

# Ion Exchange Resins: Drug Delivery and Therapeutic Applications

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## *Ion Exchange Resins: Drug Delivery and Therapeutic Applications*

### *Summary*

*Ion exchange resins are water insoluble cross-linked polymers containing a salt-forming group at repeating positions on the polymer chain. They can be classified as cationic or anionic exchange resins depending upon the nature of the exchangeable ion of the resin as a cation or anion, respectively. The degree of cross-linking and particle size of the resin substantially modify its properties and applications. Ion exchange resins can be used to overcome various pharmaceutical formulation problems including bitter taste, poor stability, deliquescence, and poor dissolution of the drugs. Resins have also been used as superdisintegrants in tablet formulations because of their swelling properties. Modified release of drugs from resinate (drug – resin complexes) is another potential application of ion exchange resins. Because of the versatile utility of ion exchange resins, they are being used for various drug delivery and therapeutic applications.*

**Key Words:** *Ion exchange resins, exchangeable ion, taste masking, modified release.*

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## *İyon Değişirici Reçineler: İlaç Taşıyıcı Olarak ve Tedavi Amaçlı Uygulamaları*

### *Özet*

*İyon deęiřtirici reęineler polimer zincirinde tekrarlayan pozisyonlarda tuz oluřturan gruplar taşıyan suda çözünen çapraz baęlı polimerlerdir. Deęiřen iyonun anyon yada katyon olması durumuna göre anyon deęiřtirici veya katyon deęiřtirici reęineler řeklinde sınıflandırılabilirler. Çapraz baęların derecesi ve partikül büyüklüęü reęinenin özelliklerini ve uygulamalarını büyük oranda deęiřtirir. İyon deęiřtirici reęineler, acı lezzet, zayıf stabilite, sulanma, düşük daęılım gibi farmasötik formlasyonlarda karşılaşılan pek çok sorunun giderilmesinde kullanılabilir. Reęineler aynı zamanda řişme özellikleri nedeniyle tablet formülasyonlarında super daęıtıcı olarak kullanılabilirler. Rezinattan (ilaç-reęine kompleksi) deęiřtirilmiş ilaç salımı iyon deęiřtirici reęinelerin bir diđer uygulama alanıdır. İyon deęiřtirici reęineler çok yönlü kullanımları nedeniyle, çok çeřitli ilaç taşıma ve terapötik uygulamalarda kullanılmaktadır.*

**Anahtar Kelimeler:** *İyon deęiřtirici reęineler, deęiřebilir iyonlar, tat maskeleyme, deęiřtirilmiş salım*

## INTRODUCTION

Ion exchange resins are insoluble polymers that contain acidic or basic functional groups and have the ability to exchange counter-ions within aqueous solutions surrounding them. An ion exchange resin is an insoluble matrix (or support structure) normally in the form of small (1-2 mm diameter) beads, usually white or yellowish, fabricated from an organic polymer substrate backbone (1). The material has a highly developed structure of pores on the surfaces from where the ions are trapped or released. The trapping of ions takes place only with simultaneous release of other ions; thus, the process is called ion exchange (2).

There are multiple types of ion exchange resins that are fabricated to selectively prefer one or several different types of ions. Ion exchange fibers have been widely used in many applications due to their high separation capacity, fast ion exchange rate and good electrical conductivity (3). Ion exchange resins are also used for various separation, purification, and decontamination processes. The most common examples are water softening and water purification. In many cases, ion exchange resins were introduced in such processes as a more flexible alternative to the use of natural or artificial zeolites. Ion exchange

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resins have found applications not only as drug carriers, but also in a number of areas within formulations and drug delivery and biomedical analysis (4). These resins are being used extensively in overcoming various formulation-related problems including poor stability and poor dissolution, for taste masking and as a powder processing aid (5). Moreover, ion exchange resins can also be used for modifying the drug release from the formulation, and are used substantially in oral, ophthalmic, nasal, transdermal, and parenteral drug delivery because of their diverse properties and applications. Ion exchange resin like cholestyramine, because of its bile acid sequestering property, is used as a hypolipidemic drug for lowering cholesterol levels in the body.

