ejpmr, 2017,4(9), 551-558

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

NOVEL METHOD OF TASTE MASKING FOR ORO DISPERSIBLE TABLETS FOR AN EXTREMELY BITTER DRUG

[1]*Anupama Diwan, [1]Aparna Tomar, [1]Rupali Kalra and [1]Ajit Jha

[1]School of Pharmaceutical Sciences, Apeejay Stya University, Sohna Palwal Road, Gurgaon-122001.

***Corresponding Author: Prof. Dr. Anupama Diwan**

School of Pharmaceutical Sciences, Apeejay Stya University, Sohna Palwal Road, Gurgaon-122001.

Article Received on 26/07/2017 **Article Revised on 06/07/2017** **Article Accepted on 16/08/2017**

ABSTRACT

The aim of the present study was to formulate orodispersible tablets (ODT) using resins. For masking the bitter taste of drugs, various resins are used like Indion 204, Indion 214, Kyron T 114, Kyron T 134 etc. We have selected Kyron T-114 (ion exchange resin) to mask the bitter taste and formulate an orodispersible tablets using drug resin complex. The prepared tablets were evaluated for the drug content, weight variation, water absorption ratio, wetting time, in vitro disintegration, hardness, friability, thickness uniformity and *in vitro* dissolution. The results revealed that Kyron T314 showed least disintegration time compare other disintegrant. This research work suggests simple and cost effective method of formulation of ODT with an objective of masking the bitter taste of a model drug API.

KEYWORDS: Orodispersible Tablets ODT, Kyron T114, Direct Compression, Resins.

INTRODUCTION

The oral route remains the preferred route for administration of therapeutic agents because of accurate dosage, low cost therapy, self medication, non invasive method and ease of administration leading to high level of patient compliance. Moreover, patients traveling with little or no access to water, limit utility of orally administered conventional tablets or capsules. Therefore, to cater the needs of such patients, recent advancements in technology have resulted in development of viable dosage alternatives popularly known as orally disintegrating tablets (ODTs). Drug delivery using orally disintegrating tablets is rapidly gaining importance since tablets either disintegrate or dissolve in the mouth rapidly, without requiring water to aid in swallowing. This novel dosage form is suitable for all age groups, particularly children, elderly and patient who are ill and have difficulty in swallowing conventional tablets and capsules.[1], [2]

At certain pH, Kyron forms a stable complex with active drug and makes a tasteless complex. The complex is susceptible to break in acidic pH i.e. less than pH 4 and drug gets absorbed in the system, thus bioavailability remains as such. The taste masked complex can be used for oral dosage forms like dispersible/mouth dissolving/chewable tablets, suspension, dry syrup etc.

Taste masking is defined as perceived reduction of an undesirable taste that would exist. The ideal solution to reduce or inhibit bitterness is the discovery of a universal inhibitor of all bitter tasting substances that does not affect the other taste modalities such as sweetness or saltiness. Informal taste tests with different flavours have shown that age is also significant in taste preference. Younger people likes flavour like tutti - fruity and chocolate. Older generations typically prefer more traditional flavours, such as orange or mint.

Unpleasant taste mainly bitterness had lead to dilemma for modern pharmaceutical science. This undesirable taste diminishes the acceptance and usefulness of many beneficial, safe and efficacious drugs. Thus elimination or reduction of bitterness is an important mainstay of product evaluation in oral pharmaceutical formulation.

Ion Exchange Resins[3]

Ion exchange resins (IER) have received considerable attention from pharmaceutical scientists because of their versatile properties as drug delivery vehicles. In past few years, IER have been extensively studied in the development of Novel drug delivery system and other biomedical applications. Several ion exchange resin products for oral and peroral administration have been developed for immediate release and sustained release purposes. Bitter taste drugs can be absorbed onto ion exchange resins, thus effectively removing them from solution during the transit through the mouth; at salivary pH 6.8, remains in intact form making the drug unavailable for the taste sensation. Various studies have revealed that ion exchange resins are equally suitable for drug delivery technology.

