and the ion-exchanger form a stable complex under buccal conditions (pH 6.7, low ion concentration) for the relatively short period of exposure, making the drug unavailable for a taste sensation.

As the formulation passes to the further parts of the GI tract, that is, under gastric and intestinal conditions, the drug is released from the ion-exchanger into the surrounding media due to the decreased pH in the stomach, increased ionic concentration of the GI tract, larger volume of the surrounding media and/or increased residence time in the stomach and intestine and is, thus, available for absorption. Efficient taste protection by ion-exchange resins has been demonstrated with a variety of drugs, such as dextromethorphan, ephedrine, pseudoephedrine, ranitidine, ciprofloxacin, erythromycin and clarithromycin [Borodkin and Sundberg, 1971; Lu et al., 1991; Anand et al., 2001; Pisal et al., 2004; Elder, 2005]. Unlike with many other approaches used in taste masking, ion-exchange materials are applicable also for suspensions, which are the preferred formulations in e.g. pediatric and geriatric medications [Lu et al., 1991; Agarwal et al., 2000].

Table 4. Examples of Ion Exchange Resins used for masking the Unpleasant Taste of Drugs

Bitter Drugs	Ion Exchange Resin	Reference
Zopiclone	Kyron T- 114	Warad S. et al., 2013.
Levocetirizine di-hydrochloride	Kyron T -104 and Kyron T- 114	N.Kanakadurga Devi et al., 2010.
Metoclopramide HCl	Indion 204	Dahima Rashmi et al., 2010.
Tinidazole	Kyron T-114, Kyron T-134 & Indion 214	A. M. Suthar et al., 2010.
Topirainate	Kyron T-104, Kyron T-114, Kyron T-134, Doshion P-542	Patel T.N. et al., 2010.
Metoclopramide HCl	Indion-234	Mahore J.G. et al., 2009.
Diphenhydramine HCl	Indion 234 and Tulsion 343	Bhise K. et al., 2008.
Fexofenadine HCl	Indion 204, 234 and 264	Madgulkar A. R. et al., 2007.
Rizatriptan Benzoate	Indion 204/214 & Tulsion 339/335	Chaudhari P. D. et al., 2006.
Levamisole HCl	Amberlite IRP-64/69	Jane V. C. et al., 2006.
Ciprofloxacin	Indion 234	Sambaji P. et al., 2004.
Chloroquine Phosphate	Polyacrylic acid	Agarwal R. et al., 2000.

5.1.2. Rapid Dissolution

Ion exchange drug resonate complexes have a faster rate of dissolution. Ion exchange resin matrices are hydrophilic and hence allow water/aqueous solutions to enter the dimensional resin structure, thereby enhancing the dissolution rate. Moreover, each individual drug molecules bound to a functional site of the resin molecule resulting in a reduction of crystal lattice energy, which may be responsible for enhancing the rate of drug dissolution bound to resin [Singh Inderbir et al., 2007; Hughes L., www.rohmhaas.com.].

5.1.3. Powder Processing Aid

Hygroscopic drugs are susceptible to agglomeration due to the presence of moisture. Adsorption of such drugs onto ion exchange resins may lead to a decrease in their hygroscopicity. Furthermore, because the resins have a uniform, macro reticular morphology, they provide excellent flowability to the formulation [Chaubal M.V., 2003].

5.1.4. Drug stabilization [Singh Inderbir et al., 2007; Bilandi Ajay et al., 2014; SivaneswariS. et al., 2015]

The drug resonate is frequently more stable than the original druge. Vitamin B12. Vitamin B12 has a shelf-life of only a few months, but resonate is stable for more than two years. Complexing active ingredients with ion exchange resins prevent harmful interaction with other components. Vitamin B12 deteriorates on storage. This necessitates the addition of overages, leading to significant increase in the cost of the formulations. The stability of Vitamin B12 can be prolonged by completing it with a weak acid cation exchange resin (INDION 264). This complex is as effective as the free form of the Vitamin. Thus the introduction of INDION 264 in the formulation significantly reduces the overages. Ion exchange resin can also be used as a carrier for immobilized enzymes to provide extended activity at localized sites. Another example is nicotine; it discolours quickly on exposure to air and light, but the resinate used in nicotine chewing gums and lozenges, is much more stable. [Kankkunen et al., 2002] have reported that an easily oxidized drug, levodopa, could be stabilized during storage using pH-adjustment and ion exchange fibers. Ion exchange fibers provide a promising alternative to control drug delivery and to store drugs that are degraded easily.