Typical ion exchange resins are based on cross-linked polystyrene. The required active groups can be introduced after polymerization, or substituted monomers can be used. For example, the cross-linking is often achieved by adding 0.5-25% of divinyl benzene to styrene at the polymerization process. Non-cross-linked polymers are used only rarely because they are less stable. Cross-linking decreases ion exchange capacity of the resin and prolongs the time needed to accomplish the ion exchange processes. Particle size also influences the resin parameters; smaller particles have larger outer surface, but cause larger head loss in the column processes (2).

## Chemistry

An ion exchange resin is a polymer (normally styrene) with electrically charged sites at which one ion may replace another. Natural soils contain solids with charged sites that exchange ions, and certain minerals called zeolites are quite good exchangers. Ion exchange also takes place in living materials because cell walls, cell membranes and other structures have charges. In natural waters and in wastewaters, there are often undesirable ions and some of them may be worth recovering. For example, cadmium ion is dangerous to health but is usually not present at concentrations that would justify recovery. On the other hand, silver ion in photographic wastes is not a serious hazard, but its value is quite high. In either case, it makes sense to substitute a suitable ion such as sodium for the ion in the wastewater.

Synthetic ion exchange resins are usually cast as porous

beads with considerable external and pore surface where ions can attach. The resins are prepared as spherical beads 0.5 to 1.0 mm in diameter. These appear solid even under the microscope, but on a molecular scale the structure is quite open (Fig. 1). Whenever there is a great surface area, adsorption plays a role. If a substance is adsorbed to an ion exchange resin, no ion is liberated. Testing for ions in the effluent will distinguish between removal by adsorption and removal by ion exchange. Of course, both mechanisms may be significant in certain cases, and mass balances comparing moles removed with moles of ions liberated will quantify the amounts of adsorption and ion exchange.

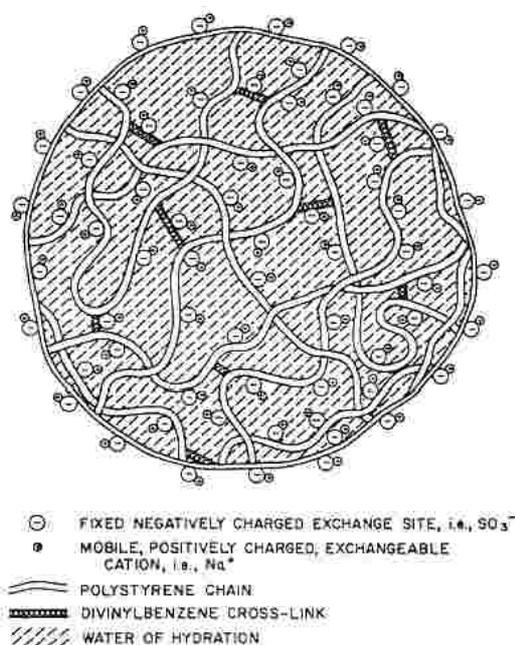


Figure 1 : Expanded view of a polystyrene bead.

While there are numerous functional groups that have charge, only a few are commonly used for man-made ion exchange resins. These are:

- $-\text{COOH}$ , which is weakly ionized to  $-\text{COO}^-$
- $-\text{SO}_3\text{H}$ , which is strongly ionized to  $-\text{SO}_3^-$
- $-\text{NH}_2$ , which weakly attracts protons to form  $\text{NH}_3^+$
- secondary and tertiary amines that also attract protons weakly
- $-\text{NR}_3^+$ , which has a strong, permanent charge (R stands for some organic group)

These groups are sufficient to allow selection of a resin with either weak or strong positive or negative charge.

## Classification

Ion exchange resins are broadly classified into two main categories (6), as cation exchange resins and anion exchange resins (Fig. 2).

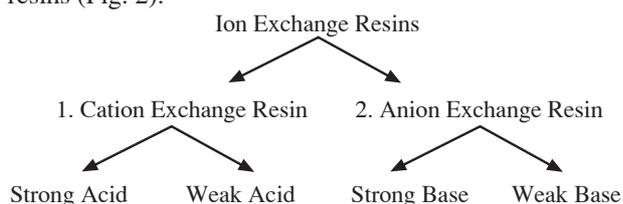
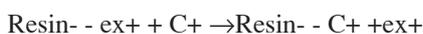


Figure 2 : Classification of ion exchange resins.

