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Ion exchange resins as drug delivery carriers

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ABSTRACT

Ion exchange resin(IER) are cross-linked synthetic high molecular weight solid water insoluble usually white or yellowish, fabricated from organic polymer (polyelectrolyte) having ionizable functional group. IER have received considerable attention from pharmaceutical scientists because of their versatile properties as drug delivery vehicles. Research over the last few years has revealed that IER are equally suitable for drug delivery technologies, including controlled release, transdermal, nasal, topical and taste masking. The major drawback of sustained release of extended release or extended release is dose dumping, resulting in increased risk of toxicity. The use 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. Synthetic ion exchange resins have been used in pharmacy and medicine for taste masking or controlled release of drug. Drug resin complexation converts drug to amorphous form leading to improved drug dissolution. Several studies have reported the use of IER for drug delivery at the desired site of action. Sulfonated and carboxylic resins with a polystyrene backbone are most widely used in clinical medicine.

Keywords: Ion exchange resins, taste masking, resin drug complex, controlled release

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INTRODUCTION

IER is defined as “Ion exchange resin are cross-linked synthetic high molecular weight solid water insoluble usually white or yellowish, fabricated from organic polymer (polyelectrolyte) having ionisable functional group”**.** Novel drug delivery systems are gaining momentum in the recent two decades as these results in reduced frequency of dosing and patient compliance. Intensity and duration of action has been the subject of increasing multidisciplinary research. One of the attractive methods for modified drug delivery systems is the use of ion exchange resins (IER) as carriers for such systems [1]. Complexes between IER and drugs are known as ion exchange resinates, which have been used in pharmaceutical formulations for several decades.

The principle of IER at which it acts is that it is a reversible process that exchanges their mobile ion of equal charge with the surrounding insoluble organic polymer having charged functional site. IER 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 exhibited like small bead with a diameter between 1-2 mm. It is usually white or yellowish and it is fabricated from an organic polymer substrate backbone. Ion exchange is a reversible process in which ions of like sign are exchanged between liquid and solid when in contact with a highly insoluble body. The drug is released from resinate by exchanging with ions in the gastrointestinal fluid, followed by drug diffusion. Due to the presence of high molecular weight water insoluble polymers, the resins are not absorbed by the body and are therefore inert. IER have specific properties like available capacity, acid base strength, particle size, porosity and swelling, on which the release characteristics of drug resonates are dependent. Drug resinates are generally prepared with purified resins and appropriate drugs [2-4].

Research over the last few years has revealed that IER are equally suitable for drug delivery technologies, including controlled release, transdermal, nasal, topical and taste masking. Synthetic ion exchange resins have been used in pharmacy and medicine for taste masking or controlled release of drug as early as 1950[5-6]. Ion-exchange systems are advantageous for drugs that are highly susceptible to degradation by enzymatic process. A major advantage of ion exchange system is low running cost. It requires little energy and the regenerated chemicals are cheap. Furthermore, if well maintained, resin beds can last for many years before replacement. However, the limitation is that the release rate is proportional to the concentration of the ions present in the area of administration. More so, the release rate of drug can be affected by variability in diet, water intake and individual intestinal content.

1.1.Advantages [7]

- Eliminate over or under dosing
- Maintain drug levels in desired range
- Increased patient compliance
- Need for less dosing
- Economic and readily available.
- Free from local and systemic toxicities.
- Drug-resinates can be formulated into various dosage forms like tablets, capsules, suspensions etc.
- Can be used for several purposes such as taste masking, sustained and rapid release.
- Effectively useful in low concentration (5-20%w/w).
- Resins have high drug loading and probability of dose dumping.

1.2.Clinical Advantages

- Reduction in frequency of drug administration
- Improved patient compliance
- Reduction in drug level fluctuation in blood
- Reduction in drug accumulation with chronic therapy
- Reduction in drug toxicity (local/systemic)
- Stabilization of medical condition (because of more uniform drug levels)
- Improvement in bioavailability of some drugs because of spatial control
- Economical to the health care providers and the patient

1.3.Disadvantages [8]

- Reduced potential for dose adjustment.
- Cost of single unit higher than conventional dosage forms.
- Increase potential for first pass metabolism.
- Requirement for additional patient education for proper medication.
- Decreased systemic availability in comparison to immediate release conventional dosage forms and poor *in vitro* and *in vivo* correlations.

