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A REVIEW ON DRUG RESIN COMPLEX AND ITS PHARMACEUTICAL APPLICATION

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ABSTRACT

Ion exchange resins (IER) are solid, cross-linked water insoluble polymers with an acidic or basic functional group that can exchange their counter ions within the aqueous solutions surrounding them. Based on the nature of the exchangeable ion they are classified as cationic or anionic exchange resins. Sulfonic and carboxylic resins with a polystyrene backbone are generally used in clinical medicine. Resinates (drug-resin complexes) are generally prepared by conventional batch process and column process and evaluated for drug content,percentage complexation,invitro release studies, stability studies etc. IERs have been used as drug carriers in pharmaceutical dosage forms for sustained release due to their better drug-retaining properties and prevention of dose dumping.

Now a days, bitter taste is a major limitation to patient compliance especially among peadiatric and geriatric population . A tasteless complex is formed between the drug and resin, thus the bitter sensation is masked. Research over the last several years has revealed that ion exchange resins have found applications in pharmacy and medicine, delivering purposes such as taste masking ,sustained or controlled drug release,sigmoidal release, enhanced drug dissolution, tablet disintegration etc. Several studies have reported the use of IER for drug delivery at the desired site of action. This review addresses the various types of ion exchange resins, mechanism of loading and unloading of drug into IER, formulation of drug resinates and their pharmaceutical and therapeutic applications.

KEYWORDS: Ion exchange resin, Sustained release

INTRODUCTION

Ion exchange resins (IER) are solid, cross-linked, synthetic, high molecular weight, water insoluble polymers that can exchange their mobile ions of equal charge with the surrounding medium reversibly. IERs exhibit non-absorbent properties within the body which make them inert. They consist of acidic or basic functional groups and have the capability to exchange their counter-ions within aqueous solutions surrounding them. The counter ions bound to functional groups by ionic bonds play a major role in the ion-exchange process. It is a reversible process in which ions of like sign are exchanged. An important advantage of this ion exchange system is the availability in low cost. The complex formed between IER and drugs are known as ion exchange resinates or drug-resin complex. The batch process is the preferred method for drug-resin complexation due to its ease of

operation. The drug is released from resinate by exchanging with ions in the gastrointestinal fluid, followed by drug diffusion. [1]

Sustained drug delivery system provides a prolonged release of the drug over extended period of time there by giving increased duration and better patient compliance. 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.[2] However simple drug resin complexes may not satisfy the requirement of sustained release. In such cases resinates are incorporated into the matrix system, microencapsulated or coated. Modified release of drugs from resinate is an important application of ion exchange resins. 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

As far,more than 50% of pharmaceutical products are administered via oral route. Today great importance has been given to organoleptic characteristics of pharmaceutical products, such as appearance,colour,odor, and taste especially in pediatric and geriatric formulations. Masking the unpleasant taste of bitter drug improves the patient's compliance and commercial success of that product . For the purpose of taste masking ,weak cation or weak anion exchange resins are used based on the type of drug to be masked.[3] pH of 6.8 in saliva is not able to break drug-resin complex. but the complex is weak enough to be broken down by the hydrochloric acid present in the stomach.

CLINICAL ADVANTAGES [4]

- Reduced dosing frequency
- Improved patient compliance
- Reduction in drug level fluctuation in blood
- Reduced accumulation of drug during chronic therapy
- Reduction in drug toxicity (local/systemic)
- Improvement bioavailability of certain drugs because of spatial control.
- Economical to the health care providers and the patient.

DISADVANTAGES

- Drug release is dependent on the concentration of ions present in the area of administration.
- Rate of drug release is altered by variation in diet, intake of water and intestinal content of an individual.
- Reduced dose adjustment potential.
- Dose dumping
- Cost of the single dosage form will be higher than conventional dosage forms.
- First pass metabolism.
- Inadequate patient education for ensuring proper medication in proper time.
- Decreased systemic availability in comparison to immediate release conventional dosage forms and poor in vitro and in vivo correlations .[2]

STRUCTURE

Chemically, IER consist of two components: a structural backbone with a polymeric matrix and a functional group to which the counter ion is bounded. The structural component of IER usually consists of a stable acrylic polymer of styrene-divinyl benzene copolymer, whereas the functional component can be acidic (mainly sulfonic or carboxylic) or basic (amine) groups. IER can be classified based on the nature while there are numerous functional groups that have charge; only a few are commonly used for man-made ion exchange resins. (5,6)

They are:

- -COOH (weakly ionized to $-COO^-$)
- -SO3H (which is strongly ionized to $-SO3^-$)
- -NH2 (weakly attracts protons to form $NH3^+$)
- -Secondary and tertiary amines (weakly attracts protons)
- $-NR3^+$ (has a strong, permanent charge)