**1. Cation Exchange Resins**, whose exchangeable ions are positively charged: Cation exchange resins are prepared by the copolymerization of styrene and divinyl benzene and have sulfonic acid groups (-SO<sub>3</sub>H) introduced into most of the benzene rings. The mechanism of cation exchange process can be represented by the following reaction:

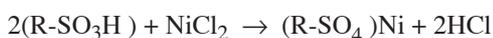


Where, Resin- indicates a polymer with SO<sub>3</sub>-sites available for bonding with exchangeable cation (ex<sup>+</sup>), and C<sup>+</sup> indicates a cation in the surrounding solution getting exchanged.

Cation exchange resins can be further classified into:

### Strong Acid Cation Exchange Resins

Strong acid resins are so named because their chemical behavior is similar to that of a strong acid. These resins are highly ionized in both the acid (R-SO<sub>3</sub>H) and salt (R-SO<sub>3</sub>Na) form of the sulfonic acid group (-SO<sub>3</sub>H). They can convert a metal salt to the corresponding acid by the reaction:



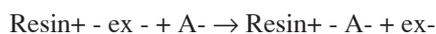
The hydrogen and sodium forms of strong acid resins are highly dissociated, and the exchangeable Na<sup>+</sup> and H<sup>+</sup> are readily available for exchange over the entire pH range. Consequently, the exchange capacity of strong acid resins is independent of the solution pH.

These resins would be used in the hydrogen form for complete deionization; they are used in the sodium form for water softening (calcium and magnesium removal). After exhaustion, the resin is converted back to the hydrogen form (regenerated) by contact with a strong acid solution, or the resin can be converted to the sodium form with a sodium chloride solution. For the above reaction, hydrochloric acid (HCl) regeneration would result in a concentrated nickel chloride (NiCl<sub>2</sub>) solution.

### Weak Acid Cation Exchange Resins

These resins behave similarly to weak organic acids that are weakly dissociated. In a weak acid resin the ionizable group is a carboxylic acid (COOH) as opposed to the sulfonic acid group (SO<sub>3</sub>H) used in strong acid resins. The degree of dissociation of a weak acid resin is strongly influenced by the solution pH. Consequently, resin capacity depends in part on the solution pH. A typical weak acid resin has limited capacity below a pH of 6.0, making it unsuitable for deionizing acidic metal finishing wastewater.

**2. Anion Exchange Resins**, whose exchangeable ions are negatively charged: These are prepared by first chloromethylating the benzene rings of styrene-divinyl benzene copolymer to attach CH<sub>2</sub>Cl groups and then causing these to react with tertiary amines such as triethylamine. The mechanism of anion exchange process can be represented by the following reaction:

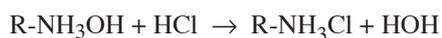


Where, Resin<sup>+</sup> indicates a polymer with N<sup>+</sup> sites available for bonding with exchangeable anion (ex<sup>-</sup>), and A<sup>-</sup> indicates anions in the surrounding solution getting exchanged.

Anion exchange resins can be further classified into:

### Strong Base Anion Exchange Resins

Like strong acid resins, strong base resins are highly ionized and can be used over the entire pH range. These resins are used in the hydroxide (OH) form for water deionization. They will react with anions in solution and can convert an acid solution to pure water:



Regeneration with concentrated sodium hydroxide (NaOH) converts the exhausted resin to the OH form.

#### *Weak Base Anion Exchange Resins*

Weak base resins are like weak acid resins in that the degree of ionization is strongly influenced by pH. Consequently, weak base resins exhibit minimum exchange capacity above a pH of 7.0. The weak base resin does not have a OH ion form as does the strong base resin.



Consequently, regeneration needs only to neutralize the absorbed acid; it need not provide OH ions. Less expensive weakly basic reagents such as ammonia (NH<sub>3</sub>) or sodium carbonate can be employed.

### **Properties of Ion Exchange Resins (7)**

#### **1. Cross-linking**

The amount of cross-linking depends on the proportions of different monomers used in the polymerization step. Practical ranges are 4% to 16%. Resins with very low cross-linking tend to be watery and change dimensions markedly depending on which ions are bound. Properties that are interrelated with cross-linking are:

##### *Moisture Content*

A physical property of the ion exchange resins that changes with changes in cross-linkage is the moisture content of the resin. For example, sulfonic acid groups (-SO<sub>3</sub>H) attract water, and this water is tenaciously held inside each resin particle. The quaternary ammonium groups of the anion resins also behave in a similar manner.

