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FORMULATION AND EVALUATION OF TASTE MASKED ORODISPERSIBLE TABLETS BY ION – EXCHANGE RESINS

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ABSTRACT

Acceptability of any drug dosage form mainly depends upon its taste i.e. mouth feel. In the formulation of oro-dispersible tablet of bitter drug, the main challenge is to mask the bitter taste of drug, because the drug is dispersed and released in mouth. This is more essential in the formulation for pediatric and geriatric, bed ribbon and non-cooperative patients. There are many methods of taste masking but the main objective of this article is to explore method, technology and evaluation to mask taste of bitter drug by ion-exchange resins. Here we will study the formulation and evaluation of various oro-dispersible tablets of bitter drug. This is more economical, easiest and efficient method for taste masking.

KEYWORDS

Oro-dispersible tablets, ion exchange resins, drug resin complex.

INTRODUCTION

The Formulation and use of oro-dispersible tablet is increasing day by day because of patient compliance especially for pediatrics & geriatric patients. The formulation of ODT of drug having sweet or acceptable taste is quite easy but if the drug is bitter in taste, it becomes more difficult. So there is need of taste masking of bitter drug before formulation of ODT. There are many methods of taste masking but we study the taste masking by IERs and formulation of ODTs.

ANATOMY & PHYSIOLOGY OF TASTE

The biological definition of taste (Gustation) - It is a chemical reaction arising from sensory responses of the four main taste perceptions: sweet, bitter, salt & sour.

Fig-1

ORO-DISPERSIBLE TABLETS

An orally disintegrating tablet (ODT) is defined as a solid dosage form that dissolves or disintegrates quickly in the oral cavity without the need for administration of water. The *EP* describes ODTs as »*uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed*« and as tablets which should disintegrate within 3 min. [1]

FDA defines ODT as »*a solid dosage form which contains a medicinal substance or active ingredient which disintegrates rapidly within a matter of seconds when placed upon a tongue* [2]

TASTE MASKING

It is defined as the apparent reduction of an unpleasant taste by using suitable agent. Taste masking technologies are very important for improving Patient compliance & better therapeutic efficacy. Many oral drug delivery formulations have objectionable taste such as

bitterness, saltiness or sourness. For those drugs taste masking is necessary.

METHODS OF TASTE MASKING

1) Taste masking with flavors, sweeteners & amino acids.
2) Polymer coating of drug.
3) Formation of Inclusion complexes.
4) Ion- exchange resin complex.
5) Solid dispersion. Microencapsulation.
6) Mass extrusion.
7) Multiple emulsions.
8) Development of liposome.
9) Prodrug concept.
10) Spray drying technique.
11) Adsorption
12) By using lipophilic vehicles like lipids & recithins.
13) Formation of salt or derivatives.
14) Use of amino acids and protein hydrolysates.
15) By viscosity modification. [3]

There are many methods of taste masking of bitter drug which are written above but here we will study taste masking by ion-exchage resins.

TASTE MASKING BY ION-EXCHANGE RESINS-

INTRODUCTION-

IERs are solid & suitably insoluble high molecular weight polyelectrolyte that can exchange their mobile ions of equal charge with the surrounding medium. [4] Synthetic ion exchange resins have been used in pharmacy & medicine for taste masking or controlled release of drug as early as 1950. [5] Bitter tasting drugs can be absorbed onto ion-exchange resins, thus effectively removing them from solution during the transit through the mouth, at salivary pH 6.7, remains in intact from making the drug unavailable for the taste sensation. Various studies have revealed that ion exchange resins are equally suitable for drug delivery technologies. [6]

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

- -COOH, which is weakly ionized to $-COO^-$
- -SO3H, which is strongly ionized to $-SO3^-$
- -NH2, which weakly attracts protons to form NH3+
- -secondary and tertiary amines that also attract protons weakly
- -NR3+, 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. [6]

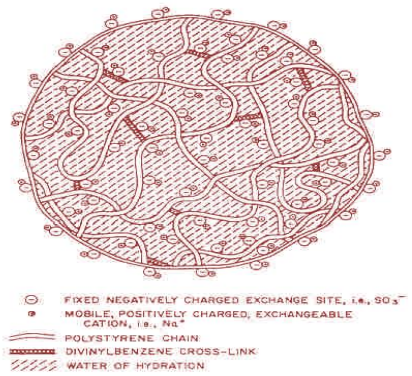
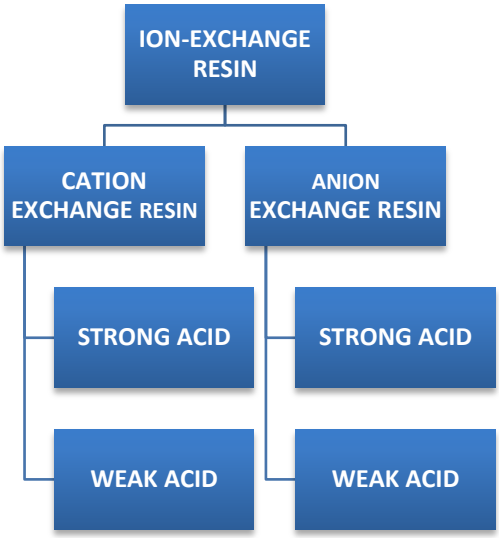


Fig-2 Expanded View of a Polystyrene Bed

CLASSIFICATION- Ion exchange resins are broadly classified into two main Categories, as Cation exchange resins and anion exchange Resins (**Fig. 3**).