TYPES OF ION EXCHANGE RESINS

a) Cation exchange resins

b) Anion exchange resins

CATION EXCHANGE RESIN

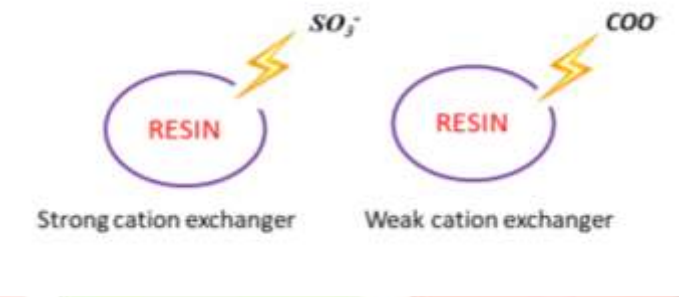

Fig 1:Types of cation exchange resin

Strong cation exchange resin

These resins behave similar to strong acids and have two highly ionizable forms of an acid (RSO_3H) and salt (RSO_3Na).Both forms of resin are highly dissociated and the exchangeable Na^+ and H^+ions are readily available for exchange throughout the entire pH range. It mainly binds with drugs existing as hydrochloride salt form such as Hydroxyzine HCl, Metformin HCl, Ciprofloxacin HCl .

Eg :Dowex 50,Indion 244(sulphonic acid resin)

$$Resin\text{-}SO_3\text{-}Na^+ + Drug\ HCl \rightleftharpoons [Polymer\text{-}SO]^- [Drug\ H]^+ + NaCl$$

Weak cation exchange resin

They have a carboxylic acid (COOH) functional group and behave similar to weak acids . It binds with drug having NH_2 group such as Amoxicillin.

Eg: Amberlite IRC 50,Indion 464 (Carboxylic acid resin)

$$Resin\text{-}COOH + Drug\text{-}NH_2 \rightleftharpoons [Resin\text{-}COO]^- [DrugNH_3]^+$$

ANION EXCHANGE RESIN

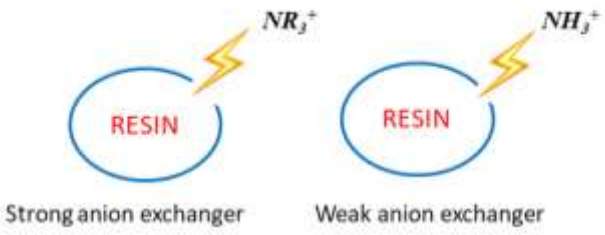

Fig 2: Types of anion exchange resin

Its exchangeable ions are negatively charged. Drugs with cationic functionality (e.g. COOH group or NaCl salt etc.) bind with this type of resin .Anion exchange resins can be further classified into:

Strong anion exchange resin

They are prepared by first chlor-meythylating the benzene rings of styrene-divinylbenzene copolymer to attach CH_2Cl groups and then causing these to react with tertiary amine such as triethylamine. Like strong cation resin, these resins are highly ionized and can be used over entire pH range .They behave similar to strong base and available in hydroxyl form(R-NH_3OH).It has R_3N^+ group which bind with drugs existing as sodium salt in the following way:

$$\text{Resin-}\ R_3N^+Cl^- + \text{Drug}^-\text{-}Na^+ \rightleftharpoons [\text{Resin-}R_3N] + [\text{Drug}]^- + \text{NaCl}$$

Eg: Dowex 1,Amberlite IR 400(Quarternary amine resin)

Weak anion exchange resin

It has R_2N group which bind with drug having COOH group

$$\text{Resin-}R_2N + \text{Drug-COOH} \rightleftharpoons [\text{Resin-}R_2NH] + [\text{Drug-COO}]^-$$

Eg:Amberlite IIR48,Dowex 2(Tertiary amine resin)

MECHANISM OF ION EXCHANGE PROCESS[7]

When the resin is placed in a electrolyte solution containing counter ion which are different from those bound to it.the migration of first few external ions to the resin and the bound ions to the surrounding solution creates an electrical potential difference (Donnan potential) between the resin and the external solution. This interchange continues until it reaches an equilibrium stage known as Donnan equilibrium.The higher the donnan potential stronger the attraction of counter ions towards the resin.

$$\text{Resin } A^- + B^- \rightleftharpoons \text{Resin } B^- + A^-$$

Ion-exchange resins and even sulphate and phosphate ions that do not diffuse readily through the intestinal wall tend to drive anions from the intestinal tract into the blood stream. The opposite effect,that of retardation of drug absorption, may occur if the drug complexes with the macromolecule. [8]

SELECTION OF SUITABLE IER

The selection of IER for pharmaceutical applications are mainly based on the properties of functional-groups present. The other factors are

- Capacity of the IER(Concentration of the counter ions in the resin in meq/g of dry resin)
- Degree of cross linking with the polymeric matrix
- Particle size of resin
- Nature of drug for complexation.
- Site of drug delivery.
- Swelling ratio
- Biocompatibility and biodegradability
- Regulatory status [9,10]

Table 1:Popular resin brands and their manufacturers

RESIN BRAND	MANUFACTURER
DOWEX	The Dow Chemical Company
AMBERLITE	Rohm and Haas Company.Philadelphia
INDION	Ion Exchange India Pvt.Ltd.Mumbai
TULSION	Thermax India Pvt.Ltd.Mumbai
KYRON	Coral Pharma Chem, Ahmedabad
DOSHION	Doshion Polyscience Pvt.Ltd.Ahmedabad
PUROLITE	Ecolab company.US

PREPARATION OF DRUG RESINATES

Purification of resins

Resin pretreatment of a cation exchanger mainly done by repeatedly cycling between sodium and hydrogen forms and for an anion exchanger purification done between chloride and hydrogen forms. Inorder to remove all the impurities it is washed with distilled water several times.