5.1.5. Anti-Deliquescence

Deliquescence can be defined as the conversion of a solid substance into a liquid as a result of absorption of water vapour from the air. Although this is not a common problem, it has been very difficult to solve and requires the use of specialized equipment or careful scheduling of production during dry seasons. However, ion exchange resins may prove instrumental in solving the problem of deliquescence of a drug by the formation of resonating complexes. Sodium valproate, a highly deliquescent drug, has been found to show free flowing properties after complexation with ion exchange resins. The amount of water absorbed decreased with increasing amount of valproate in the resonate. Similar results have been obtained with resinate of rivastigminebitartrate [Hughes L., 2004; Sharma et al., 2014].

5.1.6. Disintegration [Improved tablet Disintegration properties]

Ion exchange resins, because of their excellent swelling property when immersed in water, can be used as a tablet disintegrating agent. [Purnima A. et al., 2006] studied the swelling power of Indian 414, an ion exchange resin, sodium starch glycolate, croscopovidone and croscarmellose sodium, and reported the swelling indices to be 800, 750, 20 and 700, respectively. Mouth dissolving tablets of roxithromycin, dicyclomine, and montelukast sodium were prepared with different disintegrating agents and compared to their disintegrating properties [Sharma et al., 2014].

Advantages of ion exchange resins over conventional disintegrating agents are:

- The rate of permeation of water and subsequent swelling is very fast and cut down the disintegration time.
- Ion exchange resins do not have an adhesive tendency on hydration; hence tablet disintegrates evenly without formation of lumps.
- Ion exchange resin is effective in low concentration as disintegrants.
- Ion exchange resin incorporation confirms greater hardness to the tablet.
- Ion exchange resin work equally efficiently with hydrophilic as well as hydrophobic formulations, especially with the later where the conventional disintegrants are ineffective.

Because of their unusually large swelling capacities polymethacrylic carboxylic acid ion exchange resins have found usage in pharmacy as tablet disintegrants; for example pollacrilline a potassium salt of weakly acidic cation exchange resin with methacrylic acid divinyl benzene matrix [Sharma et al., 2014; J. Saurabh et al., 2014; K. Doraswamy, et al., 2013; Kristina Malinovskaja et al., 2013; Bhosale Rahul et al., 2012].

5.2. Controlled Drug Delivery Applications of IER

5.2.1. Oral Drug Delivery

5.2.1. 1. Chewing Gum for Buccal Absorption

Nicorette is a widely used patented product for smoking cessation program. It contains nicotine adsorbed on an ion exchange resin with carboxylic acid functionality and formulated in a flavoured chewing gum base provides gradual drug release through buccal mucosa as the gum is chewed offering fresh saliva as a solvent for elution[J. Saurabh et al., 2014; K. Doraswamy, et al., 2013; Bhosale Rahul et al., 2012; Sharma et al., 2014].

5.2.1. 2. Sustained Release Formulations such as Capsules, Liquids, Oral Tablet, etc.

The major drawback of sustained release or extended release is dose dumping hence resulting in increased risk of toxicity. The use of IER has occupied an important place in the development of controlled or sustained-release systems due to their better drug retaining properties and prevention of dose dumping. The drug resinates can also be used as a drug reservoir, which has caused a change of the drug release in hydrophilic polymer tablets[J. Saurabh et al., 2014; K. Doraswamy, et al., 2013; Bhosale Rahul et al., 2012].

5.2.1. 3. Gastrointestinal Sustained Release Mechanism

Bioavailability of drug absorbed on ion exchange resins depends on both transits of the particles through the G.I. tract and drug release kinetic. Drug release or dissolution from the resin can, in turn, occurs only by replacement of the drug by another ion with the same charge. Since the exchange is an equilibrium process; it depends on the body fluids, ionic constitution, and fluid volume. Additionally, the release is not instantaneous, and the drug must diffuse through the resin from the internal exchange sites. The net result of all the phenomena is a sustained release system. Biphetamine R a capsule containing an equal quantity of amphetamine & dextroamphetamine complexed to a sulphonic acid cation exchange resin has been used for antiobesity agent and for behavioural control of children [J. Saurabh et al., 2014; K. Doraswamy, et al., 2013; Bhosale Rahul et al., 2012].

5.2.1. 4. Bioadhesive System for Treatment of Gastric Mucosa

Ion exchange resin may have inherent bio adhesive properties similar to those of highly charged polyanions.⁹⁴ Hence ion exchange resins may be useful in mucoadhesive systems for topical treatment of stomachs such as H. pylori infection for prolonging the gastric residence of amoxicillin and cimetidine [J. Saurabh et al., 2014; K. Doraswamy, et al., 2013; Bhosale Rahul et al., 2012].