Ion exchange resins are water-insoluble cross-linked polymers containing a salt-forming group at repeating positions on the polymer chain. Synthetic Ion exchange resins are usually cast as porous beads with considerable external and internal pore surfaces for loading. The resins are typically spherical in shape and 0.5 to 1.0 mm in diameter. The structure of these Ion exchange resins is quite porous at a molecular scale to achieve the drug loading. They have the ability to exchange counter-ions within aqueous solutions surrounding them.

Drugs are loaded onto the resins via an exchange reaction, forming drug-resin complexes called resinates. Insoluble resinates are formed through weak ionic bonding with oppositely charged drugs so that release of a drug from a resinates does not occur at salivary pH (~ 6.7).7-9 The resins are not absorbed by the body due to their high molecular weight and water insolubility and are therefore inert; making them ideal drug delivery vehicles.

Classifications of Ion Exchange Resins

- **Classification based on functional groups**

Strongly acidic, Strongly basic, Weakly acidic, Weakly basic.

- **Classification based on Interactive Ion**

Cation Exchange resins, Anion Exchange Resins.

Betterment in formulation with Ion Exchange Resins (IER)

Ion exchange resins are used for a variety of applications in the pharmaceutical industry, such as;

- **Taste-masking**: Ion Exchange Resins are helpful in masking the bitter taste of a drug by forming a bond between polymer and drug, which later on dissociates in the intestine.

- **Disintegrant /Superdisintegrant**: IER can act as a disintegrant due to its high ability for hydration and swelling. The mechanism of disintegration appears to be governed by wicking and swelling actions, similar to its counterpart. This resin is exclusively suggested as a potential disintegrant for tablet formulations of basic drugs to avoid the ionic binding of the resin and drug that may deplete drug release

- **Solubility improvement:** The drug resinates may certainly provide an attractive approach for solubility enhancement of even very weakly acidic as well as basic, but ionisable poorly soluble drug molecules with low (preferably <1500) molecular weight; with appropriate consideration to ion exchange capacity of the resin, hydrophobicity/ hydrophilicity of the drug molecules, pKa of the drug and resin and concentration of competing ions during equilibration process.

- **Drug stabilization:** Vitamin B12 is an example of a molecule which can deteriorate on storage.

- **Improved flow rates:** Flow rate of a drug can be enhanced by the use of Ion Exchange Resins.

- **Modified-/Sustained-release profiles:** Diltiazem HCl, Pseudoephidephrine HCl are the examples that have been prepared using ion exchange resins.

Some Examples of Ion exchange resins suitable in ODT: Some ion exchange resins used widely for taste masking in ODT purpose in industries are:

- Indion 204 (weak acid Cation exchange resin)
- Indion 214
- Indion 234
- Kyron T-114
- Kyron T-104

Kyron T114 is derived from cross linked polymers of Acrylic acid. They are a high purity pharmaceutical grade weak acid cation exchange resin supplied as a dry powder in hydrogen form. It is suitable for use in pharmaceutical applications for tablet disintegration and taste masking of bitter drugs. Kyron T114 is based on cross linked polymethacrylic acid with divinyl benzene. Kyron derivatives are manufactured in a FDA approved manufacturing facility.

Appearance – White to off white free flowing powder
Matrix – Cross linked polymethacyrlic acid with divinyl benzene
Functional group – Carboxylic acid
Ionic form as supplied – Hydrogen
Solubility - Insoluble in water and in common solvents
Storage – Hygroscopic in nature. It is therefore essential to store it in a tightly packed container to prevent absorption of atmospheric moisture.

If moisture is absorbed, can be dried at 90ºC to 100ºC for approximately to reduce the moisture content below 10%.[11]

Application

Kyron derivatives are used in drug disintegration and taste masking of the bitter drug, a drug polymer complex can be synthesized due to the bonding between the bitter drug and the polymer thus masking the objectionable bitter taste of drug. It can be used in various formulations like suspensions, dry syrups and Orodispersible tablets. Since the polymer drug complex so formed is tasteless in the mouth but it dissociates in the acidic pH of the stomach, the bioavailability of the drug is not affected.