Loading of drugs into ion exchange resin[11]

There are mainly two methods

a)Column process:
A highly concentrated drug solution is eluted through a bed or column of the resin, until equilibrium is attained.

b)Batch process:
The resin particles are stirred with a known quantityof drug solution. After some time stirring is stopped and the residue is washed to remove adhering free and unbounded drug and thereafter it is air dried.

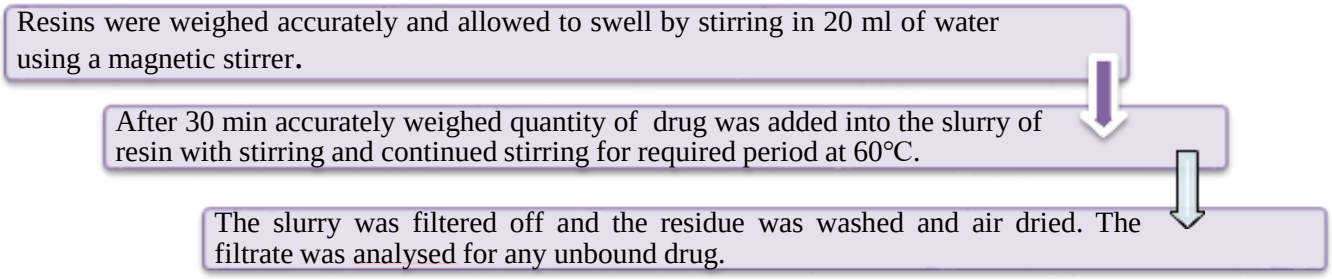

Fig 3:Preparation of resinate by batch process

FACTORS AFFECTING LOADING OF DRUG ONTO RESINS [12]

1. Cross linkage of Resin

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.

2. Particle Size

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

3. pH

The exchangeability of strong cationic and anionic exchange resins is independent of solution pH where as weak cation exchange resins are strongly influenced by solution pH.

4. 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.

5. Size of exchanging ions

Larger the size of exchanging ions, slower will be the diffusion rates and release.

6. Selectivity of Counter ions

The ions with low selectivity for resins such as H^+ gets replaced easily resulting in higher drug loading.

7. Mixing Time

Within a certain range, mixing time can affect the drug loading of resin. There for inorder to prepare resinates with appropriate drug loading, mixing time should be identified by experiments.

MECHANISM OF BINDING OF IER WITH DRUGS[12]

The binding of drug to IER involves electrostatic interactions between the resins and oppositely charged drugs and well the hydrophobic interactions .The driving force behind this exchange is due to the electronic differences between the ions. The reversibility of this interaction is exploited in oral drug delivery, in which the resins may carry the drug and release the payload in a certain region of the GIT due to a pH change or the presence of competing ions.

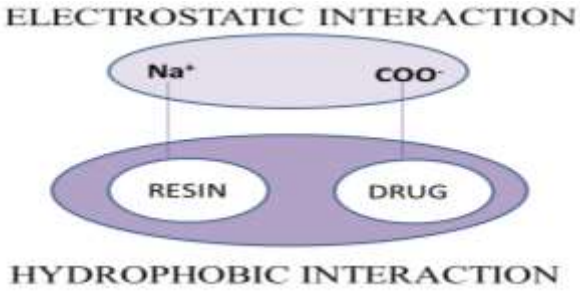

Fig 4 : Interaction between drug and resin

MECHANISM OF DRUG LOADING

For understanding drug loading and unloading from IER ,we can consider drug resin complexation reaction between dextromethorphan hydrobromide (drug) and sodium polystyrene sulphonate(cationic resin) for taste masking.