5.2.2. Nasal Drug Delivery

A novel nasal formulation, in the form of a nicotine-Amberlite resin complex powder, has been developed that provided an optimal combined pulsatile and sustained plasma nicotine profile for smoking cessation. Amberlite IRP69 and Amberlite IR120 are similar cationic exchange materials with the same ion exchange capacity but due to a smaller particle size range (10-150 µm). Amberlite IRP69 had a better flow property and a better adsorptive capacity than Amberlite IR120. The nicotine plasma profiles demonstrated that an initial rapid peak plasma level of nicotine followed by a sustained elevated level could be achieved by adjusting the ratio of free to bound nicotine in the Amberlite powder formulation [J. Saurabh et al., 2014; K. Doraswamy, et al., 2013; Bhosale Rahul et al., 2012].

5.2.3. Transdermal Drug Delivery

IER is also involved in the formulation of transdermal drug delivery systems. The release rates of ketoprofen from the carbopol-based gel vehicles containing ion exchange fibers to which the ketoprofen had been bound were determined across 0.22 μm microporous membrane. The fluctuation of the release rate of ketoprofen from the vehicles was much lower compared with that of simple gels, though the cumulative amount of ketoprofen delivery was less. In addition, ions could increase the rate and extent of ketoprofen delivery [J. Saurabh et al., 2014; K. Doraswamy, et al., 2013; Bhosale Rahul et al., 2012; P.S. Salve, 2011].

5.2.4. Ophthalmic Drug Delivery

IER also find application in ophthalmic drug delivery systems. An example is Betoptic S which is a sterile ophthalmic suspension and it contains 0.25% betaxolol hydrochloride. It is a cardioselective beta-adrenergic receptor blocking agent manufactured by Alcon Laboratories in the US. It is an ocular resinate ophthalmic product designed to lower elevated intraocular pressure. The drug resinate complex is formed when the positively charged drug is bound to a cation ion-exchange resin (Amberlite1 IRP 69). The 0.25% ophthalmic suspension of the drug showed an increased bioavailability. Microparticulates of ion exchange resin drug complex has been used for ophthalmic drug delivery of Betaxolol, an antiglaucoma agent [S. Sivaneswari et al., 2015].

Table 5. Examples of Controlled Drug Delivery Systems Studied, Utilising Ion-Exchange Materials

Drugs	Ion exchange resin	Reference
Glipizide	Indion 454	J. Saurabh et al., 2014.
Apomorphine	Smopex [®] -101 & Smopex [®] -102	Kristina Malinovskaja et al., 2013.
valsartan	Sulfonated methacryloxyacetophenone and methyl methacrylate	K. Doraswamy, et al., 2013.
Propranolol	Indion 254	Bhosale Rahul et al., 2012.
salbutamol sulphate	Amberlite IRP 69	P.S. Salve, 2011.
Chlorpheniramine	Indion 244	A. U. Kadam et al., 2008.

5.3. Targeted Drug Delivery System [Anticancer Drug]

This concept is based on the chemoembolised of drug-loaded microspheres via a tumour arterial supply. Because of their physical size microspheres can be entrapped in the capillary beds along with their load of cytotoxic drugs can be delivered to well vascularised tumour tissues. B.N. Gray has studied the in vitro release of cytotoxic agents from ion exchange resins.

5.4. Isolation and Purification of Bioactive Proteins from Bovine Colostrum [Mianbin Wu et al., 2011]

Bovine colostrums are the milk secreted by cows during the first few days after parturition. It contains many essential nutrients and bioactive components, including growth factors, immunoglobulins (Igs), lactoperoxidase (Lp), lysozyme (Lys), lactoferrin (Lf), cytokines, nucleosides, vitamins, peptides, and oligosaccharides, which are of increasing relevance to human health. Much research work has been done on the structure and function of bovine colostrum proteins. IgG was widely utilised in the immunological supplementation of foods, specifically in infant formulae.

Apart from the two kinds of bovine colostrum proteins, α -lactalbumin has been claimed as an important food additive in infant formula due to its high content in tryptophan and as a protective against ethanol and stress-induced gastric mucosal injury. β -Lactoglobulin is commonly used to stabilize food emulsions for its surface-active properties. Bovine serum albumin (BSA) has gelation properties and it is of interest in a number of food and therapeutic applications. Therefore, fractionation for the recovery and isolation of these proteins has a great scientific and commercial interest.

As a result of this growth in the commercial use of bovine colostrum proteins, there is great interest in establishing more efficient, robust and low cost processes to purify them. Although great deals of studies have been done for the separation and purification of colostrum proteins due to their wide application in food industry, medicine and as supplements, large scale production system for the downstream processing of recombinant antibodies still represents the major issue. [Lu et al., 2007] designed a two-step ultrafiltration process followed by a fast flow strong cation exchange chromatography to isolate LF from bovine colostrum on a production scale. A stepwise procedure for purification of the crude LF was conducted using a preparative-scale strong cation exchange chromatography.