Kyron T114 has proved to be an effective taste masking agent for the following drugs:

- Levocetrizine dihydrochloride
- Metronidazole

Kyron T104 has proved to be effective in taste masking of

- Cefixime
- Lornoxicam
- Antipsychotic drugs

The present study was conducted with an objective to mask the bitter taste of model drug by using ion exchange resins and optimization of ratio of drug and resin suitable for formulation of oro dispersible tablets. Evaluation parameters also revealed the masking of bitter taste and development of oro dispersible tablets.

MATERIAL AND METHODS

Development of ODT by using resins

Preparation of Drug- resin complex

Bitter taste of drug was masked by using ion exchange resin complex. The drug and Kyron T-114 was taken at various drug to polymer ratio 1:1, 1:2, 1:3 and 1:4. Kyron T-114 was initially mixed in 100 ml distilled water and stirred for 30 minutes with mechanical stirrer. The model drug was added slowly in to resin mixture and stirred for 4 to 5 hours at 200rpm. The resinate obtained was separated by filtration using Whatman filter paper and dried overnight at room temperature.[6]

The drug polymer complex was then evaluated for some parameters to proceed further:

1) Bitterness level: The bitter taste threshold value of complex was determined based on the bitter taste recognized by six volunteers (females). A series of complex aqueous solutions were prepared at different concentrations as standard solutions, i.e. 1, 2, 3, 4, 5, 6, 7, 8 µg/ml respectively. From standard solution 1 ml of each was placed on the center of the tongue, it was retained in the mouth for 15 seconds and then the mouth was thoroughly rinsed with distilled water. The threshold value was correspondingly selected from the different Drotaverine HCl concentrations as the lowest concentration that had a bitter taste.

2) Drug Loading: Drug complex equivalent to 10 mg complex was placed into a 10 ml volumetric flask containing10 mL of 0.1 N HCl. The mixture was immediately sonicated for 15 minutes and then filtered. Then solution was analysed in a spectrophotometer at λ max 252 nm to determine the drug concentration in 0.1 N HCl and drug loading was determined by using standard curve equation.

3) Amount of drug in media: Drug complex equivalent to 10 mg complex was placed into a 10 ml volumetric flask containing10 mL of phosphate Buffer pH 6.8. The mixture was sonicated for 15 minutes and then filtered. Then solution was analysed in a spectrophotometer at λmax 252 nm to determine the drug concentration in simulated salivary fluid and compared with bitterness score.

Table I: Evaluation of Complex.

Drug-resin ratio	Bitterness level	Drug loading	Amount of drug in media
1:1	2	62.85	3.55
1:2	1	72.3	4.72
1:3	0	80.92	3.08
1:4	0	86.04	5.72

Batch of 1:3 and 1:4 masked the bitter taste of the drug.

Flow properties of Drug-Resin complex

1. Bulk Density: It refers to packaging of particles. Bulk density is used to determine the amount of drug that occupies the volume in g/mL. Weighed quantity of complex was transferred into 100 ml measuring cylinder without tapping during transfer. The volume occupied by the drug was measured. Bulk density was measured by formula,

ρi = m/Vi,

where, m= mass of blend

Vi= untapped volume

2. Tapped Density: When quantity of drug was taken into a graduated cylinder, volume occupied by the drug was noted down. Then the cylinder was subjected to 500, 750 and 1250 taps in tap density apparatus. According to USP, the blend was subjected to 500 taps. Percent volume was calculated and subjected for additional 750 taps. % variation is calculated:

ρt = m/Vt,

where, Vt= tapped volume

3. Carr's Index (Compressibility): The compressibility index and Hausner ratio are measures of the property of the powder to be compressed. The packaging ability of drug was evaluated from change in volume, which is due to rearrangement of packaging occurring during tapping. It was indicated as Carr's compressibility index and was calculated as follows:

Carr's Index = [(Tapped density- Bulk density)/ Tapped density] X 100

4. Hausner Ratio: It is measurement of frictional resistance of the drug. The ideal range should be 1.2-1.5 It was determined by the ratio of tapped density and bulk density.

Hausner Ratio = Tapped density/ Bulk density.

Table II: Relation between flow property with Hausner ratio and Compressibility index.