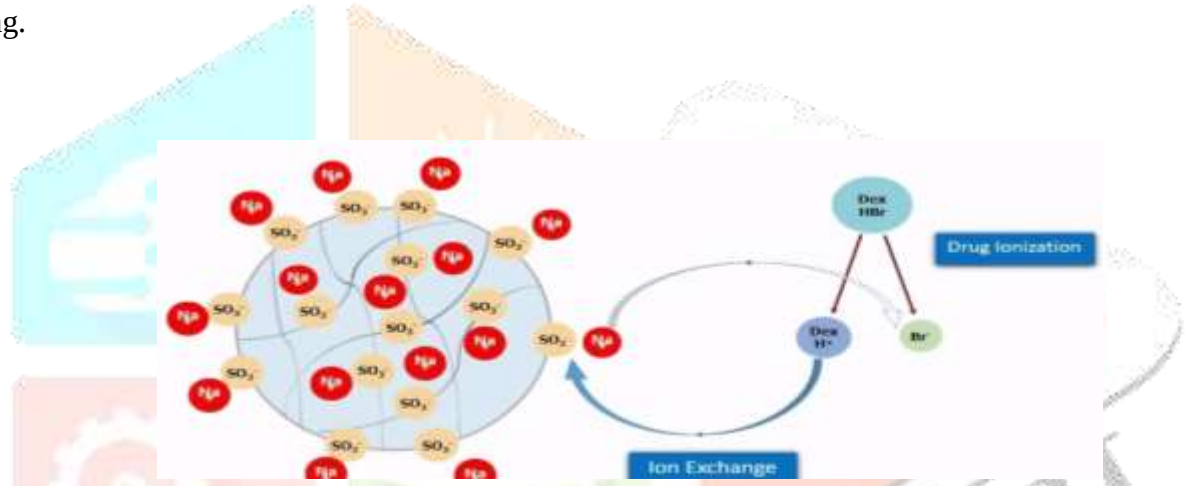

Fig 5:Loading of drug on the resin

In this case the drug dextromethorphan HBr is loaded onto the cationic resin sodium polystyrene sulphonate.In the aqueous solution of dextromethorphan,the drug ionizes into Dex H^+ and Br^- ions.When the drug solution comes in contact with insoluble cationic resin,the positive ion of the drug dex H^+ displaces the positive Na^+ ion from the resin surface.this process starts at the surface first followed by available sites within the resin. The displaced Na^+ ion associates with the Br^- ion from the drug to form NaBr byproduct salt. After completion of resination process the resinates need to be washed and filtered to remove byproduct NaBr and then dried. As the resin is insoluble the formed resinates are also insoluble in nature.

MECHANISM OF DRUG UNLOADING

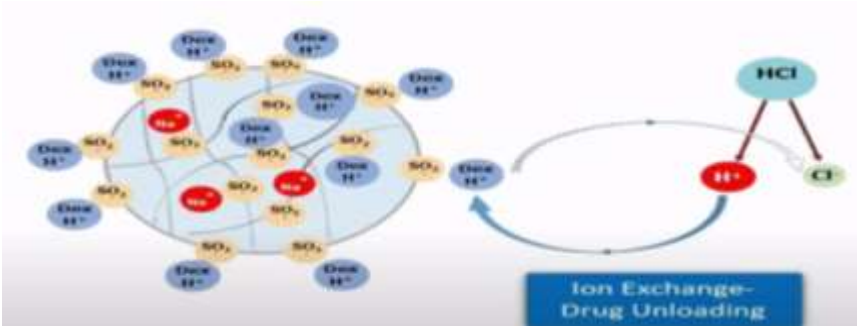

Fig 6: Unloading of drug from resin

The drug unloading process mostly takes place in the stomach because of presence of hydrochloric acid in the stomach. H^+ ion from the hydrochloric acid displaces the dex H^+ ion from the resinate. The process of ion exchange takes place at the surface of resinate followed by exchange site within the resinate. The unloaded drug is then available for absorption in the intestine.

RELEASE OF DRUG FROM RESINATES

Release of drug from the resinate depends upon two factors [13,14]

a) The ionic environment

Drug release mainly depends on the pH and electrolyte concentration within the GI tract. The drug is released from the resinate by exchanging its counter ions in the gastro intestinal fluid through the process of diffusion. Resinates breakdown in the presence of hydrochloric acid(pH 1.2) present in the stomach. The ion exchange resins are not absorbed by our body due to the presence of polymers with high molecular weight.

b) The properties of resin.

Drug molecules are released from resinate by diffusion of free drug molecule out of the resins. This process can be expressed by the following equation (1) & (2) for anion exchange and cation exchange respectively, where X & Y are ions in the GI tract.

$$Resin^+\text{-}Drug^- + X^- \longrightarrow Resin^+\text{-}X^- + drug^- \quad (1)$$

$$Resin^-\text{-}Drug^+ + Y^+ \longrightarrow Resin^-\text{-}Y^+ + Drug^+ \quad (2)$$

Resins feature reversible ion exchange between a solid and a liquid phase; the solid's structure is not permanently altered. The degree of exchange in these equilibrium reactions is determined by the resins' respective ions-specific affinity. A selectivity co-efficient that is obtained from the mass action expression provided in equation can be used to describe the relative affinity between ions.

$$K_{DM} = \frac{[D]_R[M]_S}{[D]_S[M]_R}$$

Where

K_{DM} =Selectivity co-efficient
$[D]_R$ = Drug concentration in resin
$[D]_S$ = Drug concentration in the solution
$[M]_S$ = Counter ion concentration in the solution
$[M]_R$ = Counter ion concentration in the resin

EVALUATION OF RESINATES

DRUG LOADING(%)

After the drug resin complexation process was completed, the mixture was filtered using suitable filter. Percentage drug bound was calculated by analysing amount of drug remaining in the filtrate.