Ion exchange Chromatography

Proteins contain charged groups on their surfaces that enhance their interactions with solvent water and hence their solubility. Charged residues can be cationic or anionic and it is noteworthy that even polar residues can also be charged under certain pH conditions. These charged and polar groups are responsible for maintaining the protein in solution at physiological pH. Because proteins have unique amino acid sequences, the net charge on a protein at physiological pH is determined ultimately by the balance between these charges. This also underlies differing isoelectric points (pIs) of proteins [Himmelhoch 1971]. Therefore, bioactive proteins can be absorbed by different ion-exchange chromatography due to the different charge type and pI. The ion-exchange resins are then selectively eluted by slowly increasing the ionic strength (this disrupts ionic interactions between the protein and column

matrix competitively) or by altering the pH (the reactive groups on the proteins lose their charge) [Dolman et al., 2002]. The whey proteins can be fractionated and separated by different ion exchange chromatography.

The Mechanism of Hydrophobic Charge Induction Chromatography (HCIC)

HCIC binding is based on mild hydrophobic interaction and is achieved under near physiological conditions, without the addition of lipotropic or other salts. Desorption is based on electrostatic charge repulsion and is accomplished by reducing the pH of the mobile phase. Under mildly acidic conditions (pH 4.0–4.5), the ligand and target molecule took a net positive charge; binding is thus disrupted and elution occurs. Elution is conducted using a dilute buffer (e.g., 50mM acetate). The new BioSeptra MEP HyperCel sorbent from Life Technologies, Inc. (LTI; Rockville, MD) has been optimized for capture and purification of monoclonal and polyclonal IgG. The heterocyclic ligand, derived from 4-mercaptoethylpyridine (4-MEP), provides efficient capture and purification of antibodies from a broad range of sources, such as animal sera, ascites fluid and a variety of cell culture supernatants, including protein-free, chemically defined, protein-supplemented and serum supplemented media.

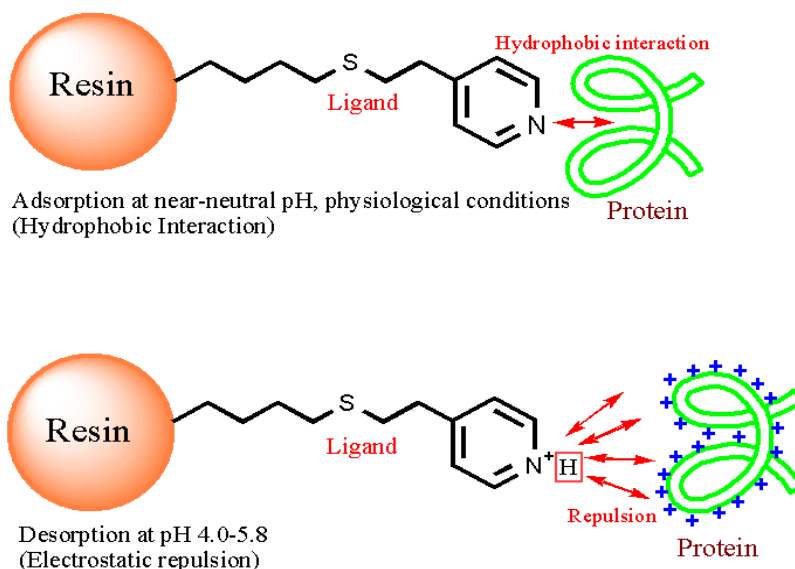


Figure 7: Mechanism for Hydrophobic Charge-induction Chromatography

At neutral pH, (top) the ligand is uncharged and binds molecules through mild hydrophobic interaction. As the pH is reduced (bottom), the ligand becomes positively charged and hydrophobic binding is disrupted by electrostatic charge repulsion.

5.5. Removal of Chromium III) from the Waste Solution of an Indian Tannery by Amberlite IR 120 Resin [Sahu Sushanta Kumar et al., 2012]

In recent years, chromium has received considerable attention owing to uses of its compounds in pigments and paints, leather tanning, oxidative dyeing, electroplating, fungicides, catalysis, refractory materials, glass Industries and various other industrial applications. These industrial processes discharge large quantities of chromium into the environment. Chromium occurs in aqueous systems in the trivalent and hexavalent forms. Out of the two forms, hexavalent chromium is more hazardous to living organisms than the chromium (III). Rapid oxidation of chromium (III) to chromium (VI) state in aquatic and solid wastes situations accounts for mobility of chromium. Therefore, removal and recovery of chromium (III) from industrial wastewater and effluents are critical from both ecological and economic point of view. It may reduce the risk of polluting environment while the recovered compounds of chromium (III) can be reused.