Compressibility index	Flow Character	Hausner's Ratio
<10	Excellent	1.00-1.11
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-31	Poor	1.35-1.45
32-37	Very poor	1.46-1.59
>38	Very very poor	>1.60

5. Angle of Repose: The angle of repose is used to characterize the flow properties of solids. Angle of repose is a characteristic related to inter particulate friction or resistance to movement between particles. This is the maximum angle possible between surface of pile of powder or granules and the horizontal plane.

$\tan \theta = h/r$

$\theta = \tan^{-1} h/r$

where, θ = angle of repose, h= height & r= radius.

Table III: Flow Properties of Drug –Resin complex.

Parameters	1:3	1:4
Bulk density	0.497±0.004	0.457±0.021
Tapped density	0.583±0.004	0.513±0.029
Carr's Index	13.31±0.25	12.25±0.067
Hausner's Ratio	1.112±0.003	1.103±0.006
Angle of repose	29.926±0.86º	27.45±0.067º

Formulation of ODT with Drug Resin Complex[17],[18]

Various technologies can be used to manufacture orodispersible tablets, which are classified as below:

Table IV: Technologies for formulation of ODT.

Technologies	
Conventional Technologies	**Patented Technologies**
1. Melt Granulation 2. Effervescent Method 3. Cotton Candy Process 4. Direct Compression 5. Tablet Moulding 6. Sublimation 7. Phase Transition 8. Freeze Drying 9. Mass Extrusion 10. Spray Drying 11. Fast Dissolving Films 12. Nanonization	1. Zydis Technology 2. Durasolv Technology 3. Dispersible tablet Technology 4. Orasolv Technology 5. Wow Tab Technology 6. Ora Quick Technology 7. Flash Tab Technology 8. Quick dis Technology 9. Frosta Technology 10. Pharmaburst Technology

Among the above methods, Direct Compression Method was suitable for the formulation that we have selected.

Direct Compression Method

1. Weighing: All the ingredients were weighed separately on a butter paper.

2. Sifting: All the ingredients and drug polymer complex were passed through #40 mesh sieve.

3. Dry Mixing: The drug-polymer complex was mixed with the rest of the ingredients and mixed properly.

4. Lubrication: Magnesium Stearate was then passed from #200 mesh sieve. It was then transferred to above mixture and mixed for 5 minutes.

5. Compression: Lubricated blend was then compressed at 16-station compression machine with 10X9.0 mm sc. Punch to obtain an average weight of 286 mg and hardness of 3-5 Kp.

Strategies for development of ODTs

From the assay of drug- polymer complex, it was found that

50mg of drug polymer complex = 10 mg of model drug

Table V: Formula Composition of Orodispersible tablet.

Sr no.	Ingredients	Batch I	Batch II	Batch III	Batch IV	Batch V	Batch VI
1	Drug-polymer complex(mg)	150	150	200	200	200	200
2	D- Mannitol(mg)	60	60	60	60	60	60
3	Microcrystalline Cellulose(mg)	40	40	40	40	40	40
4	Cross carmellose Sodium(mg)	40	40	40	40	40	40
5	Citric Acid(mg)	10	5	10	7.5	5	3
6	Aspartame(mg)	10	10	10	10	10	10
7	BMDM KS-197(mg)	5	5	5	5	5	5
8	Sucrose(mg)	15	20	15	15	20	20
9	Magnesium Stearate(mg)	4.2	4.2	4.2	4.2	5	5
10	Aerosil (mg)	2.2	2.2	2.2	2.2	3	3

Batch I & II were of ratio 1:3 and Batch III, IV V and VI were of 1:4.

These batches were further evaluated for bitterness and disintegration time for selection of appropriate batch.

Table VI: Evaluation of different batches.

Batch	Bitterness level	Disintegration time	Wetting time
I	2	15 sec	15 sec
II	2	15 sec	14 sec
III	1	18 sec	16 sec
IV	1	16 sec	10 sec
V	0	16 sec	10 sec
VI	**0**	**14 sec**	**8 sec**

Batch VI was finalized for further as it successfully masked the bitter taste of the drug and disintegrates in less time.