INVITRO DRUG RELEASE

Dissolution study was carried out using suitable medium (eg:stimulated gastric fluid). After certain time interval sample was withdrawn and filtered and the filtrate was analyzed.

TASTE EVALUATION.

With agreement from the bioethics committee, a trained human volunteer taste panel assessed the bitterness of drug resin complex.In this technique, participants cleaned their mouths both before and after consuming the drug-resin mixture. A precisely measured quantity of resinates was taken orally, held in the mouth for thirty seconds, and then spat out. Numerical scores of 0, 1, 2, and 3 were used to indicate no bitterness, mild bitterness, moderate bitterness, and extreme bitterness, respectively, in the tasting test.[15]

INVITRO EVALUATION OF TASTE MASKING (SPECTROPHOTOMETRIC METHOD)

The bitterness of taste is related to the amount of drug released in the mouth. Bitterness sensation is reported to be experienced after 30s of tasting .Accurately weighed quantity of Pure drug is dissolved in 5ml of phosphate buffer(pH 6.8) and stirred .Stirring was stopped at different time intervals such as 30s,60s and120s and amount of drug release was determined. There for amount of pure drug release in salivary pH after 30s was taken as the standard and all the formulated drug resinates were evaluated for taste masking on basis of this.

RESINATE STABILITY STUDY[16]

A short term stability analysis was conducted on the dry drug resin combination. Samples were placed in tightly sealed, tiny glass vials and kept out of the light for a month in an incubator. All samples underwent release trials in simulated stomach fluid after a month, and the outcomes were compared to newly made resinate powder.

CHEMICAL DETERIORATION OF RESINS[17]

A variety of factors lead to the chemical degradation of the resins. The covalent bonds between the resin matrix and functional groups are broken which results in loss of the groups and the ion exchange capacity is reduced. Exposure of strong anionic exchange resins into the combined influence of a strong alkali and higher temperature results in chemical altering or loss of the functional groups. The organic substances sorbed can be regenerated and cleansed.

APPLICATIONS OF IER

- Production of water
- Treatment of wastewater
- Waste Treatment(Radioactive)
- Recovery of metals
- Analysis of chemicals
- Enzyme immobilization
- Purification in Food Industry

APPLICATIONS OF ION EXCHANGE RESINS IN VARIOUS FORMULATION- RELATED PROBLEMS

1.Sustained Drug Delivery Systems[18]

Some Properties Which Make Ion Exchange Resin a Suitable Candidate for SRDDS:

Physico-chemical stability
Inert nature
Uniform size
Spherical shape assisting coating
Equilibrium driven reproducible drug release in ionic environment

Because of its ability to delay the onset of side effects and prevent dose dumping, IER is a crucial component in the creation of sustained release formulations. The drug resinates can also be used as drug reservoirs, which causes a change in drug release characteristics. The slowness of uptake and release of medicament from ion exchange resin has proven to be effective in solving the problem of dose dumping by conventional dosage form. Ion exchange resins are extremely insoluble in aqueous liquids and have no side effects unless given in large dosage enough to disturb the calcium and sodium balance of body fluids as they have an affinity for these ions.

Microencapsulation of resinates provides better control over the drug release because of the presence of a rate controlling membrane. The absorption of the drug from coated resinates is a consequences of the counter ions into the coated resinates, release of drug ions from the drug-resin complex by ion exchange process, and diffusion of drug ions through the membrane into the surrounding absorption environment. [19]

Table 2: Examples for controlled release formulation using resinates

Ion-exchange resin	Drug	Type of system	Remarks
Indion 244	Bromhexine Hydrochloride	Microencapsulated Resinate	Controlled release oral liquid suspension
Dowex 1-X2	Diclofenac Sodium	Microencapsulated Resinate	Resinates are coated with eudragit RS 30 D for better controlled release
Amberlite IL-120	Metoclopramide	Resinate	Diffusion controlled release of drug
Dowex1-X2, 1-X4,1-X8	Theophylline	Microencapsulated Resinate	Controlled release formulation
AmberliteCG-50W	CPM Maleate	Microencapsulated Resinate	Polymethylmethacrylate-coated resinates
Indion 412	Fluvastatin Sodium	Microencapsulated resinate	Resinates are coated with ethyl cellulose and eudragit RS100 for controlled release

Hye-Ryeong Park et al,(2022),prepared drug-resin complexes of donepezil hydrochloride for the treatment of Alzheimer's disease and formulated it into a sustained- release oro dispersible film.[20]

Jun-Pil Jee et al,(2023), developed paliperidone- cation exchange resin complexes of different particle sizes to enable sustained release. [21]

2.TasteMasking[22]

Excessive bitterness of the active pharmaceutical 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. 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.

Advantages of Resins as Taste Masking Agents:

Resins being poly electrolytes have extensive binding sites leading to very high drug loading ability.
They have no systemic or local adverse effects and are chemically inert
Resins can be used to prepare all common dosage forms, including liquid, semisolid, and solid.
They have been used in selective separation of pharmaceuticals from mixtures.
Easily formed into any sterile dosage form, it remains stable under all sterilizing methods.