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 ($-SO_3H$) introduced into most of the benzene rings. The mechanism of Cation exchange process can be represented by the following reaction:

Resin- - ex+ + C+ ®Resin- - C+ +ex+

Where, Resin- indicates a polymer with SO3- 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:

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-SO3H) and salt (RSO3Na) form of the sulfonic acid group (-SO3H). They can convert a metal salt to the corresponding acid by the reaction:

$2(R\text{-}SO_3\ H) + NiCl2 \ ® \ (R\text{-}SO_4)\ Ni + 2HCl$

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. 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 convened to the sodium form with a sodium chloride solution. For the above reaction, hydrochloric acid (HCl) regeneration would result in a concentrated nickel chloride (NiCl2) 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 (SO3H) 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 chlormethylating the benzene rings of styrene-divinyl benzene copolymer to attach CH2Cl 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:

Resin+ - ex - + A- ® Resin+ - A- + ex-

Where, Resin+ indicates a polymer with N+ sites available for bonding with exchangeable anion (ex-), and A- indicates Cation 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:

R-NH3OH + HCl ® R-NH3Cl + HOH

Regeneration with concentrated sodium hydroxide (NaOH) converts the exhausted resin to the OH form. [7]

METHOD OF IER-DRUG COMPLEX FORMATION-

Ion exchange resins may be supplied in case of cation exchangers as sodium, potassium or ammonium salts and of anion exchangers usually as the chloride. It is frequently necessary to convert a resin completely from one ionic form to another.

Charged drugs are normally loaded on to ion exchange resins by two methods, viz, column method and batch method.

Column method- In this method a highly concentrated drug solution is passed through a column of resin particles. Since the reaction is an equilibrium phenomenon, maximum potency and efficiency is best obtained by the column method.

Batch method-In this method the drug solution is agitated with a quantity of resin particles until equilibrium is established. The reaction involved during complexation of drug with resin may be indicated as follows [8]

CONFIRMATION OF COMPEXATION-

FTIR studies- Drug, Resin, and physical mixture of both and DRC are subjected to Fourier transform infrared spectroscopy (FTIR) studies. Samples are prepared using KBr disc method and spectra are recorded over the range 400 to 4,000 cm−1. Spectra are analyzed for drug–resin interactions and functional groups involved in the complexation process.

Powder X-ray diffraction studies- X-ray diffractograms of Drug, Ion-exchange resin, and DRC are recorded using Philips PW 3710

deffractometer and analyzed for interactions between drug and resin and confirmation of complexation.

Thermal analysis- Differential scanning calorimetry (DSC) is carried out using Mettler Toledo 823e instrument equipped with intracooler. Indium zinc standards are used to calibrate the temperature and enthalpy scale. The samples are hermetically sealed in aluminum pans and heated over the temperature range 30°C to 300°C with heating rate of 10°C/min. Inert atmosphere is provided by purging nitrogen gas flowing at 40 mL/min.

PROPERTIES OF ION-EXCHANGE RESINS-

1) **PARTICLE SIZE & FORM-** Decreasing the size of the resin particles significantly decreases the time required for the reaction to reach the equilibrium with the surrounding medium; hence larger particle size affords a slower release pattern.
2) **POROSITY & SWELLING-**Porosity is defined as the ratio of volume of the material to its mass. The limiting size of the ions, which can penetrate into a resin matrix, depends strongly on the porosity. The porosity depends upon the amount of cross-linking substance used in polymerization method. The amount of swelling is directly proportional to the number of hydrophilic functional groups attached to the polymer matrix and is inversely proportional to the degree of DVB cross linking present in the resin.
3) **CROSS LINKING-**The percentage of cross-linking affects the physical structure of the resin particles. Resins with low degree of cross-linking can take up large quantity of water and swell into a structure that is soft and gelatinous. Cross-linkage has dramatic effect on loading efficiency. It affects porosity and swelling properties of resin. Low cross-linking agents remarkably upon hydration. Higher grade have finer pore structure thus reducing loading efficacy with increase in cross- linking. Low cross linkage increase loading efficacy but also increases release rates.(9)
4) **MOISTURE CONTENT-**A physical property of the ion exchange resins that changes with changes in cross-linkage are the moisture content of the resin. For example, sulfonic acid groups (-SO3H) 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.(10)
5) **EXCHANGE CAPACITY-**The exchange capacity refers to the number of ionic sites per unit weight or volume (mEq. Per gram or meq per ml). The weight basis values (mEq. per gm) are much higher than the volume based exchange capacity since the wet resin is highly hydrated. The exchange may limit the amount of drug that may be adsorbed on a resin, hence affect potency of the complex. Carboxylic acid resins derived from acrylic acid polymers have higher exchange capacities (10meq. /gm) than sulfonic acid (about 4meq. / gm) or amine resins because of bulkier ionic substituent and the polystyrene matrix. Therefore, higher drug percentages may often be achieved with carboxylic acid resins. (11)
6) **ACID BASE STRENGTH**-It depends on various inorganic groups incorporated into resins. Resins containing sulphonic, phosphoric or carboxylic acid exchange groups have approximate pKa values of <1, 2, 3 and 4-6 respectively. Anionic exchangers are quaternary, tertiary or secondary ammonium groups having pKa values of >13, 7-9 or 5-9 respectively. The pKa values of resin will have significant influence on the rate at which the drug will be released in the gastric fluid.(12)