5.6. Clinical Use of Ion Exchange Resins

Ion exchange resins have notably found use in the treatment of various pathological states such as hyperacidity; ulcer; Na and K supplement depletion; nephrotic, pancreatic and cardiac oedema, etc. Cationic resins have also been used as oral therapeutics to reduce phosphate levels for end-stage renal disease patients. Cation-exchange resin (sodium polystyrene sulphonate) has been reported as an adjuvant in the treatment of hyperkalaemia associated with oliguria or anuria secondary to acute renal failure [Pandit JK et al 2006]. Anion-exchange resins have been used in the treatment of hyperglycaemias. At present, cholestyramine and colestipol (AER) are used in the treatment of type II hyperlipoproteinaemia and familial hypolipoproteinaemia in children and young adults [Witzman JL, 1996]. Colestipol hydrochloride acts by increasing fractional catabolic rate of low-density lipoproteins (LDL), thereby decreasing LD [Zernp HN 1983; Kunin R 1988].

Toothpaste, lacquers, and prostheses coming in contact with tooth surface are rendered anticariogenic by incorporating ion exchange resins containing fluorine, phosphate or calcium ions [Naumann G et al 1976].

5.6.1. Application in Treatment of High Cholesterol

Cholesterol reducer Cholestyramine resin USP, when used as an active ingredient binds bile acids, this leads to replenishment of bile acids; through increased metabolism of serum cholesterol resulting in lowered serum cholesterol levels. Cholestyramine was the first polymeric resin-based drug that was approved for the treatment of high cholesterol. The resin, in this case, serves as a sequestrant to bind bile acids in the gastrointestinal tract. The binding and effective removal of bile-acids forces the liver to consume cholesterol to synthesize more bile acids. This leads to the indirect reduction in cholesterol levels. The advantage of this therapy was that it did not use conventional drugs and hence had lower side effects as compared to conventional therapies. The drawback of this therapy was the high-dose requirements for the first-generation resins (four tablespoons administered via fruit juice).

Colestimide, a 2-methylimidazole-epichlorohydrin polymer, is a new bile acid sequestering resin that is fourfold as powerful at lowering low-density lipoprotein cholesterol (LDL-C) as the conventional resin (cholestyramine). Colestimide has been reported to lower blood glucose levels in patients with type 2 diabetes complicated by hypercholesterolaemia [Tatsuya S et al., 2007].

5.6.2. Application of Non-absorbable Ion Exchange Resin in Pruritus

These molecules are not absorbable from GIT and release chloride and bind bile acid in the lumen of the intestine, diminishing their enterohepatic recirculation. Non-absorbable ion exchange resin augments cholesterol excretion via enhanced conversion to bile acids. These drugs can decrease the bile acid pool by Ca. 40%. Trihydroxy bile acid dissociates rapidly from these molecules and can be absorbed in the ileum.

Cholestyramine (orange-flavoured granules) has been used for some decades and has been proven to be effective and safe. However, palatability is poor, limiting the tolerability to this drug. Through the nasogastric tube, administration of cholestyramine through this pathway has been shown to be well tolerated and successful in decreasing serum cholesterol levels and improving pruritus. Colestipol in granules or tablets has not been used frequently in children. Colesevelam hydrochloride (in the form of non-absorbable hydrogel or tablets) is probably the best tolerated of these drugs. This drug has enhanced the specificity, greater affinity and higher capacity for binding bile acids compared with the above two non-absorbable IER. Non-absorbable IERs can interfere with intestinal absorption of other drugs, like ursodeoxycholic acid (UDCA). So another drug should be given 1 or 4-6 h after cholestyramine administration to avoid interaction with another drug including fat-soluble vitamins and to allow a maximal capture of bile acids. Non-absorbable IER dose is 8—16 g orally 2—3 daily, increased progressively by 2 g daily side effects of non-absorbable IER include constipation and hyperchloraemic acidosis due to the large quantity of chloride released in GIT and absorbed instead of bicarbonate.

5.6.3. Adsorption and Recovery of Rifamycin B and Rifamycin S

The antibiotic rifamycin S is a physiologically active derivative of the rifamycin-B (Gilpin JA et al 1983). Strongly or weakly basic anion-exchange resins are reported for recovery of antibiotic rifamycin S from rifamycin B, by curtailing complex, multi-step processes involved in separation.

5.6.4. Ion-Exchange Resins in the Treatment of Oedema

Sulphonated and carboxylic resins with a polystyrene backbone are most widely used in clinical medicine. The pharmacological activity of these resins is attributed to their ability to adsorb ions, which are more selective to the resin than the counter- ion of the resin. Resins are mostly used in conditions of sodium and water retention, such as in cardiac failure, renal disease (nephritic syndrome), and toxemia of pregnancy and cirrhosis of the liver (Payne WW 1956). In hypertension and oedema, dietary restriction of sodium to less than 0.5 g/day is difficult. IER has been used as reinforcement of a low sodium diet or to enable high salt intake in the diet. Certain cation-exchange resins in the H⁺ or NH⁺ form may be used for the relief and control of oedema. Doses of about 50 g/day are usually required, in conjunction with a limited salt intake. IER has also been used for haemoperfusion and management of drug overdoses (poisoning).