Table 3:Examples for resins used for taste masking

Name of resin	Taste masked Drug
Indion 204,Amberlite IRC50,PuroliteC102D, Kyron-T-104,Tulsion-T-335	Norfloxacin,Ofloxacin,Roxithromycin Spiramycine,Ranitidine,Levocitrizine,Dicyclomine HCl,Dimenhydrinate,Dextromethorphan
Indion 214	Azithromycin
Amberlite IRP 88,Indion 234,Tulsion T-335	Chloroquinephosphate,CiprofloxacinHCl, Quinine sulphate,LebexacinHCl,Methoclopramide HCl,
Amberlite IRP 69	Ranitidine
Indion 254	Bromhexine HCl,Dextromethorphan HBr

Fahad Siddiqui et al,(2023), optimized resinates of azithromycin with ion exchange resins Kyron T135 and Doshion-P 542 through Design of Experiment(DOE) and evaluated its taste masking effect.[15]

3. Rapid Dissolution[23]

Ion exchange resin matrices are hydrophilic and hence more aqueous solutions can penetrate the dimensional resin structure, thereby enhancing the dissolution rate. Additionally , each individual drug molecule is bound to a functional site of the resin molecule which lowers the crystal lattice energy, which may be responsible for enhancing the rate of drug dissolution bound to resin.The drug is converted to amorphous form during complexation with IER. Hence during the process of desorption the drug with poor solubility is immediately released.

4. Powder Processing Aid [24]

Drugs that are hygroscopic are prone to aggregation because of moisture. Adsorption of such drugs onto ion exchange resins may lead to a decrease in their hygroscopicity due to the fixed rigid structure of the resins . Ion exchange resins may prove useful in solving the problem of deliquescence of a drug by the formation of resinate complexes. Following complexation with ion exchange resins, sodium valproate, a highly deliquescent medication, has been observed to exhibit free flowing characteristics. [25]

5. Stability [26]

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.

6.Disintegration

Ion exchange resins, because of their excellent swelling property when immersed in water,can be used as a tablet disintegrating agent. Subsequently the resin is to be washed to remove free and un-associated drug and thereafter it is air dried. Eg: Indion 414

7.Polymorphism

A drug resinate is an amorphous solid that cannot crystallize or even form hydrates.the use of resinates can eliminate any problems with polymorphism.

THERAPEUTIC APPLICATION [12]

Antacid preparation

Purolite A 830E MR is an antacid used to control gastric acidity for the treatment of peptic ulcers.

Chewing gum for buccal absorption

Nicotine 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 flavored chewing gum base provides gradual drug release through buccal mucosa as the gum is chewed offering fresh saliva as solvent for elution.

Cholesterol reducer

Cholestyramine resin USP(Anion exchange resin), When used as an active ingredient binds bile acids, this leads to replenishment of bile acids due to the increased metabolism of serum cholesterol resulting in lowered serum cholesterol levels.

Hyperkalaemia treatment

Polystyrene sulphonates of sodium and calcium are given orally or by retention enema for treatment of hyperkalaemia associated with anuric and severe oliguric renal insufficiency. They may also be used to treat hyperkalaemia in patients requiring dialysis . [27,28,29]

SITE -SPECIFIC DRUG DELIVERY APPLICATION

a) Oral Drug Delivery:

Resinates can be directly filled in a capsule,suspended in liquids,suspended in matrices or can be compressed into tablets. Drug will be slowly released and absorbed from resinate when compared to pure drug particles but this will be significantly faster than the resinates which are coated or microencapsulated.

Junyaprasert V et.al.(2008), formulated sustained release suspension of diltiazem-strong cation exchange resin microcapsule to reduce dosing frequency and to improve patient compliance and compared release profile and stability of microcapsule. [30]

b)Nasal Drug Delivery :

Yu-Hui cheng et.al,(2002),postulated a novel nasal formulation containing Nicotine- Amberlite resin complex powder to provide an optimal combined pulsatile and sustained plasma nicotine profile for smoking cessation.[31]

c) Transdermal Drug Delivery:

LiminYu et.al 2006) formulated a model for transdermal delivery system of ketoprofen from the carbopol-based gel vehicles containing ion exchange fibers and found that the fluctuation of release rate of ketoprofen from the vehicles was much lower when compared with that of simple gels. [32]

d) Ophthalmic Drug Delivery:

IER also find application in ophthalmic drug delivery systems. An example is Bet optic S which is a sterile ophthalmic suspension and it contains 0.25% betaxolol hydrochloride. It is a cardio selective beta-adrenergic receptor blocking agent manufactured by Alcon Laboratories in the US.

R Jani et.al,(1994),investigated the complexation of betaxolol hydrochloride, an anti glaucoma agent with ion exchange resin incorporated to Carbomer 934P polymer. The 0.25% suspension showed an increased bioavailability.[33]

e)Targeted drug delivery system [Anticancer drug]

This concept is based on the chemoembolished of drug-loaded microspheres via the 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 cytotoxic agents from ion exchange resins.