7) **STABILITY-**The ion exchange resins are inert substances at ordinary temperature and excluding the more potent oxidizing agent are resistant to decomposition through chemical attack. These materials are indestructible. They get degraded and degenerated in presence of gamma rays.(9)

8) **PURITY AND TOXICITY-**Since drug resin combination contains 60% or more of the resin, it is necessary to establish its toxicity. Commercial product cannot be used as such. Careful purification of resins is required. Resins are not absorbed by body tissue and are safe for human consumption. Test for toxicological tolerance showed that it does not have any pronounce physiological action at recommended dosage and is definitely non-toxic.(9)

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 other than size and charge also contribute to the selection of one counter ion in preference to another. The extent of adsorption increases with -

1. 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.
2. The counter ion at least affected by complex formation with its co-ion or non-exchange ion.
3. 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. (10)

PHARMACEUTICAL GRADE ION-EXCHANGE RESINS-

NAME	FUNCTIONALITY	POLYMER BACKBONE
AMBERLITE™ IRP 64	WEAK ACID COO^-	CROSSLINKED POLYACRYLIC
AMBERLITE™ IRP 69	STRONG ACID SO^{3-}	SODIUM STYRENE-DIVINYL BENZENE
AMBERLITE™ IRP 88	WEAK ACID COO^-	CROSSLINKED POLYACRYLIC
AMBERLITE™ IR 120	STRONG ACID SO_3H	STYRENE-DIVINYL BENZENE
AMBERLITE™ IR C50	WEAK ACID COOH	METHAACRYLIC ACID DIVINYL BENZENE
AMBERLITE™ IR 400	STRONG BASE N^+R_3	STYRENE-DIVINYL BENZENE
AMBERLITE™ IR4B	WEAK BASE N^+R_2	STYRENE-DIVINYL BENZENE
DOWEX 1	STRONG BASE N^+R_3	POLY STYRENE-DIVINYL BENZENE
DOWEX2	WEAK BASE N^+R_2	POLY STYRENE-DIVINYL BENZENE
DOWEX 50	STRONG ACID SO_3H	POLY STYRENE-DIVINYL BENZENE

DOSHION P544(R)	WEAK ACID COO^-	METHAACRYLIC ACID DIVINYL BENZENE
DUOLITE AP 143	STRONG BASE N^+R_3	STYRENE-DIVINYL BENZENE
KYRON T-104	WEAK ACID COO^-	METHAACRYLIC ACID DIVINYL BENZENE
KYRON T-114	WEAK ACID COO^-	METHAACRYLIC ACID DIVINYL BENZENE
KYRON T-134	WEAK ACID COO^-	METHAACRYLIC ACID DIVINYL BENZENE
KYRON T-154	STRONG ACID SO_3H	STYRENE-DIVINYL BENZENE
TULSION 335	WEAK ACID COOH	METHAACRYLIC ACID DIVINYL BENZENE
TULSION 339	WEAK ACID COOK	METHAACRYLIC ACID DIVINYL BENZENE
TULSION 344	STRONG ACID SO_3Na	SODIUM STYRENE-DIVINYL BENZENE
PUROLITE C100 HMR	STRONG ACID SO_3H	STYRENE-DIVINYL BENZENE
PUROLITE C102 DR	WEAK ACID COO^-	METHAACRYLIC ACID DIVINYL BENZENE