Evaluation of Orodispersible Tablets[19]

HARDNESS

Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under the condition of storage transformation and handling before usage depends on its hardness. Hardness of the tablet of each formulation was determined using Monsanto Hardness tester. The hardness of MDTs is generally kept lower than conventional tablets as increased hardness delays the disintegration of the tablet. The force is measured in kg and the hardness of about 3-5 kg/cm2 is considered to be satisfactory for uncoated tablets.[20]

FRIABILITY

Friability is the loss of weight of tablet in the container due to removal of fine particles from the surface.

Friability test is carried out to access the ability of the tablet to withstand abrasion in packaging, handling and transport. Roche friabilator is employed for finding the friability of the tablets. Friabilator consist of a plastic chamber that revolves at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. Pre-weighed sample of tablets was placed in the friabilator and were subjected to 100 revolutions. Tablets were de-dusted utilizing a soft muslin cloth and reweighed, the loss in the weight of tablet is the measure of friability and is expressed in percentage as,[21]

% Friability =loss in weight/ initial weight ×100

WEIGHT VARIATION

USP weight variation test is done by weighing 20 tablets individually; calculating the average weight and comparing the individual tablet weight to the average weight variation tolerance.

Table VII: Weight variation specifications as per IP/BP and USP[22]

Monograph	Average Weight	Deviation (%)
IP/BP	<80 mg	10
	Between 80 and 250 mg	7.5
	>250 mg	5
USP	<130 mg	10
	Between 130 and 325mg	7.5
	>325 mg	5

CONTENT UNIFORMITY

The test for uniformity of content is based on the assay of the individual content of drug substance(s) in a number of individual dosage units to determine whether the individual content is within the limit. The test for content uniformity is required for tablets containing <25mg or <25% of one tablet. The content of active ingredient is determined in each of 10 dosage units taken at random using method described in assay. The

preparation complies with the test if individual content is 85-115% of average content.[22]

THICKNESS

The thickness and diameter of the tablets was determined using a Micrometer screw gauge. Five tablets from each type of formulation were used and average values were calculated. It is expressed in mm.[23]

WATER ABSORPTION RATIO

A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper and the time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio (R), was determined using following equation,[24]

$R=10\times Wa/Wb$

where, Wb is weight of tablet before water absorption and Wa is weight of tablet after water absorption

STABILITY STUDY

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light and enables recommended storage conditions, re-test periods and shelf lives to be established. ICH specifies the length of study and storage conditions. Optimized batch was stored at appropriate ICH guidelines for 6 months and all parameters were evaluated accordingly at specific time intervals.

RESULTS

Oro dispersible tablets were formulated for a bitter taste model drug with ion exchange resin complex. As discussed in material and methods, different batches were prepared according to different ratio of drug: resins. Batch VI of ODT was optimized as best with ratio of 1:4 (Drug: resin) with minimal level of bitterness 0 and less disintegration time. So batch VI was further evaluated for different evaluation parameters for tablets. Results of different evaluation parameters done with ODT is shown in table VIII.

Table VIII: Physicochemical Properties of Batch VI.

Physicochemical parameters	Results
Hardness (kg/cm^2)	3.433±0.057
Friability (%)	0.73±0.01
Thickness (mm)	2.13±0.055
Weight Variation	0.903±0.01
Wetting time (sec)	8.66±0.577
Dispersion time (sec)	15.33±0.577

[*Mean±SD (n=3)].

***In vitro* disintegration study**

In vitro disintegration time was measured using USP disintegration test apparatus. Randomly six tablets were selected from each batch for disintegration test. Tablet was placed to 10 ml 0.1 N HCl solutions, at 37±2°C. Time required for complete dispersion of a tablet was measured. Also in vitro dispersion time was measured by dropping a tablet into 10 ml phosphate buffer pH6.8 in a beaker at 37±0.5°C. Time required for complete dispersion of a tablet was measured.[25]

***In vitro* dissolution study**

Standard USP dissolution apparatus USPII (Paddle) was used to study in vitro release profile using rotating paddle. The dissolution test was carried out using 900 ml of 0.1 N HCl, at 37±0.5°C and 50 rpm. A sample of the solution was withdrawn from the dissolution apparatus at 0, 5, 10, 15, 20, 25, 30 minutes and withdrawn volume was replaced with fresh dissolution media. Samples were suitably diluted and analysed spectrophotometrically.[26]