2.Structure and Chemistry of Ion Exchange Resin

IER are simply insoluble polyelectrolyte's that are insoluble polymers which contain ionisable groups distributed regularly along the polymer backbone. The most common resins used in formulations are cross-linked polystyrene and polymethacrylate polymers [8]. When IER are mixed with a fluid such as water, ions in the fluid can exchange with the polyelectrolyte's counter ions and be physically removed from the fluid.

An ion exchange resin is a polymer (normally styrene) with electrically charged sites at which one ion may replace another. There are numerous functional groups that have charge, only a few are commonly used for man-made IER. These are:

• -COOH, which is weakly ionized to $-COO^-$,
• $-SO_3H$, which is strongly ionized to $-SO_3^-$,
• $-NH_2$, which weakly attracts protons to form NH_3^+,
• -secondary and tertiary amines that also attract protons weakly,
$-NR_3^+$, 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.

3.Types of Ion-exchange Resins

There are two major classes of ion-exchange polymers [9] (Fig. 1)

(a) Cation and (b) anion exchange resins. These are discussed in the following two sub-sections.

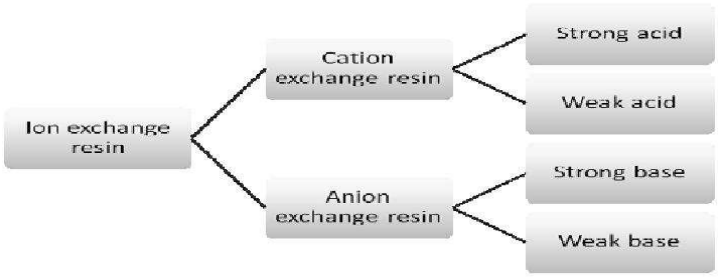

Fig. 1. Classification of IER.

3.1.Cation exchange resins

Cation exchange resins contain covalently bound negatively charged functional groups and exchanges positively charged ions. They are prepared by the copolymerization of styrene and divinyl benzene and have sulfonic acid groups ($-SO_3H$) introduced into most of the benzene rings. The mechanism of cation exchange process can be represented by the following reaction in Eq. (1)

R- - ex+ + C+ →R- - C+ +ex+ (1)

where, R is a resin polymer with SO_3- sites available for bonding with exchangeable cation (ex+), and C+ indicates a cation in the surrounding solution getting exchanged.

Cation exchange resins can be further classified into

(a) strong acid cation exchange resins and (b) weak acid cation exchange resins.

3.1.1.Strong acid cation exchange resins

The chemical behaviour of these resins is similar to that of a strong acid. These resins are highly ionized in both the acid ($R-SO_3H$) and salt (RSO_3Na) form of the sulfonic acid group ($-SO_3H$). They can convert a metal salt to the corresponding acid by the reaction in Eq. (2):

$2(R-SO_3H) + NiCl_2 \rightarrow (R-SO_4)\ Ni + 2HCl$ (2)

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

3.1.2.Weak acid cation exchange resins

These resins behave similarly to weak organic acids that are weakly dissociated. In a weak acid resin the ionisable group is a carboxylic acid (COOH) as opposed to the sulfonic acid group (SO_3H) 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.

3.2.Anion exchange resins [10]

Anion exchange resins have positively charged functional groups and they exchanges negatively charged ions. These are prepared by first chlormethylating the benzene rings of styrene-divinylbenzene copolymer to attach CH_2Cl 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 in Eq. (3)

R+ - ex - + A- → R+ - A- + ex- (3)

where, R+ indicates a resin polymer with number of sites available for bonding with exchangeable anion (ex-), and A- indicates cations in the surrounding solution getting exchanged. Anion exchange resins can be further classified into two which are as follows:

3.2.1.Strong base anion exchange 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 Eq. (4)

$$R\text{-}NH_3OH + HCl \rightarrow R\text{-}NH_3Cl + H_2O \quad (4)$$

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

3.2.2.Weak base anion exchange resin

Weak base resins are like weak acid resins in that the degree of ionization is strongly influenced by pH. Hence, weak base resins exhibit minimum exchange capacity above a pH of 7.0. The weak base resin does not have an OH ion form as does the strong base resin Eq. (5)

$$R\text{-}NH_2 + HCl \rightarrow R\text{-}NH_3Cl \quad (5)$$

Consequently, regeneration needs only to neutralize the absorbed acid; it need not provide OH ions. Less expensive weakly basic reagents such as ammonia (NH_3) or sodium carbonate can be employed.