PHARMACEUTICAL GRADE IER- INDION-

PRODUCT NAME	INDION 204	INDION 214	INDION 224	INDION 234
Applications	Taste masking of bitter drugs such as Norfloxacin, Ofloxacin	Taste masking of bitter drugs such as Azithromycin	Sustained release agent in drug formulations	Taste masking of bitter drugs such as Ciprofloxacin, Chloroquinphosphate
Matrix type	Cross linked polyacrylic	Cross linked polyacrylic	Styrene DVB	Cross linked polyacrylic
Functional Group	$-coo^-$	$-coo^-$	$-SO_3^-$	$-coo^-$
Standard Ionic Form	H^+	H^+	H^+	K^+
Particle size range, mm	≤ 0.15	≤0.15	0.2 – 1.2	≤0.15
% Moisture	≤ 5	≤ 5	≤ 3	≤ 10
Total Exchange Capacity meq/g, dry	10.0	10.0	4.8	NA

PRODUCT NAME	INDION 234S	INDION 244	INDION 254	INDION 264
Applications	Taste masking of bitter drugs as well as tablet disintegration	Sustained release agent in drug formulations	Sustained release agent in drug formulations. Product meets specs. Of Sodium	Stabilization of Vitamin B_{12}

			Polystyrene sulfonate , USP	
Matrix type	Cross linked polyacrylic	Styrene/DVB	Styrene/DVB	Cross linked polyacrylic
Functional Group	$-COO^-$	$-SO_3^-$	$-SO_3^-$	$-COO^-$
Standard Ionic Form	K^+	H^+	Na^+	H^+
Particle size range, mm	≤ 0.075	≤ 0.15	≤ 0.15	≤ 0.15
% Moisture	≤ 10	≤ 10	≤0.15	≤ 5
Total Exchange Capacity meq/g, dry	NA	4.5*	NA	10.0*

PRODUCT NAME	INDION 284	INDION 294	INDION 404	INDION 414
Applications	Sustained release agent in drug formulations	Tablet disintegrant/ Taste masking. Product meets specs. Of Polacrilin Potassium, USP	Treatment of hyperkalaemia. Product meets specs. Of Calcium polystyrene sulfonate, BP	As superdisintegrant in mouth disperse tablets, iron & calcium pellets
Matrix type	Styrene/DVB	Cross linked polyacrylic	Styrene/DVB	Cross linked polyacrylic
Functional Group	$-SO_3^-$	$-COO^-$	$-SO_3^-$	$-COO^-$
Standard Ionic Form	Na^+	K^+	Ca^{++}	K^+
Particle size range, mm	0.3 – 1.2	≤ 0.15	≤ 0.15	≤ 0.15
% Moisture	≤ 70	≤ 10	≤ 8	≤ 10
Total Exchange Capacity meq/g,	1.0	NA	NA	NA

PRODUCT NAME	INDION 454	INDION 464
Applications	Cholesterol reduction and taste masking of bitter drug	Taste masking of bitter substances Ex. Nicotine
Matrix type	Cross linked Polystyrene	Cross linked Polymethacrylic
Functional Group	$-N^+R_3$	$-COO^-$
Standard Ionic Form	Chloride	H^+
Particle size range, mm	≤0.15	≤ 0.15
% Moisture	≤12	≤ 5
Total Exchange Capacity meq/g,	N.A.	9.5

DESIRED PROPERTIES OF PHARMACEUTICAL GRADE IERS-

a) Fine, free flowing powders

b) Particle size of 25 - 150 microns

c) Contain functional group that capable of exchanging ions and/or ionic groups

d) Insoluble in all solvents, all pH's

e) Not absorbed by body

f) Do not have a defined molecular weight

ADVANTAGES OF ION EXCHANGE RESIN AS A TASTE MASKING AGENT IN ORODISPERSIBLE TABLET-

1. These method requires few and simple equipment.
2. The numbers of excipients required are less and are easily available.
3. The Bioavailability of drug is not altered.
4. The resins are easy to process and has high margin of safety.
5. The manufacturing can be carried out at room temperature and no other special experimental conditions are required.
6. It has low cost of manufacturing. (9)

TASTE MASKED ORODISPERSIBLE TABLETS HAVING IERs AS A TASTE MASKING AGENT-

1. FORMULATION OF TASTE MASKED ORO-DISPERSIBLE TABLETS OF METFORMIN HYDROCHLORIDE-(13)

- METFORMIN HYDROCHLORIDE is an oral biguinide agent, used in the management of non-insulin dependent (type-2) diabetes mellitus.
- Firstly Drug Resinate was prepared with INDION-234 using batch method in ratio drug to resin at 1:1.
- Then filtered and dried drug resinate was compressed with different disintegrant like Sodium Starch Glycolate (SSG), Starlac & Avicel pH101; singly and also in combination.
- After evaluation, the batch with 5% SSG & avicel was found to be optimum batch as it shows lowest disintegration time with desired friability values.
- The first one having DT- 20±0.6 (In vitro), 25±0.7 (In vivo)
- Second one having DT- 23±0.3 (In vitro), 32±1.6 (In vivo)

2. FORMULATION OF TASTE MASKED ORO-DISPERSIBLE TABLETS OF ONDANSETRON HYDROCHLORIDE-(14)

- Ondansetron hydrochloride is commonly used as anti emetic.
- The taste masking of this drug was done by formulating drug resinate by batch method with three different IERs- INDION-204, INDION-234 & INDION-335 in drug to resin ratio 1:6, 1:5, 1:6 respectively.
- The filtered and dried drug resinate was compressed with disintegrant Crosspovidone & microcrystalline cellulose.
- All the three batches of tablets having INDION-204 (F1), INDION-234 (F2), TULSION (F3) passed weight variation test. Formulated products have exhibited very less disintegration time- 14, 21, 20 seconds respectively.