Anticancer drugs like doxorubicin which are ionic in nature and can be complexed with IER.Recently several attempts have been made to deliver these drugs to cancer cells in a controlled release manner with IER. [34]

f)IERs in floating drug delivery system

A novel floating extended-release system consisting of a bicarbonate-charged resin coated with a semipermeable membrane was studied for improving gastric-residence time. [35] Drug resin complex beads are loaded with bicarbonate ions and coated with a hydrophobic polymer. When the beads reaches the stomach,the chloride ions are exchanged with bicarbonate ions and CO_2 is generated. The gas is entrapped with in the polymeric coated resins and causes the beads to float. [36]

g)Sigmoidal-release systems

IER were studied in the development of sigmoidal release systems.Eudragit RS,an AER with limited quarternary ammonium groups ,is coated over beads with sugar core surrounded by organic acid and drug mixture.the ionic environment,induced by the addition of an organic acid to the system ,was found to be responsible for pulsatile release. [37]

CONCLUSION

This article aims to provide a comprehensive review of the literature, covering topics such as properties of ion exchange resins, Drug loading and unloading on resins, drug-resin complexation and various pharmaceutical applications. From the number of patents and technological developments it is evident that the use of IER in drug delivery research is gaining importance and economic success. IER play an important role in the modification of drug release by forming a complex with the drug substances and further sustained action is obtained when these resinates are incorporated into the matrix system, microencapsulated or coated. IERs have been used in pharmacy and medicine for various function such as taste masking of bitter drugs and tablet disintegration etc. Several novel concepts, such as sigmoidal release, gastro retentive and targeted release systems have shown the potential use of IER in drug delivery system .By using IER one can easily prepare dosage forms like tablet,capsule,suspension etc. and in addition to oral drug delivery, IER systems are being explored for site-specific, transdermal, nasal and ophthalmic routes. The objective is to encourage researchers to exploit these resins more efficiently in the formulation of advanced drug delivery systems.

REFERENCES

1) Anand V, Kandarapu R and Garg, S, Ion-exchange resins: carrying drug delivery forward. Drug Discov. Today 2001; 6, 905–914. .

2) Bhalekar M, Avari JG, Jaiswal SB, Cation-exchanger in pharmaceutical formulation, Indian Journal of pharmaceutical Sciences, 38, 2004, 184-187.

3) Rane EP, Babar M. Development and evaluation of taste masked formulations of fexofenadine hydrochloride. Int J Pharma Med Biol Sci. 2021;5: 45-50.

4) Berge MS, Swarbrick J, Boylan, CJ, In Encyclopaedia of Pharmaceutical Technology, Marcel Dekker, Inc., New York,13, 1996, 465.

5) Mahesh V, Chaubal, Synthetic- Polymer Based Ion Exchange Resins : Excipients & Actives, Drug delivery tech. com, (2001- 2006); article 149

6).Sharma Vijay, Chauhan Dr. C. S.1 Ion Exchange Resins And Their Applications Journal of Drug Delivery & Therapeutics; 2014, 4(4), 115-123

7)Ajay bilandi,AK Mishra.Ion exchange resin an approach towards taste mask of bitter drugs and sustain release formulations with their patents.International research journel of pharmacy.2013,4(8)

8) Sinko PJ(2006).Martin's physical pharmacy and pharmaceutical sciences.5th Edition,Lippincott Williams and Wilkins,Philadelphia.

9) Chatap V.K., Sharma D.K., Desh P.T., Deshmukh, Taste masking Property of ion exchange resin: A Review, Pharma Times. 2008; 40(6): 22-26.

10)Irwin W.J., Belaid K.A., Alpar H.O., Drug-delivery by ion-exchange. Part III. Interaction of ester pro-drugs of propranolol with cationic exchange resins, Drug Dev. Ind. Pharm. 1987;13: 2047-2066.

11)Avari JG, Bhalekar M.Cationic resins for taste masking and rapid dissolution of Spar floxacin. Indian drug.2004: 41(1): 19-23.

12)Mhetre RM et al., Ion Exchange Resin: A Novel Drug Delivery System An overview . American Journal of PharmTech Research 2019.

13) Jeong SH, Park K. Development of sustained release fast-disintegrating tablets using various polymer-coated ion-exchange resin complexes. Int J Pharm2008; 353(1 2): 195-204.

14) Swabr ick J and Boylan JC. Encyclopedia of pharmaceutical technology. Newyork: Marcel Dekker, INC; 1996, pp.155-157.