A typical cation-exchange resin is prepared by the copolymerization of styrene and divinylbenze. During the polymerization, polystyrene formed as a linear chains and these become covalently bonded to each other by divinylbenze cross links. If sulphuric acid is then allowed to react with this copolymer, sulphonic acid groups are introduced into most of the benzene rings of the styrene-divinylbenze polymer, and the final substance formed is known as cation-exchange resin.

A typical anion exchange resin is prepared by first chloromethylating the benzene rings of the three dimensional styrene-divinylbenzene copolymers to attach – CH_2Cl groups and then causing these to react with a tertiary amine, such as trimethylamine. This gives the chloride salt of strong-base exchanges.

4.Role of IER in Controlled Drug Delivery Systems

The major drawback of controlled release is dose dumping, resulting in increased risk of toxicity. The usage of IER during the development of controlled release formulations plays a significant role because of their drug retarding 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 [11].

The use of IER into drug delivery systems have been encouraged because of their physico-chemical stability, inert nature, uniform size, spherical shape assisting coating and equilibrium driven reproducible drug release in ionic environment. The physical and chemical properties of the IER will release the drug more uniformly than that simple matrix formulation [12]. Drug molecules attached to the resins are released by appropriate charged ions in the gastrointestinal tract, followed by diffusion of free drug molecules out of the resins as shown below in Eqs. (6) and (7):

$$Resin^- Drug^+ + X^+ \rightleftharpoons Resin^-....X^+ + Drug^+ \quad (6)$$

$$Resin^+ Drug^- + X^- \rightleftharpoons Resin+...X^- + Drug^- \quad (7)$$

where, X and Y are ions in the gastrointestinal tract.

IER have been used as drug carriers in pharmaceutical dosage forms for controlled release formulation [13-16]. The prolonged release of the active drug is accomplished by providing a semi-permeable coating around discrete, minute, ion exchange resin particles with which the drug component has been complexed to form an insoluble drug resin complex. The semi-permeable coating creates a diffusion barrier and the thickness of which can be adjusted to provide the desired level of retardation of drug availability in the gastrointestinal tract over a period of time. Several preparations involving strong resinates of sulphuric acid (cation exchange resins) provided more moderate release than the weak resinates of carboxylic acid . Hence, resinates of strong cationic drugs are formulated as sustained release suspension, tablets, capsules and micro particles [17-20].

5.Method of Preparation

The important step in the preparation of drug resinates is to purify the resins. Purification of resin can be achieved by washing with absolute ethanol, ethanol and water mixture. Final washing with water removes all the impurities. Purification is generally done by cycling repeatedly between the sodium and hydrogen forms with a cation

exchanger or between the chlorides and hydroxide forms with a anion exchangers. The conversion can be achieved by soaking the resins with acid or alkali solutions, respectively. After changing the ionic form, the resin is subjected to washing with distilled water until elute becomes neutral in reaction, and finally is dried at 50ºC. The drugs are loaded on to the resins by column method and batch method [21-23].

5.1.Column Method: Highly concentrated drug solution is passed through the column containing resins. Maximum efficiency is best obtained by the column method.

5.2.Batch Method: In this method the drug solution is agitated with a quantity of resin until equilibrium is attained. Subsequently the resin is to be washed to remove free and un-associated drug and thereafter it is air dried.