3. FORMULATION OF TASTE MASKED ORO-DISPERSIBLE TABLET OF METOCLOPRAMIDE HYDROCHLORIDE-(15)

- Metoclopramide hydrochloride a derivative of paraaminobenzoic acid is a commonly prescribed drug used for the management of gastrointestinal disorders such as gastric stasis, gastro esophageal reflux and for the prevention of cancer chemotherapy-induced emesis.
- Drug resinate was prepared using a batch process by INDION-234 in the ratio of drug to Resin in 1:3.
- Then filtered & dried drug resinate was compressed with disintegrant Crosspovidone & MCC.
- The formulation having MCC and Mannitol in 1:1 ratio along with 7 mg of Crosspovidone was selected as optimized batch because of its lowest disintegration time and highest drug release.

4. FORMULATION OF TASTE MASKED ORODISPERSIBLE TABLETS OF TRAMADOL – (16)

- Tramadol is a centrally acting opioid analgesic used in the treatment of moderate to severe pain in diverse conditions.

- Drug resin complex (DRC) was prepared using a batch method by TULSION-335 in the ratio of 1:1.
- Then filtered and dried DRC was compressed with disintegrant Crosspovidone with varying excipients conc. & prepared various batches.
- All the batches showed DT less than a minute & friability less than 1%.

5. FORMULATION OF ORO-DISPERSIBLE TABLET OF AMBROXOL HYDROCHLORIDE-(17)

- Ambroxol hydrochloride (HCL) is a potent mucolytic capable of inducing bronchial secretion. It is used in the treatment of asthma, bronchitis, and cough.
- The DRC was prepared using batch method with IER INDION 204 & INDION 234 in the ratio 1:5 and 1:6 respectively.
- Then filtered & dried DRC was compressed with Mannitol & talc & mint flavor.
- The ODTs obtained passed weight variation test & have exhibited very low DT (14 sec and 21 sec).

6. FORMULATION OF TASTEMASKED ORO-DISPERSIBLE TABLET OF DEXTROMETHORPHAN-(18)

- Dextromethorphan hydrobromide is an antitussive drug widely used in the treatment of cough.
- DRC was prepared by a batch process with Amberlite® IRP-69 in ratio 1:2.
- Then filtered & dried DRC was compressed with disintegrant Avicel PH102 & Mannitol.
- The ODTs obtained having DT 20 sec & 13 second.

7. FORMULATION OF TASTE MASKED ORO-DISPERSIBLE TABLET OF DIPHENYHYDRAMINE HYDROCHLORIDE-(19)

Diphenhydramine Hydrochloride (DPH HCl) an antihistaminic drug with bitter taste and low dose (25 mg) DRC was prepared by a batch process with two IERs TULSION 343 & INDION 234 in the ratio 1:1 & 1:2. Then filtered & dried DRC was compressed with sodium bicarbonate, tartaric acid, citric acid anhydrous, dicalcium phosphate, talc, avicel 101, Primojel, Mannitol, Aerosil, sod. Saccharine , PVP K30, Magnesium Stearate and orange flavor.

DT was found to be in range 35-60 seconds.

EVALUATION OF TASTE OF ORO-DISPERSIBLE TABLETS-(20)

Sensory evaluation

Taste, to think of, is a very subjective perception. Depending on individuals, the perceived taste may vary to different degrees. If we have well controlled experimental set up, it is possible to accurately and reproducibly measure taste thresholds. To quantitatively evaluate taste sensation, following methods have been reported in literature.

- Panel testing (human subjects)
- Measurement of frog taste nerve responses.
- Multichannel taste sensor/ magic tongue
- Spectrophotometric evaluation/ D30's value

Panel Testing

The panel testing is a psychophysical rating of the gustatory stimuli. In this method, a group of about 5-10 human volunteers is trained for taste evaluation by using reference solutions ranging in taste from tasteless to very bitter. Numerical values are then assigned to these levels of bitterness (eg.,0-5). Subsequently, test solution is tasted and rated on the same scale to assess its bitterness.

Measurement of Frog Taste Nerve Responses

In this method, adult bull frogs are anaesthetized intraperitoneally and the glossopharyngeal nerve is then located and dissected from the surrounding tissue and cut proximally. An ac-amplifier and an electronic integrator are used to respectively amplify and integrate the nerve impulses. The peak height of the integrated response is then taken as the magnitude of response.