##### *Capacity*

The total capacity of an ion exchange resin is defined as the total number of chemical equivalents available for exchange per some unit weight or unit volume of resin. The capacity may be expressed in terms of milliequivalents per dry gram of resin or in terms of milliequivalents per milliliter of wet resin.

The more highly cross-linked a resin, the more difficult it

becomes to introduce additional functional groups. Sulfonation is carried out after the cross-linking has been completed and the sulfonic acid groups (-SO<sub>3</sub>H) are introduced inside the resin particle as well as over its surface. Likewise, the quaternary ammonium groups are introduced after the polymerization has been completed, and they too are introduced both inside the particle as well as on its surface. Fewer functional groups can be introduced inside the particles when they are highly cross-linked, and hence the total capacity on a dry basis drops slightly.

This situation is reversed when a wet volume basis is used to measure the capacity on a resin. Although fewer functional groups are introduced into a highly cross-linked resin, these groups are spaced closer together on a volume basis because the volume of water is reduced by the additional cross-linking. Thus, the capacity on a wet volume basis increases as cross-linking increases.

##### *Equilibration Rate*

Ion exchange reactions are reversible reactions with equilibrium conditions being different for different ions. Cross-linkage has a definite influence on the time required for an ion to reach equilibrium. An ion exchange resin that is highly cross-linked is quite resistant to the diffusion of various ions through it, and hence, the time required to reach equilibrium is much longer. The larger the ion or molecule diffusing into an ion exchange particle, or the more highly cross-linked the polymer, the longer the time required to reach equilibrium conditions.

#### **2. Available Capacity**

The capacity of an ion exchange is a quantitative measure of its ability to take up exchangeable counter ions and it is therefore of major importance. However, in the preparation of drug resonates, the actual capacity obtained under specific experimental conditions depends on the accessibility of the functional groups for the drug of interest.

##### *Acid-Base Strength*

The acid or base strength of an exchanger is dependent on the various ionogenic groups incorporated into the resin. Resin-containing sulfonic, phosphoric and carboxylic acid

exchanger groups have approximate pKa values of <1, 2-3 and 4-6, respectively. Anionic exchangers are quaternary, tertiary, or secondary ammonium groups having apparent pKa values of >13, 7-9 or 5-9, respectively. The pKa value of the resin will have a significant influence on the rate at which the drug will be released from resinate in the gastric fluids.

#### Selectivity of the Resins for the Counter-Ion

Resin selectivity is attributed to many factors. Since ion exchange involves electrostatic forces, selectivity at first glance should depend mainly on the relative change and the ionic radius of the (hydrated) ion competing for an exchange site. Factors others than size and charge also contribute to the selection of one counter ion in preference to another. The extent of adsorption increases with-

- a) the counter ion that in addition to forming a normal ionic bond with the functional group of an exchanger, also interacts through the influence of van der Waal forces with the resin matrix.
- b) the counter ion at least affected by complex formation with its co-ion or non-exchange ion.
- c) the counter ions that induce the greater polarization. These factors, together with the effect of the size and charge of an ion on exhibiting certain selectivity toward a resin, are at best only general rules, and as a consequence there are many exceptions to them.

#### Applications in Various Formulation-Related Problems

##### Taste Masking

Excessive bitterness of the active principal ingredients (APIs) in oral formulations is the major taste problem faced by the pharmaceutical industry. Bitterness of formulations can influence selection by physicians and markedly affect patient compliance (8). 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 (9). As shown in Table 1, a number of ion exchange resins

have been researched for their ability to mask the unpleasant taste of drugs.

**Table 1.** References of ion exchange resins used for masking the unpleasant taste of drugs

Bitter drugs	Ion exchange resin	Reference
Diphenhydramine Hydrochloride	Indion 234 and Tulsion 343	10
Fexofenadine Hydrochloride	Indion 204, 234 and 264	11
Rizatriptan Benzoate	Indion 204/214	
Tulsion 339/335	12	
Levamisole Hydrochloride	Amberlite IRP-64/69	13
Ciprofloxacin	Indion 234	14
Chloroquine Phosphate	Polyacrylic acid	15

##### Rapid Dissolution

Ion exchange drug resinate 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 molecule is bound to a functional site of the resin molecule resulting in reduction of crystal lattice energy, which may be responsible for enhancing the rate of drug dissolution bound to resin (16).