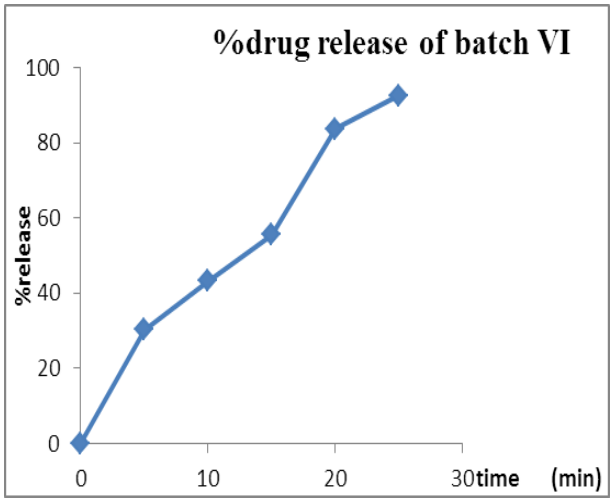

Fig 1: Dissolution study of most optimized batch.

Stability Studies

The ODTs of the model drug of selected best formulation were stored at 40°C/75%RH in closed tight containers with the child resistant closures for 6 weeks. Tablets were analyzed at specific time intervals (0,2, 4 and 6 weeks) for physical appearance and in vitro dissolution studies. No change in physical observation was observed even after 6 weeks. While performing in-vitro dissolution studies, no significant change in the release profile of the formulation was observed even after 6 weeks indicating the stability of the formulation.

Table IX: Evaluation of optimized batch subjected to stability studies.

Parameter	Initial	2nd week	4th week	6th week
Appearance	Yellow	No change	No change	No change
Hardness (kg/cm^2)	3.433	3.21	3.18	3.15
Friability (%)	0.73	0.71	0.69	0.68
Thickness (mm)	2.13	2.10	2.06	2.03
Weight Variation	0.903	0.912	0.926	0.925
Wetting time (sec)	8.66	8.78	8.96	8.94
Dispersion time (sec)	15.33	15.29	15.23	15.13
Drug content (%)	98.25	96.98	95.25	95.15

DISCUSSION

ODT of model drug was prepared by using direct compression method and drug polymer complex was prepared by Solvent Evaporation method. Bitter taste of drug was masked by coating the drug with the polymer (Kyron T 114) which was found to be acceptable. Batch with the drug polymer complex of the ratio 1:4 found to be suitable to achieve the objective of my study. Finally the ODTs was successfully evaluated for bulk density, tapped density, Hausner ratio, angle of repose, hardness, thickness, friability, drug content, disintegration, wetting time, dispersion time and stability parameters.

CONCLUSION

It was concluded that from various polymers, Kyron T 114 was best, this polymer coat the drug and bitterness is not be felt. We are able to achieve our objective of masking the bitter taste of model drug by simple method of direct compression. Kyron T114 is the ion exchange resin which can be used for the formulation of Orodispersible tablet and it also help in masking the bitter taste of the bitter drugs.