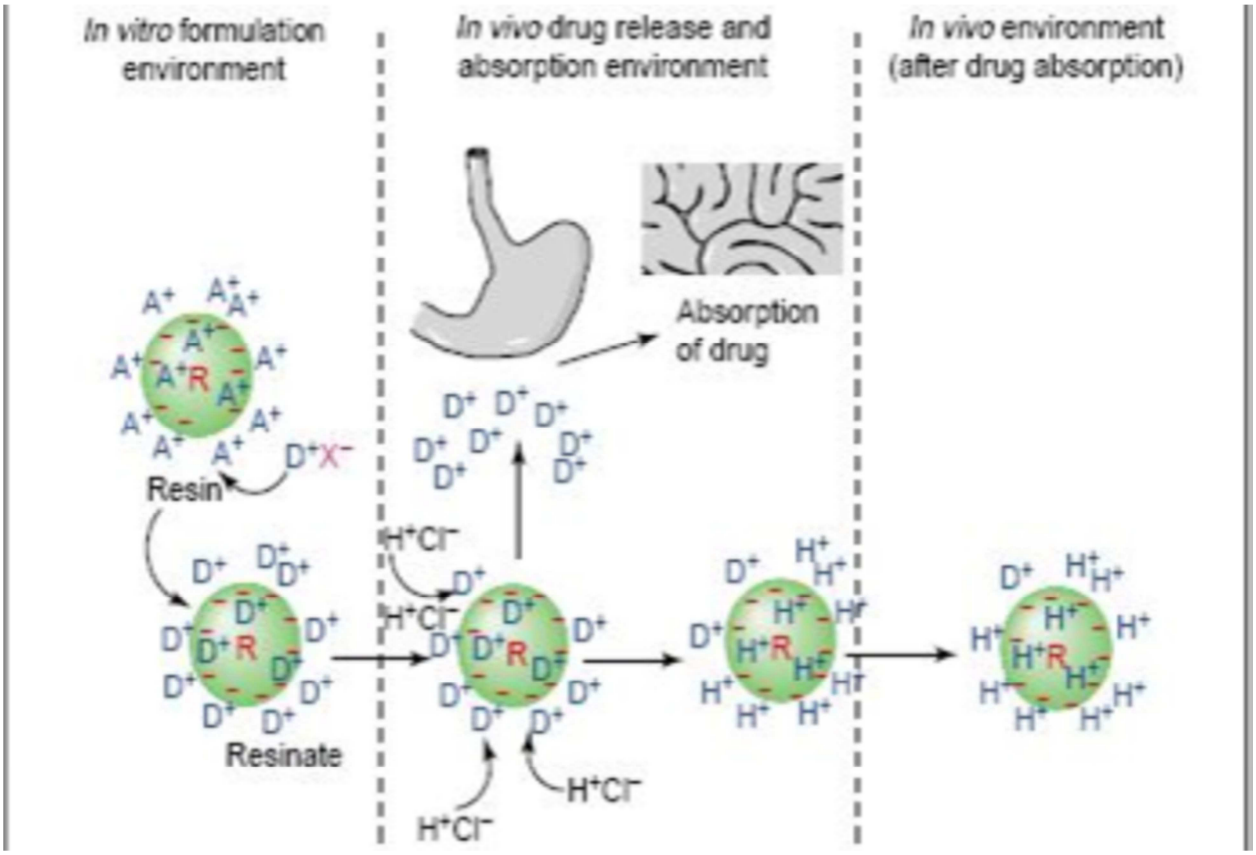

Fig 2. The mechanism of action of the drug release from the ion exchange resin

6.Mechanism and Principle

Anion exchange resins involve basic functional groups capable of removing anions from acidic solutions while Cation exchange resins contain acidic functional group, capable of removing cations from basic solutions[21-22].

The use of IER to prolong the effect of drug release is based on the principle that positively or negatively charged pharmaceuticals, combined with appropriate resins to yield insoluble polysalt resinates.

R-SO-3 H+ + H2N-A ↔ R-SO-3 – H3N-A

R-N+H3OH- + HOOC-B ↔ R-N+H3 –OOC-B+H2O

H2N-A → basic drug, R-SO-3H+ → cation exchanges, HOOC-B → acidic drug

R-NH3+OH- → anion exchange resins.

In The Stomach:

1) Drug resinate + HCl ↔ acidic resin + drug hydrochloride
2) Resin salt + HCl ↔ resin chloride + acidic drug

In The Intestine:
1) Drug resinate + NaCl ↔ sodium resinate + drug hydrochloride
2) Resin salt + NaCl ↔ resin chloride + sodium salt of drug

This system incorporates a polymer barrier coating and bead technology in addition to the ion exchange mechanism. The initial dose comes from an uncoated portion, and the remainder from the coated beads. The coating is not dissolved and coating is extended over 12-hour period by ionic exchange. The drug-containing polymer particles are minute, and may be suspended to produce a liquid with extended release characteristics as well as solid dosage forms .

EXAMPLE:
Examples of drug product of this type include;
1) Hydrocodone polistirex and chlorpheniramine polistirex suspension [Tussionex Pennkinetic Extended Release Suspension (Medeva)] and
2) Phentermine resin capsules [Ionamin Capsules (Pharmanex)].

