Review Article

ION EXCHANGE RESINS: A BOON FOR PHARMACEUTICAL INDUSTRY – AN OVERVIEW

Sharma V*, Singh L
Department of Pharmaceutical Technology, Pharmacy Division, Shri Ram Murti Smarak College of Engineering and Technology, Bareilly, U.P, India.
***Corresponding author's E-mail:** vijaysrampur@gmail.com

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ABSTRACT

Ion exchange resins are said to be revolutionary agents, is widely being used in pharmaceutical industry with several advantages, because of their unique properties discussed in the review. IER are being used as taste masking agent, disintegrant, stabilizer, in novel drug delivery system, enhance dissolution and also in various formulations.

Keywords: Ion exchange resins, cross linking, targeted drug delivery.

INTRODUCTION

Ion Exchange Resins are suitably high molecular weight solid polymers having positively and negatively charged functional groups that can exchange their mobile ions equal charge with surrounding medium.[1] Due to their high molecular weight and insolubility, resins are not absorbed by body. [2]

Complexation between drug and resin is a process of diffusion of ions between resin and surrounding medium i.e. drug solution.[3]

In future trend ion exchange resins are not only being used as a taste masking agent but also for the development of sustain release dosage forms.

IDEAL CHARACTERISTICS OF AN ION EXCHANGE RESIN[4]

1) It must be fine, free flowing powders.

2) Particle size must be ranges between 25-150 microns.

3) It must be capable of exchanging ions and/or ionic groups.

4) It must be insoluble in all solvents at all pH.

5) It should not be absorbed by the body.

CLASSIFICATION OF ION EXCHANGE RESIN[1]

Ionizable groups attached to resin determine the functional capability of ion exchange capability of resin.

Ion exchange resins are classified as

- Strong acid cation exchange resins (SACER)

- Weak acid cation exchange resins (WACER)

- Strong base anion exchange resins (SBAER)

- Weak base anion exchange resins (WBAER)

SACER can neutralize strong base and convert salts into their corresponding acids. These resins derive their functionality from sulfonic acid group ($HSO3^-$ or $NaSO_3^-$).

SBAER can neutralize strong acids and converts neutral salts into their corresponding bases. SBAER are deriving their functionality from quaternary ammonium groups. Two type of quaternary ammonium groups are used as type I (having 3 methyl groups) and type II similar to type I except one methyl group replaced by ethanol group. Type I is more stable than Type II.

WACER and WBACER are able to neutralize strong bases and acids respectively. These resins are used for dealkalization and partial dealkalization.

WACER derive their functionality from carboxylic group. (-COOH or –COOK)

WBACER are deriving from primary, secondary and tertiary amines.

Cation exchange resins are not significantly affected by temperature as compared to anion exchange resins.[5]

MECHANISM OF WORKING

The phenomenon of loading of drug into resin is due to electrostatic interaction between resin and oppositely charged drug ions. This electrostatic interaction causes equilibrium distribution of drug between resin and solution of drug. 6 it was also find that the vanderwaal force or chemisorptions process along with drug exchange during complexation process.[7] complexation process between drug and resin will be as follows

$$Resin^- - Na^+ + Drug^+ \longrightarrow Resin^- - Drug^+ + Na^+$$

The drug release process will be as follow

$$Resin^- - Drug^+ + X^+ \longrightarrow Resin^- - X^+ + Drug^+$$

Where X^+ is ions in GIT

Drug release from DRC (drug Resin Complex) is done by partial diffusion and film diffusion process[8]

Table 1: Types of Ion exchange resin.

Type	Exchange species	Ionic Form	Polymers Backbone	Commercial Name
Weak acid	-COO	(1,2,5) Hydrogen (3, 4) Potassium	(1, 3) Methacryllic acid divinylbenzene (2, 4) Crosslinked polyacrylic acid (5) Crosslinked Polymethacrylic	(1) AMBERLITE™ IPR64 (2) INDION 204, INDION 214, KYRON T-114, TULSION 335 (3) AMBERLITE™ IPR88 (4) INDION 234, INDION 234S, INDION 294 (5) INDION 464
Strong acid	- SO_3	Sodium	Styrene divinylbenzene	AMBERLITE™ IPR69
Strong base	$-N^+(R)_3$	Chloride	Styrene divinylbenzene	DUOLITE™ AP143

Essential Properties of ion exchange resins

1. Cross linking

This is the property having a great effect on physical structure, porosity and swelling property of resin. In case of low degree of cross linking will result into higher swelling with water and becomes soft and gelatinous but becomes hard and brittle in case of high degree of cross linking. Hence as cross linking increases loading efficiency of drug will decrease.[9]

2. Capacity

Total capacity of IER refers total number of chemical equivalent available for exchange per unit weight or per unit volume of resin. The capacity expressed as meqvt./gm for dry resin or meqvt./ml for wet resin. Weak acid cation resins having higher exchanging capacity than strong acid cation, weak base anion and strong base anion exchange resins. [9]

3. Particle size

Rate of ion exchange is inversely proportional to particle size of resin. Hence lower the particle size of resin means higher will be the rate of ion exchange i.e. less time will be taken to achieve equilibrium.[10]

4. pH

Excess H^+ in the solution decreases complexation at lower pH. Protonated fractions of moderately weak acid or basic drug and weak functionality resin undergoes changes thereby increase or decrease drug resin interaction and drug loading.[11]