The resins have a greater affinity for calcium and magnesium than for potassium and for potassium than for sodium. Under suitable conditions, the resin may replace one cation in a solution by another, though the extent to which this occurs depends on several factors such as the relative concentrations, the pH of the medium and the time allowed for exchange. Treating oedema, either carboxylic or sulphonic resins can be given by mouth, in either the hydrogen or ammonium form. The greater part of the exchange of cations appears to take place in the upper part of the alimentary canal and involves mainly the cations ingested in the food. For each milliequivalent of cation taken up by the resin, 1 mEq of ammonium or hydrogen is exchanged and absorbed together with 1 mEq of the anion. The ammonia is converted to urea, while the hydrogen ions are buffered by bicarbonate to form H₂CO₃, which is removed by increased pulmonary ventilation. The anions absorbed are accommodated in the extracellular fluid at the expense of bicarbonate. The latter is lowered still further by the loss of fixed base in the urine, but the kidney reduces this loss by secreting a highly acidic urine (containing H₂PO₄ in place of HPO₄) and, after a few days' delay, by forming a large quantity of ammonia. In this way, disposable cations are absorbed in place of sodium, which is removed in the faeces. The corresponding anions are excreted by the kidney with little fixed base and with a minimum change in plasma pH (compensated metabolic acidosis such as Compensation cannot be effected if renal function is severely impaired: in this case, sodium and other cations will be lost in the

urine and severe acidosis will develop. The amount of sodium removed in the faeces by a given dose of the resin decreases with decreasing dietary sodium.

As its bulk limits the quantity that can be given, there is a definite limit to the amount of sodium that can be removed and it is rare for the faeces to contain more sodium than the diet.

5.6.4.1. Application of Cation-Exchange Resin (Resodec) in the Treatment of Cardiac Oedema

'Resodec' (a balanced ammonium-potassium carboxylic resin) in congestive heart failure produces clinical results similar to those of dietetic sodium restriction but sometimes with undesirable side effects which are due to hyperchloraemia or to development of abnormal serum potassium levels. Biochemical control is essential in the early stages of treatment. This is especially important in patients with renal impairment and in those who have been on a sodium-restricted diet or on mercurial diuretics; such patients may have abnormal blood electrolyte levels resulting from previous treatment. These abnormalities are sometimes corrected but sometimes aggravated by resin therapy. Subject to biochemical control, the resin can be used as a substitute for low sodium diet or in conjunction with the diet to reinforce the latter. When given in addition to low sodium diet, the best result was obtained with repeated short courses. Ammonium chloride should be discontinued during periods of resin administration.

Complications of Cation-Exchange Resin Therapy used in the Treatment of Oedema:

- ❖ **Acidosis:** A compensated metabolic acidosis develops in every case treated with cation-exchange resins. In a great majority, this produces no undesirable effects, though it is possible that it might play a part in producing skeletal decalcification over a long period, especially if hypocalcaemia were also produced.
- ❖ **Sodium Deficiency:** The low salt syndrome may be produced if sodium removal is too drastic or if very much sodium is removed in the urine. This sodium depletion may be associated with signs of cellular over-hydration, vascular collapse and renal failure and finally death.
- ❖ **Potassium Deficiency:** This is particularly liable to occur with low sodium diets, for resins will then remove more potassium than sodium in the faeces. The simplest safeguard is to give extra potassium with the resin, i.e. to give it partly in the potassium cycle. The potassium is exchanged for hydrogen in the stomach and is available for absorption in the intestine.
- ❖ **Calcium Deficiency:** In few cases, this appears to be a real hazard after very long periods of treatment. It must be remembered that if the kidney cannot form ammonia, extra losses of sodium, potassium, and calcium in the urine may cause deficiencies of these ions. On the other hand, if the renal failure or oliguria is present, hyperkalaemia may occur if a potassium resin is given.
- ❖ Anorexia and nausea, abdominal pain, diarrhoea, constipation and even faecal impaction have been noted in a few of the cases treated.
- ❖ Urinary casts nearly always appear when highly acidic urine is being formed [Cheng YH et al 2002], but there is no evidence that they impair renal function. A high fluid intake has been recommended.
- ❖ Deficiencies of iron, magnesium, thiamine, and riboflavin might theoretically occur but have not been reported [Martz BL et al 1952] found a normal response to iron in one patient with hypochromic anaemia while on resin therapy.