15)Fahad Siddiqui , Muhammad Harris Shoaib , Farrukh Rafiq Ahmed , Faaiza Qazi , Rabia Ismail Yousuf .Formulation development and optimization of taste-masked azithromycin oral suspension with ion exchange resins: Bioanalytical method development and validation, in vivo bioequivalence study, and in-silico PBPK modeling for the paediatric population Journal of Drug Delivery Science and Technology 79 (2023) 1773-2247

16) Baher A. Ehab R. , Magdy I. Mohamed , Alia A. B Domperidone resinate complex as new formulation for gastroretentive drug delivery. journel of drug delivery science and technology .AUG 2020 (58)

17)Venkatesh DP & Karki, Roopa & Goli, Divakar & Jha, Sajal).Over view :ion exchange resins in controlled drug delivery system.World journel of pharmacy and pharmaceutical sciences .2013

18)Prachi R. Kumbholkar*[1], Sheikh Samir Md. Mustafa[2], Tina K. Ramchandani[3], Ahsanulhaq Abdulhad[4], Adnan khan Yaqub khan[5], Nikita Gaydhane[6], Dr. Ravi Kalsait[7]. A review on ion excghange resins as drug delivery system.International Journal of Creative Research Thoughts (IJCRT)DEC 2023(11) 2320-2882

19)Pande SV, Kshirsagar MD and Chandewar AV. (Ion exchange resins Pharmaceutical applications and recent development). International journal of advances in pharmaceutical sciences, 2011;2: 8-11

20)Park HR, Seok SH, Hwang KM, Kim JY, Park CW, Park ES. Formulation of sustained-release orodispersible film containing drug–resin complexes of donepezil hydrochloride. Journal of Pharmaceutical Investigation. 2022 Mar;52(2):259-72.

21)Jee JP, Kim YH, Lee JH, Min KA, Jang DJ, Jin SG, Cho KH. Paliperidone-Cation Exchange Resin Complexes of Different Particle Sizes for Controlled Release. Pharmaceutics. 2023 Mar 13;15(3):932. doi: 10.3390/pharmaceutics15030932. PMID: 36986792; PMCID: PMC10055564.

22)Shital JB,BhanojiR,Ganesh Y.D,Jayant B,Vaishali D.T,Development and evaluation orodispersible tablets containing taste masked zopiclone,Bulletin of environment pharmacology and life sciences.feb 2022;11(3)11-22

23 Dr Hughes L,Gehris A, A new method of characterization of buccal dissolution of drug: Rohm and Haasresearch laboratory spring house,PA,USA17.

24)Chaubal MV. Synthetic polymer-based ion exchange resins: excipients & actives. Drug Del Tech 3(5): 6-8, 2003.

25)Hughes L (2004). Ion exchange resin unique solution to formulation problem; pharmaceutical technology excipients and solid dosage form. www.pharmtech.com

26)I Singh*, Ashish K. Rehni, R Kalra, G Joshy , M Kumar, Hassan Y. Ion Exchange Resins: Drug Delivery and Therapeutic Applications: 2007 ,J Pharm. Sci., 32, 91-100,

27)Namdeo J., Drug delivery and therapeutic application of ion-exchange resins: An update, J. Pharm. Sci. 2007;5 (4):148-156.

28)Sharma Vijay, Chauhan Dr. C. S.1 Ion Exchange Resins And Their Applications Journal of Drug Delivery & Therapeutics; 2014, 4(4), 115-123.

29)S. Sivaneswari, D. Veena, P. Sai Sumana, P. Subhashree, L. Ramya, R. Rajalakshmi,P. J. Chandana and E. Karthikeyan , Ion exchange resins as drug delivery carriers Journal of Chemical and Pharmaceutical Research, 2015,7(4):1436-1445.

30)Junyaprasert VB, Manwiwattanakul G. Release profile comparison and stability of diltiazem-resin microcapsules in sustained release suspensions. Int J Pharm 352(1-2): 81-91, 2008

31)Cheng YH, Watts P, Hinchcliffe M, Hotchkiss R,Nankervis R, Faraj NF, Smith A, Davis SS, Illum L. Development of a novel nasal nicotine formulation comprising an optimal pulsatile and sustained plasma nicotine profile for smoking cessation. J Control Release 79(1-3): 243-254, 2002

32) Yu L, Li S, Yuan Y, Dai Y, Liu H. The delivery of ketoprofen from a system containing ion-exchange fibers . 319(1-2): 107-113, 2006

33)Jani, R., Gan, O., Ali, Y., Rodstrom, R., & Hancock, S. (1994). Ion exchange resins for ophthalmic delivery. Journal of ocular pharmacology, 10(1), 57–67. https://doi.org/10.1089/jop.1994.10.57

34)Chen Y.et al.,Evaluation of ion exchange microspheres as carriers for the anticancer drug doxorubicin :in vitro studies,.J.Pharm.Pharmacol,44,1991,211-215

35)Fell TJ,et al.Prolonged gastric retention using floating dosage forms,Pharm.Technol.March,2000:82-88

36) Aytabi F,Maryam K.Ion exchange ,an approach to prepare an oral floating drug delivery system for diclofenac. Iranian Journal of pharmaceutical research.2004,2:93-97

37)Narisawa S,et al.,an organic acid induced sigmoidal release for oral controlled release preperations.2.permeability enhancement of Eudragit RS coating led by physicochemical interactions with organic acid,J.Pharm.Sci,85,1994,184-188