7.Important Properties of IER[23-30]

7.1.Crosslinkage

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

7.2.Moisture Content

A physical property of the ion exchange resins that changes with changes in crosslinkage is the moisture content of the resin. For example sulfonic acid groups attract water, and this water is tenaciously held inside each resin particle. The quaternary ammonium groups of the anion resins behave in a similar manner.

7.3.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 millequivalents per milliliter of wet resin. The more highly crosslinked a resin, the more difficult it becomes to introduce additional funcitonal groups. Sulfonation is carried out after the crosslinking has been completed and the sulfonic acid groups 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 crosslinked 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 crosslinked resin, these groups are spaced closer together on a volume basis because the volume of water is reduced by the additional crosslinking. Thus the capacity on a wet volume basis increases as cross-linking increases.

7.4.Equilibration Rate

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

7.5.Summary of Crosslinkage Effects

Copolymers of styrene containing low amounts of divinylbenzene (1-4%) are characterized as follows

- High degree of permeability
- Contain a large amount of moisture
- Capacities are lower on a wet volume basis
- Equilibrium rates are high
- Physical stability is reduced

Selectivity for various ions is decreased, but ability to accommodate larger ions is increased. Copolymers of styrene containing high amounts of divinylbenzene (12-16%) exhibit characteristics in the opposite direction.

7.6.Particle size[31]

The physical size of the resin particles is controlled during the polymerization step. Screens are used to sieve resins to get a fairly uniform range of sizes. Mesh sizes in the following table refer to U.S. Standard screens. A higher mesh number means more and finer wires per unit area and thus a smaller opening.

Table 1 Particle size of resins

Mesh Range	Diameter of Particles	
	Inches	**Micrometers**
20 – 50	0.0331-0.0117	840-297
50 – 100	0.0117-0.0059	297-149
100 – 200	0.0059-0.0029	149-74
200 – 400	0.0029-0.0015	74-38
minus 400	< 0.0015	< 38

7.7.Flow Rate

Ion exchange processes are usually carried out in columns with the resin resting on a suitable support. Liquids may be processed either up-flow or down-flow through such columns. The spherical particles of ion exchange resin resist the flowing of a liquid through or around them. The smaller the particle size, the greater will be this resistance against which a liquid must flow. This resistance goes up very rapidly when particles smaller than 100 mesh are employed[32].

8.Evaluation of Drug Resinates[33-39]

The *invitro* test demonstrates the release pattern of a drug from resinate preparation dosage form. It depends on size of resinate, degree of cross linkage of resin with drug, nature of the resins, nature of the drug and test conditions that is ionic strength of the dissolution medium. *In vivo* procedures used for estimating drug activity of resinates include serum concentration level determination, urinary excretion, and toxicity studies. Bioavailability of drug from drug-resinate complexes depends on both transit of the particles through the gastrointestinal tract and drug release kinetics. The complex will release the active content only when it replaced by the ion which has the same charge. Since the exchange is an equilibrium process, it will depend on the ionic constitution and the fluid volume of the body fluid. In additional, release is not instantaneous, and the drug must diffuse through the resin from the internal exchange sites. Thus, agitation and time of exposure play a key role in drug release.

Stomach emptying with fine particles, likely follows a first order or distributional process. In the intestine, the neutral pH should keep all ionic sites ionized, and the exchange process should occur continuously. The absorption into the body of solubilised drug should drive the equilibrium further toward drug release. In the large intestine, desorption from resins and absorption into the body may be slowed considerably due to low fluid content, entrapment in faecal matter, and poor absorption in colon. The highly insoluble resin never dissolves, and should not be absorbed. It will simply be eliminated from the body with whatever counter-ions have replaced the drug.

9.Applications of IER [39-45]

9.1.Pharmaceutical applications

Some pharmaceutical applications of IER include

9.2.Taste masking

Masking of bitter taste in active principal ingredients in oral formulations posses a major challenge to pharmaceutical industry especially for paediatric and geriatric patients. 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. Previously some workers used carbomer to mask the nauseating and unpleasant taste of erythromycin and clarithromycin, by adsorption into Carbopol and then encapsulating the resulting particles with hydroxylpropyl methylcellulose phthalate.