##### 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, macroreticular morphology, they provide excellent flowability to the formulation (17).

##### Stability

The drug resinate is frequently more stable than the original drug. Vitamin B12 has a shelf-life of only a few months, but the resinate is stable for more than two years. Another example is nicotine; it discolors quickly on exposure to air and light, but the resinate, used in nicotine chewing gums and lozenges, is much more stable. Kankkunen et al. (18) 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.

### *Deliquescence*

Deliquescence can be defined as the conversion of a solid substance into a liquid as a result of absorption of water vapor 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 resinate 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 resinate. Similar results have been obtained with resinates of rivastigmine bitartrate (5).

### *Disintegration*

Ion exchange resins, because of their excellent swelling property when immersed in water, can be used as a tablet-disintegrating agent. Purnima et al. (19) studied the swelling power of Indion 414, an ion exchange resin, sodium starch glycolate, crospovidone 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 for their disintegrating properties.

## **Drug Delivery Applications**

### **Oral Drug Delivery**

#### *Modified Release*

Junyaprasert and Manwiwattanakul (20) formulated sustained release suspension of diltiazem using strong cation exchange resins for the preparation of microcapsules by emulsion solvent evaporation method. The sustained release suspensions possessed good stability with low drug leaching, and their release profiles were unchanged when compared with the dried microcapsules for 120 days at 30 and 45°C.

Hanninen et al. (21) studied the release of salicylates from

the strong anion exchange fiber, Smopex DS-218v at 1/10, 1/1 or 10/1 molar ratios of the external chloride-ions versus the salicylate bound in the fiber. The Donnan potential between the fiber and external solution (electrostatic interaction) appeared to be the main factor affecting the release of salicylates from the strong base anion exchange fiber; an increase in the molar amount of the external chloride-ions resulted in a more effective release of all the salicylates from the fiber. The highest chloride-ion concentration (10/1) released the monovalent salicylates practically completely, while the lowest concentration (1/10) released only 10-35% of the loaded salicylates.

Sriwongjanya and Bodmeier (22) tested the effect of ion exchange resins when incorporated as release modifiers into hydroxypropyl methylcellulose (HPMC) matrix tablets. The drug release from HPMC tablets containing drug-resin complexes was significantly slower than from HPMC tablets containing drug without resin. Use of smaller resin particles eliminated the burst release seen with larger resin particles. Upon comparing different carrier materials, the drug release was in the order of Gelucire > polyethylene oxide 400K > HPMC. Nicorette chewing gum is an example in which the drug-resin complex is encapsulated into a matrix. This product utilizes nicotine bound to an ion exchange resin within a sorbitol-based matrix. Nicotine is released only during chewing, thereby providing the minimal supply to facilitate smoking cessation.

Jeong and Park (23) investigated the complex formation between drugs and ion exchange resins and the effects of coating by various aqueous polymeric dispersions on the complexes for developing new sustained-release fast-disintegrating tablets (FDTs) of dextromethorphan. As the particle size of resins increased, the drug loading and release rate decreased due to the reduced effective diffusion coefficient and surface area. Higher coating level decreased the release rate further.

Halder and Sa (24) used Indion 254, a cation exchange resin, for preparing propranolol-HCl resinates, which were microencapsulated with polystyrene using an oil-in-water emulsion-solvent evaporation method, with a view to achieving prolonged drug release in simulated gastric and intestinal fluid. Polystyrene appeared to be a suitable polymer to provide prolonged release of propranolol

independent of the pH of the dissolution media.

Steel et al. (25) studied the development of a novel combination vector consisting of adenovirus conjugated to liposomes (AL complexes) bound to cation-exchanging microspheres (MAL complexes). Of the complexes tested, the 5:1 and 2:1 ratio AL complexes were able to be efficiently bound by the microspheres and exhibited sustained release over 24 h. The 1:1 and 1:2 AL complexes, however, bound poorly to the microspheres and were rapidly released. In addition, the MAL complexes were also able to reduce the toxicity of the AL complexes, which was seen with the 10:1 ratio.