REFERENCES

1. G J Mahore, J K Wadher, Ion exchange resins: Pharmaceutical applications and recent advancement, International Journal of Pharmaceutical Sciences Review and Research, 2010; 1(2): 8-13.
2. L. Lachman, H. A. Lieberman, J. L. Kanig, The Theory and Practise of Industrial Pharmacy. Bombay: Varghese publication house; 1987; 293-345.
3. http://ionresins.com/application-pharmaceutical.html.
4. Garg A and Gupta MM. Taste masking and formulation developement & evaluation of mouth dissolving tablets of levocetrizine dihydrochloride. J. of Drug Delivery & Therapeutics, 2013; 123-130.
5. Sisodiya N, Rathore GS, Sisodiya DS and Avinash N. ORO Dispersible Tablets: A Review. Int. J. Pharm. Natural. Med. 2013; 1(1): 102-106.
6. Lang P M Preparation and use of ion exchange resin loaded with quinolone carboxylic acid derivatives. U.S. Pat. No.5, 152,986 to Bayer Aktiengesellschaft; 1992.
7. Humbert-Droz, P., M. Seidel, and R. Martani, Fast disintegrating oral dosage form. 1997, WO 1997038679 A2.
8. Stoltenberg, I. and J. Breitkreutz, Orally disintegrating mini-tablets (ODMTs)--a novel solid oral dosage form for paediatric use. European Journal of Pharmaceutics and Biopharmaceutics, 2011; 78(3): 462-9.
9. Prabhu NB, Rao L, Amin PD. Studies on taste masking of drotaverine hydrochloride and its formulation. Indian Drugs, 2007; 44(11): 848-51.
10. Madgulkar AR, Bhalekar MR, Joshi VS, Wable N. Comparative study of efficacy of Indiaon 414 and Amberlite IRP 88 as superdisintegrants in mouth dissolves tablets. Indian Drugs, 2007; 44(6): 455-57.
11. http://www.corelpharmachem.com/kyron.htm.
12. D.Spiro Alexandratos, Ion-Exchange Resins: A Retrospective from Industrial and Engineering Chemistry Research, Ind. Eng. Chem. Res., 2009; 48(1): 388-398.
13. https://en.wikipedia.org/wiki/Ion-exchange_resin.
14. Irwin W, Mchale R, Watts P. Drug delivery by ion exchange. Part VII: Releases of acidic drugs from anionic exchange resinate complexes. Drug Dev Ind Pharm. 1990; 16: 883–98.
15. Shukla D, Chakraborty S, Singh S, Mishra B. Fabrication and evaluation of taste masked resinate of risperidone and its orally disintegrating tablets. Chem Pharm Bull. 2009; 57: 337–45.
16. Zeng HX, Wang M, Jia F, Lin SJ, Cheng G, Pan WS. Preparation and in vitro release of dual-drug resinate complexes containing codeine and chlorpheniramine. Drug Dev Ind Pharm, 2011; 37: 201-207.
17. Alam MD, Nayyar P, Kumar SP. Novel technology for formulation and evaluation of mouth dissolving tablet - A review; Adv Biol Res., 2014; 8(5): 180-6.
18. Vummaneni V, Chawla L: Mouth Dissolving Tablets- A Review; Am. J. Pharm Tech Res; 2012; 2(3): 28-45.
19. Bagul U, Gujar K, Patel N, Aphale S, Dhat S: Formulation and Evaluation of Mouth dissolving Tablets of Levocetirizine Dihydrochloride. Int J of Pharm Sci, 2010; 2(2): 76-80.
20. Pooja A, Arora SV. Orodispersible tablets: A comprehensive review. Int J Res Dev Pharm Life Sci., 2013; 2(2): 270-84.
21. Puneet M, Kumar SP, Rishabha M. A review on recent advances of oral mouth dissolving tablet. J Drug Discov Ther., 2014; 2(18): 17-22.
22. Kumar SS, Ravendra V, Vikash C, Prakash SS. Orally disintegrating tablets: A dosage form that

extends the market exclusivity and patent protection. World J Pharm Pharm Sci., 2014; 3(7): 526-46.
23. Deepika J, Mishra A. A review - Formulation and development of orodispersible tablet. Int J Pharm Erudition, 2014; 4(1): 21-38.
24. Bandari S, Mittapalli RK, Gannu R, Rao YM. Orodispersible tablets: An overview. Asian J of Pham. 2008; 2: 2–11.
25. Alam MD, Nayyar P, Kumar SP. Novel technology for formulation and evaluation of mouth dissolving tablet - A review. Adv Biol Res., 2014; 8(5): 185-6.
26. Narazaki R, Harada T, Takami N, Kato Y, Ohwaki T. A new method for disintegration studies of rapid disintegrating tablet. Chem Pharm Bull (Tokyo), 2004; 52: 704–7.
27. Shirsand S B, Para M S, et.al., NOVEL CO-PROCESSED SUPERDISINTEGRANTS IN THE DESIGN OF FAST DISSOLVING TABLETS, International Journal of Pharm Tech Research, Res., 2010; 2(1): 222- 227.