Multichannel Taste Sensor / Magic tongue

This is an automated taste sensing device to detect the magnitude of bitterness of a drug substance. The device has a transducer which is composed of several kinds of lipid/polymer membranes with different characteristics that can detect taste in a manner similar to human gustatory sensation. Taste response is transferred into a pattern composed of electric signals of membrane potentials of the receptor part. Different response electric potential pattern are obtained for substance producing different taste qualities.

Spectrophotometric Method (21)

A known quantity of the taste-masked formulation is mixed with 10 ml of distilled water in 10 ml syringe by revolving the syringe, end to end, five times in 30 seconds. The test medium is then filtered through a membrane filter, followed by Spectrophotometric determination of the concentration of the drug in the filtrate. If this concentration is below the threshold concentration, it may be concluded that the bitter taste would be masked *in vivo*. This technique has been applied to evaluate the taste masked granules of sparfloxacin, with threshold concentration being 100µg/ml.

SUPPLIERS OF PHARMA GRADE ION EXCHANGE RESINS IN INDIA-

SR. NO.	SUPPIER'S COMPANY NAME	ADDRESS & WEBSITE/E-MAIL ID
1	Ion Exchange (India) Ltd.	Ion House, Dr. E. Moses Road, Mahalaxmi, Mumbai 400 011, India. E-mail : hocro@ionexchange.co.in
2	• Potent Water Care Private Limited	32, C.S.C. - 12,G - 29, D.D.A. Market, Sector - 3, Rohini, New Delhi, Delhi - 110 085, India Website: http://www.pwswimmingpool.com/water-treatment-chemicals.html
3	• Water Care Technology	Shop No. 27, C. S. C. 12, G- 29, D. D. A. Market, Sector - 3, Rohini, New Delhi, Delhi - 110 085, India Website: http://www.swimmingpoolexpertindia.com/water-treatment-chemicals.html
4	Doctor H2O	No. 32, C. S. C. 12, G - 29, D. D. A. Market, Sector - 3, Rohini, Delhi, Delhi - 110 085, India Website: http://www.swimmingpoolequipmentindia.com/sauna.html
5	Pool Tycoon	Shop No. 32, C. S. C. 12, G - 29, D. D. A. Market, Sector - 3, Rohini, New Delhi, Delhi - 110 085, India Website: http://www.swimmingpoolequipments.com/ion-exchange-resins.html
6	• Triveni Interchem Pvt. Ltd. (Group Of Triveni Chemicals)	Pacharatna Char Rasta, G.I.D.C, Vapi, Gujarat - 396 195, India Website: http://www.triveniinterchem.com/resin.html
7	• Triveni Chemicals	No. 135, Pancharatna Char Rasta, G. I. D. C., Vapi, Gujarat - 396 195, India Website: http://www.trivenichemical.com/resin1.html
8	• Aqua Ion Exchange Systems	No. 20, Old No. 3, Dhanalakshmi Nagar, 100 Feet, New Scheme Road, New Sidhapudur, Coimbatore, Tamil Nadu - 641 044, India Website: http://www.aquaionexchange.com/ion-

		exchangeresin.html
9	• Kent Air Eco Corporation Limited LP	No. J - 9, Silver Oak Estate, Gamma - 2, Greater Noida, Uttar Pradesh - 201 301, India Website: http://www.kentaircorporation.com/aventura-components.html
10	• Hydrotherm Engineering Services	34, Corner Market, Millenium Business Centre, Malviya Nagar, Delhi, Delhi - 110 017, India Website: http://www.hydrothermengineeringservices.com/water-purification-materials.html
11	Aqua Chem Industries	Shed No. L - 322/16/9, G. I. D. C. Estate, Office - 126 - A, City Center, Silvassa Road, Vapi, Valsad, Gujarat - 396 195, India Website: http://www.indiamart.com/aqua-chem-industries/water-treatment-chemicals.html
12	Shri Krishna Enterprises	217, Katra Peran, Tilak Bazar, Delhi, Delhi - 110 006, India Website: http://www.indiamart.com/skechemicals/ro-chemicals.html
13	Marcuras	West- 194 B, S Block, MIDC Bhosari, Pune, Maharashtra - 411 026, India Website: http://www.reverseosmosisindia.com/water-treatment-plant.html
14	I - Con Trading Corporation	38/3, B. T. Road, Kolkata, West Bengal - 700 002, India Website: http://www.indiamart.com/icon-trading-corporation/components-of-water-treatment-plant.html
15	Noida Chemicals (A Unit Of Chemicals & Associates, New Delhi)	Suite No. 27, Ashoka Chamber Opp Rachna Cinema Pusa Road New Delhi, New Delhi, Delhi - 110 060, India Website: http://www.rasayan.in/ion-exchange-resins.html
16	Ashi Inc (A Unit Of Chemicals & Associates, New Delhi)	Chamber No. 27, 4th Floor, Ashoka Chambers, Opposite Metro Pillar No. 150, Pusa Road, New Delhi, Delhi - 110 060, India Website: http://www.radocarb.com/water-treatment-chemicals.html
17	Clear Aqua Technologies Private Limited	No. 13/6, Sri Nagar, T. V. Koil, Tiruchirapalli, Tamil Nadu - 620 005, India Website: http://www.reverseosmosis.co.in/industrial-water-plants.html
18	Unique Marketing	No. 13, Karnavati Avenue, Near Silver Complex, Opposite Baroda Express Highway, C. T. M., Ahmedabad, Gujarat - 380 008, India Website: http://www.indiamart.com/uniquemarketing-ahmedabad/ion-exchange-resin.html
19	Ion Robinson India	D - 2, Yadav Nagar, Samaypur, Badli, New Delhi, Delhi - 110 042, India Website: http://www.indiamart.com/ionrobinsonindia/water-filtration-systems.html
20	R. D. Engineering	No. 130/7, Dum Dum Road, 1st Floor, Dum Dum, Kolkata, West Bengal - 700 074, India Website: http://www.watertestinginstruments.co.in/laboratory-chemicals.html