5. Porosity and swelling

Porosity is the ratio of volume of material its mass. Amount of cross linking substance used affected by its porosity. Higher number of hydrophilic functional groups attached to the polymer matrix will cause higher swelling.[12]

6. Form of resin

Protonated resin having higher loading capacity because of it acquires lower pH than the sodium ions.[11]

7. Counter ion selectivity

Higher drug loading was found inions with low selectivity for protonated resin because of easy replacement of H^+. [12]

8. Stirring time

It is found that as the stirring time increases drug loading significantly increases because of surface absorptive phenomenon.[13]

METHODS OF COMPLEXATION

❖ **Batch process**

In this process resins are kept to soak some amount of water into a tank for a period of time. Then drug was added and stirred continuously for a predefined time period to set equilibrium. After this subjected to filter, washed with deionized water to two or three times and dried.

❖ **Column process**

Resin was packed into glass column by gentle tapping and then aqueous drug solution was passed through this resin packed glass column and left to set equilibrium.

USES OF ION EXCHANGE RESIN

a. Targeted drug delivery system

For treatment of cancer, delivery of anticancer drug was done in controlled release fashion to anticancer cells with IER [14, 15]

For gastro retentive system to exchange the gastric residence time bicarbonate as well as drug loaded onto IER**.** [16]

For sigmoid release system Eudragit RS (AER) limited quaternary ammonium group (SBAER) is coated over beads with sugar core surrounded by organic acid and drug mixture. The ionic environment induced by addition of an organic acid to system, was found to be responsible for pulsatile release. [17]

b. Taste masking

It is seen that most of the drugs are extremely bitter in taste, such drugs are loaded in IER to make tasteless either by batch process or column process. Pisal et al did Formulation of tasteless complex of ciprofloxacin with Indion 234 ion exchange resin.[13] Betty et al formulated a mixture of coated and uncoated sulfonic acid resin loaded with Dextromethorphan for taste masking.[18] Patricia et al form a stable pseudoephedrine Dowex 50 WX8 complex, found less bitter taste masked suspension.[19]

Nasal drug delivery

An IER complex approach was used to deliver therapeutic peptides or synthetic drugs via Nasal mucosa, A composition was developed to deliver nicotine in a pulsatile fashion to the systemic circulation via nasal route.[20]

c. Stabilization of drugs

Vitamin B_{12} having most common problem of stability, it gets deteriorate upon storage hence necessitates overages result into increase in the cost of formulations. To avoid overages complexation V was done with weak acid cation (Indion 264) was done which was found to be same as free form of Vitamin B_{12}.[21] for the immobilization of enzymes to provide extended activity at localized site, IER can be used as carrier.

d. Controlled or sustain release drug delivery system

Sustain release of drug may be difficult to achieve due to many variables. This problem overcomes by coating to ion exchange resin drug complex particles, making drug release from these particles diffusion controlled. [22] Seong Hoon Jeong et a developed sustain release fast disintegrating tablet of dextromethorphan using various polymer coated IER complexes and observed diffusion within the resin matrix is the rate controlling step [23]

Various formulation formulated using resinated of strong sulfonic cation exchange resin are available in marked which provide more moderate release than carboxylic acid resin.[24]

e. Tablet disintegrant

Some IER having property to swell significantly when exposed to water. This property to swell significantly used to increase disintegration of tablets. Polymethacrylic carboxylic acid IER due to its large swelling capacity used as tablet disintegrant such as polacrilin potassium salt of weakly acidic cation exchange resin.[25]

f. Transdermal drug delivery system

Transdermal iontophoresis involves movements of ionic drug across skin using an extremely applied potential difference. The addition of IER to get or other composite vehicles complicates the process of passive drug release. Release of drug was measured by current density and NaCl concentration using a novel an iontophoretic cells.

Vuorio M et al studied on resinates of cationic drugs such as ambroxol and chlorpheniramine and investigated amount of drug release from prepared resinates by simultaneous loading of both drugs was not differ from the classical ambroxol or chlorpheniramine resinates but was found to be higher that concurrent administration of two classical resinates. Hence it was concluded that concurrent administration of resinates can be used as carrier in ion exchange drug delivery system.[26]

g. Dissolution Enhancer

Poorly soluble ionizable drug shows slow dissolution and low solubility. The rate of release of poorly soluble ionizable drugs from resinates can be made faster than that of rate of dissolution of solid form of pure drug. Change in molecular state of entrapped drug from crystalline form to amorphous state cause improvement in dissolution rate. [27]

h. Polymorphism

Ion exchange resins are great innovation for Pharma industry to resolve the problem of polymorphism. A drug resinates are amorphous in nature and cannot be crystallize or even form hydrates. Release of drug from resinates found to be independent of crystal form which was used to eliminates the problem arises from polymorphism.[28]

i. Deliquescence

It is the property of solid to absorb so much amount of water it is difficult to solve and requires use of special equipment or more attentive scheduling of production during dry seasons. Resinates of deliquescent drug retain properties of resin, is not deliquescent hence resin of deliquescent drug can handle without need of special manufacturing condition.[28]

CONCLUSION

Ion exchange resins having its own importance in novel drug delivery system due to its complexation property with drugs without any interaction with drug and drug can be release at desired site of action. Because of its complexation property it used as disintegrator, dissolution enhancer, taste masking agent, in novel drug delivery system, to improve stability, and for handling of deliquescent and hygroscopic substances

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