5.6.5. Anion-Exchange Resins as Antacids (Amberlite IR-4)

The anion-exchange resin is effective in neutralizing the acid and inactivating pepsin of both ulcer and non-ulcer patients (divided doses of about 25 g/day are usually recommended). Segal and co-workers demonstrated that the weakly basic resins are capable of raising the pH of gastric juice from pH 1—5. The advantages claimed for this type of treatment include (a) great speed of action; (b) greater neutralizing power when used in practical application; (c) complete inhibition of peptic activity; (d) no removal of PO_4^- ; (e) lack of acid rebound; (f) no constipating effect; and (g) no chloride removal.

5.6.6. Application of Ion Exchange Resins in Kidney Dialysis

Besides the proved applications of ion exchange resins (IER) in various industries, biochemists have found their uses in medicines also. The development and use of synthetic ion exchange resins for kidney dialysis is a relatively recent achievement. The artificial kidney uses cellulose membranes in place of the phospholipid-bilayer membranes used by real kidneys to separate the components of blood. Polymeric ion exchange resins are insoluble, so when taken orally, pass through the gastrointestinal tract (GIT) without being absorbed. In the malfunctioned kidney, sodium and calcium polystyrene sulfonate resins are designed to exchange sodium for potassium in the colon, for use in the treatment of hyperkalemia. It is predicted that additional therapeutic applications may be found for ion exchange resins in the coming years.

5.7. Use of Ion Exchange Resins in Water Treatment: [Rohm & Haas. 2008]

A bed of resin can be used either to remove unwanted ions from a solution passed through it or to accumulate a valuable mineral from the water which can later be recovered from the resin. Examples of the removal of unwanted ions are the removal of heavy metals from metal trade wastes, the demineralisation of the whey used to manufacture specialized dairy products and the removal of salts from fruit juices.

Strong cation resins in the hydrogen form are used for the hydrolysis of starch and sucrose.

Resins also find many uses in the laboratory where the chemist's ingenuity is less constrained by economic considerations. They can be used to remove interfering ions during analysis or to accumulate trace quantities of ions from dilute solutions after which they can be concentrated into a small volume by elution.

A cation resin in the hydrogen form can be used to determine the total concentration of ions in a mixture of salts. The sample passing through a column is converted to the equivalent quantity of acid and the amount readily found by titration.

One of the earliest applications of ion exchange was the separation of rare earth elements during the 1940's. These metals occur naturally as mixtures and have almost identical chemical properties. The equilibrium quotients for cationic resin were found to vary sufficiently for separation to be achieved chromatographically by adding a solution of the mixture to a resin column and eluting the metals with an acid wash. These work lead first to the discovery of promethium (element 61) and later to the discovery of five new elements in the actinide series.

5.7.1. Water Treatment

Far more resin is used for water purification than for any other purpose. It is, therefore, appropriate to discuss water treatment examples when outlining the application of the principles of ion exchange technology. Industrial ion exchange units are produced in sizes ranging from a few litres up to vessels holding several tonnes of resin. Service runs between regenerations usually range from 12 to 48 hours.

The two major types of treatment applied to water are **water softening** - the replacement of 'hard' ions such as Ca^{2+} and Mg^{2+} by Na^+ and **demineralisation** - the complete removal of dissolved minerals. Both of these treatments are outlined below.

5.7.1.1. Water Softening

In water softening a cation resin in the sodium, the form is used to remove hard metal ions (calcium and magnesium) from the water along with troublesome traces of iron and manganese, which are also often present. These ions are replaced by an equivalent quantity of sodium so that the total dissolved solids content of the water remains unchanged as does the pH and anionic content. At regular time intervals, the resin is cleaned (Figure). This involves passing influent water back up through the resin to remove suspended solids, passing a regenerant solution down through the resin to replace the ions that have bound to the resin and then rinsing again with water to remove the regenerant solution. In water softening the regenerant is a strong solution of sodium chloride.

Table: Ion Exchange Process for Water Treatment

Typical Minerals in Influent		Types of Exchanger		Minerals Converted to
A. $\text{Ca}(\text{HCO}_3)_2$ CaSO_4	→	Cation Exchanger (Na^+ Form)	→	NaHCO_3
	→		→	Na_2SO_4
B. $\text{Ca}(\text{HCO}_3)_2$ CaSO_4	→	Cation Exchanger (H^+ Form)	→	H_2CO_3
	→		→	H_2SO_4
C. $\text{Ca}(\text{HCO}_3)_2$	→	Cation Exchanger (H^+ Form) (Weak acid)	→	H_2CO_3
D. Na_2SO_4 NaHCO_3	→	Anion Exchanger (Cl^- Form)	→	NaCl
	→		→	NaCl
E. H_2CO_3 H_2SO_4	→	Anion Exchanger (OH^- Form)	→	H_2O
	→		→	H_2O
<ul style="list-style-type: none"> • Conventional Softening – Process (A) • Dealkalization by split stream softening – blending effluents from (A) & (B) • Dealkalization by anion exchange – Process (D) Proceeded by (A) • Dealkalization by weak acid cation exchanger followed by conventional softening process (C) followed by (A) • Demineralizing – combination of (B) & (E) 				