21	Maitreya Enterprises	No. 1413, Sadashiv Peth, Shop No. 7 & 11, Avishkar Heights, Opposite Vidyarthigriha, Pune, Maharashtra - 411 030, India Website: http://www.indiamart.com/maitreyaenterprises/edm-machines-spares.html
22	Aquaion Technology, Inc.	No. 302, Nanadan Complex, Opposite Railway Crossing, Ellis Bridge, Ahmedabad, Gujarat - 380 006, India Website: http://www.indiamart.com/aquaiontechnology/water-treatment-ion-exchange-resin-chemicals-filter-media.html
23	RK Chemical Works	No. 3583, Netaji Subhash Marg, Darya Ganj, New Delhi, Delhi - 110 002, India Website: http://www.indiamart.com/rkcw/ro-chemicals.html
24	Manas Watertech Engineers Private Limited	No. 12, Kalpataru Industrial Estate, Near R Mall, Opp. Lawkim Company, Monorama Nagar, Thane West, Thane, Maharashtra - 400 607, India Website: http://www.indiamart.com/manaswatertech/ion-exchange-resin.html
25	Soft Tech Ion Exchange Engineers	No. 42/41, Parmeshwar Estate-2, Opp. Yamuna Estate Phase-1, G. I. D. C., Vatva, Ahmedabad, Gujarat - 382 445, India Website: http://www.indiamart.com/softtechion/watertreatment-plantspare.html
26	H_2O Remediation Engineering	Address: No. 12, Kalpataru Industrial Estate, Near R Mall, Opp. Lawkim Company, Monorama Nagar, Thane West, Thane, Maharashtra - 400 607, India Website: http://www.indiamart.com/manaswatertech/ion-exchange-resin.html
27	Water Ions Purification	A - 252, Pratap Vihar, Kalwar Road, Govindpura, Jaipur, Rajasthan - 302 012, India Website: http://www.indiamart.com/water-ions-purification/water-treatment-chemicals-resin.html
28	Aquatronix Engineers	C - 1, Sharad Nagar, Behind L. G. Nagar Society, Nizampura, Vadodara, Gujarat - 390 002, India Website: http://www.indiamart.com/aquatronix-engg/water-treatment-spares.html
29	Tejasvi Group	Shop No. 5, Banshidhar Complex, Ghanshayam Nagar, Main Road, Behind I. O. C. Quaters, Kalawad Road, Rajkot, Gujarat - 360 005, India Website: http://www.indiamart.com/tejasvi-group/water-treatment-plants.html
30	Aetom Engineering Technologies Private Limited	Plot No. 3039, Sector - 46, Gurgaon, Haryana - 122 002, India Website: http://www.indiamart.com/aetom-engineering-technologies/industrial-chemical.html
31	Aagam Chemicals	K-43, Bharat Nagar., Nagpur, Maharashtra - 440 033, India Website: http://www.indiamart.com/aagamchemicals/water-treatment-chemicals.html
32	Indus Chemical Private Limited	No. 357, 3rd Floor, Aggarwal Modern Bazar, C - 33, Lawrence Road, Industrial Area, New Delhi, Delhi - 110 035, India