Jeong et al. (26) developed a comprehensive mathematical model using a mechanistic approach by considering diffusion, swelling, and ion exchange processes solved by numerical techniques involved in polymer (poly vinyl acetate) coated dextromethorphan- resin complexes for studying release characteristics.

#### **Nasal Drug Delivery**

Cheng et al. (27) demonstrated the application of ion exchange resins to develop novel nasal formulations of nicotine. 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 microm), 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.

Higaki et al. (28) evaluated the potential application of ion exchange resins for the enhancement of intranasal immune response to influenza hemagglutinin (HA) vaccine in mice. The results demonstrated that intranasal administration of influenza HA vaccine in combination with the 20-45 micron sized particles of sodium polystyrene sulfonate resin induced the highest levels of mucosal IgA, and enhanced systemic

hemagglutinin-inhibiting antibodies. Furthermore, mice intranasally immunized with HA vaccine together with sodium polystyrene sulfonate resin showed higher protection against viral challenge than those that received HA vaccine alone. Intranasal administration of influenza HA vaccine with sodium polystyrene sulfonate resin might be both a safe and an effective means of immunization.

#### **Transdermal Drug Delivery**

Yu et al. (29) postulated model for transdermal delivery using ion exchange fibers as controlling device was designed, and the main objective of their study was to assess the rationality of the model. 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  $\mu\text{m}$  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. Additional ions could increase the rate and extent of ketoprofen delivery.

Kankkunen et al. (18) attempted controlled transdermal delivery of the zwitterionic levodopa by iontophoresis and ion exchange fiber. Ion exchange kinetics and transdermal permeation of a cationic (presumably more stable) model drug, metaraminol, were compared to the corresponding data of levodopa. Iontophoretic enhancement of drug permeation across the skin was clearly more significant with the positively charged metaraminol than with the zwitterionic levodopa.

#### **Ophthalmic Drug Delivery**

Jani et al. (30) investigated the complexation of betaxolol hydrochloride, an antiglaucoma agent with ion exchange resins. Drug resin particles were then incorporated into the structured vehicle, containing Carbomer 934P as a polymer, to enhance the physical stability and ease of resuspendability of the product. The 0.25% ophthalmic suspension of the drug showed an increased bioavailability, and pharmaceutically, is an elegant suspension product, which settles slowly, providing uniform dosage and increased ocular comfort.

Moreau et al. (31) employed an experimental rabbit model of Staphylococcus keratitis, and compared the effectiveness of two commonly prescribed formulations of fluoroquinolones to an experimental formulation, ciprofloxacin with polystyrene sulfonate (ciprofloxacin-PSS). The ciprofloxacin-PSS formulation uses an ion exchange resin to aid in the delivery of drug to the cornea. Topical treatment of experimental S. keratitis with ciprofloxacin-PSS, ciprofloxacin, or ofloxacin was effective. The effectiveness of ciprofloxacin-PSS suggests that improved drug delivery systems employing an ion exchange resin could be useful in an ocular fluoroquinolone formulation.

### Ion Exchange Resins as Therapeutic Agent

In addition to the utility of ion exchange resins as excipients, these materials are being explored for their therapeutic potential as well. Cholestyramine was the first polymeric resin-based drug that was approved for the treatment of high cholesterol. The cationic 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 (4 tablespoons administered via fruit juice). Subsequent generation therapies have utilized molecular modeling strategies to impart specificity to the resin, thereby decreasing the dose levels to capsule sizes (e.g., WelChol developed by Genzyme). Specificity for these resins has been achieved by the use of polymers that bind not only via electrostatic interactions but also other forces, such as hydrophobic interactions.

Cationic resins have also been used as oral therapeutics to reduce phosphate levels for end stage renal disease patients (e.g., Renagel developed by Genzyme).

Colestimide, a 2-methylimidazole-epichlorohydrin polymer, is a new bile-acid-sequestering resin that is four-fold 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 hypercholesterolemia (32).

### CONCLUSIONS

Apart from the traditional application of separation, purification and processing, ion exchange resins are being researched for their pharmaceutical applicability. Be it taste masking, modified or sustained release, dissolution enhancement, or as a potential disintegrating agent, ion exchange resins have proven their worth in the pharmaceutical industry. Furthermore, therapeutic application of these resins could open new pharmacological perspectives.

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