5.7.2. Application other than Water Treatment

There is an incredible number of applications in fields other than water treatment. Let us mention a few of them:

- Softening of beet sugar juices before evaporation
- Colour removal from cane sugar syrups
- Chromatographic separation of glucose and fructose
- Demineralisation of whey, glucose and many other foodstuffs
- Recovery of polyphenols for use in the food industry
- Recovery of uranium from mines
- Recovery of gold from plating solutions
- Separation of metals in solution

- Catalysis of anti-knocking petrol additives
- Extraction of antibiotics and other compounds from fermentation broths
- Purification of organic acids

6. MARKETED ION EXCHANGE RESINS

The popular resin brands available in the market:

Table 6: Various Brands and Manufacturer of IER
 [http://www.ionresins.com/pdf/cross_reference.pdf]
 [Friedrich & Helfferich., 1995)

S.N.	Brand	Manufacturer
1.	DOWEX	The Dow Chemical Company
2.	AMBERLITE	Rohm and Haas Company
3.	INDION	Ion Exchange India Pvt. Ltd
4.	TULSION	Thermax India Pvt. Ltd
5.	PUROLITE	Purolite Inc.
6.	DIAION	Mitsubishi
7.	LEWATIT	Lanxess
8.	ZEO-KARB	The Permutit Co. Ltd.
9.	ZEROLIT	United Water Softeners
10.	NALCITE	National Aluminate Corp.,

Table 8: Brands of AMBERLITE

Commercial Name	Compendia Name	Matrix Type	Nature	Ionic Form	Application
AMBERLITE™ IRP64	Polacrillex Resin	Methacrylic acid divinyl benzene polymer	Weak acid -COO ⁻	H ⁺	<ul style="list-style-type: none"> • Taste masking agent • Drug stabilizing agent • Nicotine
AMBERLITE™ IRP88	Polacrilin Potassium	Methacrylic acid divinyl benzene polymer	Weak acid -COO ⁻	K ⁺	<ul style="list-style-type: none"> • Tab. Disintegrant • Taste masking agent
AMBERLITE™ IRP69	Sodium Polystyrene Sulfonate	Styrene-divinyl benzene polymer	Strong acid -SO ₃ ⁻	Na ⁺	<ul style="list-style-type: none"> • Sustained release • Drug stabilizing agent • Taste masking agent
DUOLITE™ AP143	Cholestyramine Resin	Styrene-divinyl benzene polymer	Strong base -N ⁺ (R) ₃	Cl ⁻	<ul style="list-style-type: none"> • Sustained release • Drug stabilizing agent • Taste masking agent

Table 9: Brands of INDION

Commercial Name	Matrix Type	Particle Size	Functional Group	Total exchange capacity (meq/mL)	Ionic form	Application
INDION 224	Styrene Divinyl benzene	0.2 - 12	- SO ₃	4.8	H ⁺	Sustained release agent
INDION 244	Styrene Divinyl benzene	≤0.15	- SO ₃	4.5	H ⁺	Sustained release agent
INDION 254	Sod. Polystyrene Sulfonate USP	≤0.15	- SO ₃	NA	Na ⁺	Sustained release agent, USP specified
INDION 284	Styrene Divinyl benzene	0.3 – 1.2	- SO ₃	1.0	Na ⁺	Sustained release agent

Table 10: Brands of TULSION

Commercial Name	Compendia Name	Application
Tulsion®335	Polacrilex	<ul style="list-style-type: none"> • Taste masking • Preparation of nicotine Polacrilex • Vitamin b 12 stabilization
Tulsion®339	Polacrilex Potassium USP	<ul style="list-style-type: none"> • High performance tablet disintegrant • Taste masking
Tulsion®344	Sodium Polystyrene Sulphonate USP	<ul style="list-style-type: none"> • Sustained release or Modified release agent • Drug stabilization • Taste masking
Tulsion®345	Calcium Polystyrene Sulphonate BP	<ul style="list-style-type: none"> • Treatment of blood disorders • Potassium reduction in blood
Tulsion®142(CHL)	Cholestyramine Resin USP	<ul style="list-style-type: none"> • Reduction of bile acids Cholesterol reduction • Taste masking

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