		Website: http://www.indiamart.com/induschemicals/marine-chemicals-equipments.html
33	Esbose Water Equipment Pvt. Ltd.	5th Floor, Unit - 502, 18 - B, Ashutosh Mukherjee Road, Kolkata, West Bengal - 700 020, India Website: http://www.indiamart.com/esbosecommercial/water-softeners.html
34	Neel Operations	G - 3, A - 9, Aurangabad Co - Operative Industrial Estate, M. I. D. C., Railway Station, Aurangabad, Maharashtra - 431 005, India Website: http://www.neeloperations.co.in/water-treatment-spares.html
35	N. M. Enterprises, Ahmedabad	No. 406, Janpath Complex, Near Nehru Bridge, Ashram Road, Ahmedabad, Gujarat - 380 009, India Website: http://www.waterfiltrationplant.co.in/ion-exchange-resin.html
36	Solu Tech Water Services	Nisha Apartment, Plot No. 1, S. No. 56, Shevantiban Housing Society, Chinchwad, Pune, Maharashtra - 411 044, India Website: http://www.solutechwaters.com/consumables-products.html
37	Water Testing Services	1, G. D. Bhutta House, Opposite Panchal Steel, Near Reliance Consultancy, Mogra Road, Mumbai, Maharashtra - 400 069, India Website: http://www.indiamart.com/watertestingservices/water-treatment-chemicals.html
38	Asha Resins Private Limited	No. 1232, Bhawani Peth, Palkhi Vithoba Chowk, Pune, Maharashtra - 411 042, India Website: http://www.indiamart.com/asha-resins/ion-exchange-rasin.html
39	N Shashikant	No. 3, Indira Niwas, Peru Baug, Aarey Road, Goregaon East, Mumbai, Maharashtra - 400063, India Website: http://www.indiamart.com/n-shashikant/resin-synthetic.html
40	Numatik Engineers Private Limited	Shop No. 6, Bobby Pathak Avenue, Opposite Rotary Garden, Near Corporation Bank, Near Anand Nagar, Dahisar East, Mumbai, Maharashtra - 400 068, India Website: http://www.indiamart.com/numatikengineers/water-fuel-treatment-plant.html
41	Safe Water India	201, Kalyan Complex, 426, Mangalwar Peth Near Narpatgiri Chowk, Pune, Maharashtra - 411 011, India Website: http://www.indiamart.com/safe-water/water-treatment-equipments.html
42	Unitech Water Technologies	401, Shanti House, Opposite Madhusoodan House, Near Sardar Patel Seve Samaj, C. G. Road, Ahmedabad, Gujarat - 380 006, India Website: http://www.indiamart.com/unitech-water-technologies/ro-spares.html
43	Amjey Chemicals	: No. 402, Nanak Chambers, Opposite Fun Republic, Off New Link Road, Andheri West, Mumbai, Maharashtra - 400 069, India

		Website: http://www.amjeychemicals.com/
44	A To Z Chemicals	No. 8/1, Lal Bazar Street, Mezzanine Floor, Room No. 10, Kolkata, West Bengal - 700 001, India Website: http://www.indiamart.com/atoz-chemicals/industrial-resin.html
45	Enviro-Chem Analyzers & Consultants	B/106, Shiv Shakti Complex, S. V. Road, Dahisar East, Mumbai, Maharashtra - 400 068, India Website: http://www.indiamart.com/envirochemanalyzers/products-information.html
46	Aqualia Water Technologies	Plot No. 101, Naga Gher, Ranipokhari, Dehradun, Uttarakhand, India Website: http://www.indiamart.com/company/4743998/
47	Aquamatix Incorporation	No. 38, 12th KM, Opposite J. C. Industrial Layout, Kanakapura Road, Bengaluru, Karnataka - 560 062, India Website: http://www.indiamart.com/aquamatix-incorporation/
48	Chemtech	C-103, Maruti Industrial Estate, Phase-1, GIDC Vatva, Ahmedabad, Gujarat - 382 445, India Website: http://www.indiamart.com/chemtech-ahmedabad/
49	Hira Engineering	No. 19, Jai Ambe Cooperative Housing Society, Majaswadi, Near Raheja Brookheavan Building, Jogeshwari- Vikhroli Link Road, Jogeshwari, Mumbai, Maharashtra - 400 060, India Website: http://www.indiamart.com/company/4297127/
50	Prime Water Systems	Street -1071, Sai Saroja Nilayam, Sanathnagar, Hyderabad, Andhra Pradesh - 500 018, India Website: http://www.indiamart.com/prime-water-systems/
51	Uniway Engineers Private Limited	29, 48th Street, 9th Avenue, Ashok Nagar, Chennai, Tamil Nadu - 600083, India Website: http://www.indiamart.com/company/4103601/

CONCLUSION

For taste masking & formulation of oro-dispersible tablets; ion exchange resins are best suited in comparison to other methods of taste masking as well as this method is also economical. Various examples prove that ion exchange resins play an important role in taste masking as well as to decrease the disintegration time which is useful for oro-dispersible tablets. The study also showed that the drug to resin ratio in the range of 1:1 to 1:5 can easily mask the taste of bitter drugs and indions are generally used for taste masking.

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