9.3.Eliminating polymorphism

Many pharmaceutical solids can exist in different physical forms. Polymorphism is often characterized as the ability of a drug substance to exist as two or more crystalline phases that have different arrangements and/or conformations of the molecules in the crystal lattice. This is a common problem in the pharmaceutical industry and huge sums of money are spent trying to identify polymorphs and trying to make stable, suitably soluble forms. Failure to resolve such a problem can result in significant stability and stability problems for the final dosage form. Ion exchange resins present a unique way to deal with the problem because using resinates completely eliminates any problem with polymorphism.

9.4.Improving the dissolution of poorly soluble drugs

Ion exchange drug resinate complexes can be used to enhance the dissolution rate of a poorly soluble drug. Using micronization to increase the rate of dissolution can be problematic, because it frequent requires specialized equipment and often there can be agglomeration of the fine particles after grinding. The grinding can also result in melting and conversion to other crystal forms. These problems are completely eliminated by using the ion exchange resin approach.

9.5.Improving stability

The drug resinate is frequently more stable than the original drug. For instance, vitamin B_{12} has a shelf-life of only a few months while it's resinate has more than two years. Another example is nicotine which discolors on exposure to air and light, but the resinate used in manufacturing nicotine chewing gums and lozenges is much more stable.

9.6.Improving physical characteristics

Most drug substances are in solid form there are some that are liquids or difficult-to-handle solids. Because the physical properties of the resinates are similar to the resin not the drug, the resinates of these drugs will be free-flowing solids. A very well established example of this is the nicotine resinate used in nicotine chewing gums and lozenges. Nicotine is in liquid form but its resinate is a stable, free- flowing solid. The resins have a uniform, macroreticular morphology that provides excellent flow ability to the formulation.

9.7.Drug delivery applications [46-49]

9.7.1.Oral drug delivery: 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 of 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. The use of ion exchange resins into drug delivery systems have been encouraged because of their physico-chemical stability, inert nature, uniform size, spherical shape assisting coating and equilibrium driven reproducible drug release in ionic environment.

9.7.2.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.

9.7.3.Transdermal drug delivery: IER are 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.

9.7.4.Ophthalmic drug delivery: IER also find application in opthalamic 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.

10.Diagnostic and therapeutic applications

Synthetic as well as natural polysaccharides based on ion-exchange resins have been used with good results for diagnostic determinations. eg. In gastric acidity. They have also found applications as adsorbents of toxins, as antacids, and as bile acid binding agents. Ion-exchange resins have been successfully used therapeutic in the treatment of liver diseases, renal insufficiency, urolithic disease and occupational skin disease. For instance, sodium polystyrene sulfonate is a sulfonic cation-exchange resin used in the treatment of hyperkalemia and also used in acute renal failure. Phenteramine, a sympathomimetic amine is indicated for short term use in the management of exogeneous obesity in a regimen of weight reduction utilizing caloric restriction. It also has application in the control of cholesterol and potassium ion levels.

11.Some IER Available in the Market

The use of IER to form drug adsorbates for sustained release [50-53] was closely associated with Strasenburgh Laboratories, an affiliate of Pennwalt Corporation, which was granted several patents in this area. Their first significant application involved amphetamine adsorbed onto a sulfonic acid cation exchange resin (Biphetamine) which is use in appetite suppression and for also for behavior control in children. The drug is administrated once or twice daily. Other products that have been introduced commercially since the initial work with amphetamine include Penntuss which is a combination of Codeine and Chlorpheniramine. This is a liquid suspension used as a cough suppressant and relief of cold. It is taken twice daily. Both drugs are bound to a sulfonic acid cation-exchange resin. The chlorpheniramine-resinates are uncoated due to much high affinity for the resin while the codeine-resinates are coated with ethylcellulose. Other products used for cough and cold include phenylpropanolamine, chlorpheniramine, and dextromethorphan. Some other examples include Ionamin (phentermine) and Tussionex (hydrocodone polistirex and chlorpheniramine polistirex) both are marketed by Medeva Pharmaceuticals, Inc.) .

CONCLUSION

IERs have been used in pharmacy and medicine for various functions, which include tablet disintegration, bioadhesive systems, sustained release systems. In recent years IER have been successfully utilized for masking of taste of bitter drugs.IER play a major role in the modification of drug release by forming a complex with drug substances.

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