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RESEARCH ARTICLE

Development of mouth dissolving tablet containing microencapsulated drug for taste masking by green synthesis

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ABSTRACT

The purpose of this study was to prepare formulation by masking the intensely bitter drug. Patient noncompliance i.e. pediatric, geriatric population are most sensitive to bad taste of medicament due to feeling bitted which may not necessary be wise, one of the key causes failure of oral dosage regimen (swallowing) Its reasoned taste masking carried out using technology depending on the type drug & dosage form but stability is major challenging task. Thus, the common method used to mask the unpleasant sensation is microencapsulation. This technology provides physical barrier between drug molecule & taste buds. Polymer can be used coating material, alone or in combination to produce a larger coat, depending on the drug bitterness. Eudragit e100 is a pH sensitive (<5) & have been popularly used for coating bitter medicament to achieve taste masking with perfection. Solubility of polymer in solvent (like organic solvent) & rate of solvent removal get cost range is very high. So that reduces this problem use green synthesis method, which are inexpensive, safe, eco-friendly & increase patient compliance & regulatory compliance. Development of mouth dissolving tablets contain microencapsulated drug are easy to swallow, no grittiness & with good mouth feel, cost effective, easy taken, major ideally for pediatric & geriatric patient & Bioavailability enhanced by taste masking technology compatible with MDTb formulation.

Keywords: Olopatadine hydrochloride, Eudragit 100, Taste masking, Microencapsulation, Mouth dissolving tablets (MDTb).

1. INTRODUCTION

Taste masking is defined as a perceived reduction of an undesirable taste that would exist. More than 50% of pharmaceutical products are administered orally, undesirable taste or "Dysphagia" is one of the important formulation problems that can be encountered with certain drugs. Oral administration of bitter

drugs with acceptable level of palatability is a key issue for health care providers especially with paediatrics and geriatric patient [1-2]. For this reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have fascinated an immense deal of consideration. A quick-dissolving tablet also known as a fast-dissolving, fast-dissolving multiparticulate, rapid-dissolving, mouth-dissolving, fast-melting, or orodispersing tablets, is an oral tablet that does not require water for swallowing. These types of tablet dissolve within 60 seconds when placed in the mouth. Thus, to eliminate or reduce bitter taste of orally administered pharmaceuticals various techniques and strategies like sensory approaches, complexation and adsorption, chemical approaches and barrier approaches. Microencapsulation is a process of applying relatively thin coating to small particles of solid, droplets of liquid and dispersion. This technology provides physical barrier between drug molecule & taste buds. Development of mouth dissolving tablets contain microencapsulated drug are easy to be swallowing, no grittiness & with good mouth feel, cost effective, easy taken, major ideally for paediatric, geriatric patient [3-4]. The green synthesis method is inexpensive & convenient for large area, efficient method for producing microencapsulated particles with specified properties. Their principle based on the concept of green chemistry/ green formulation (without use organic solvent & toxic chemicals) to produce eco- friendly, safe, inexpensive [5].

Table 1. Prepare Eudragit Particles with different Concentration

S. NO.	Conc.		Eudragit e100 (Polymer)	No. of particles
	HCl (0.1N)	NaOH (0.1N)		
1	10 ml	15 ml	100 mg	+
2	20 mg	25 ml	200 mg	++
3	30 ml	35 ml	300 mg	+++
4	40 ml	45 ml	400 mg	++++

Table 2. Optimization of stirring time and drug polymer ratio

Batch	Drug : polymer ratio	Swelling Time (Min)	Stirring Time (Min)	Taste	% Drug entrapment
F1	1:10	30	30	+++	34.2%
F2	1:20	30	60	+++	45.7%

Table 3. Solubility profile of drug in various solvent

S.No.	Solvent	Solubility	Inference
1.	Distilled water	+++	Sparingly soluble
2.	Methanol	++++	Freely soluble
3.	HCl (0.1N)	----	Insoluble
4.	NaOH (0.1N)	----	Insoluble
5.	Buffer solution (7.4)	+++	Soluble

Table 4. Melting point

Material	Specification	Observation
Oloptadine	242-245°C	245-250°C

Table 5. Standard Calibration Curve

S.No.	Conc.	Absorption
1	20 µg/ml	0.140
2	25 µg/ml	0.171
3	30 µg/ml	0.210
4	35 µg/ml	0.249
5	40 µg/ml	0.271

Table 6. Interpretation (Drug)

S.No.	Functional group	Peak	Type of vibration	Intensity
1	C-H (Aromatic)	3014.74	Stretch	Medium
2	C-O	1006.84	Stretch	Weak
3	C=O	1716.65	Stretch	Strong
4	O-H	2868.15	Stretch	Strong and broad
5	C-C(Aromatic)	1600.92	Stretch	Medium - weak

Table 7. Interpretation (Formulation)

S.No.	Functional group	Peak	Type of vibration	Intensity
1	O-H	2872.01	Stretch	Strong
2	C-N	1151.50	Stretch	Medium
3	N-O	1566.2	Stretch	Strong
4	C-O	1018.41	Stretch	Medium
5	C=O	1728.22	Stretch	Strong
6	C-H	3273.2	Stretch	Strong

In the present work, the method used for masking the taste is barrier approaches i.e. by microencapsulation, involving "Green synthesis" a new idea for replacing the use of organic solvents.

2. MATERIALS AND METHOD

2.1. Solubility studies in acidic, neutral and basic medium

The solubility of oloptadine drug was determined in different solvent at room temperature. The solubility of drug was determined based on approximate volume of solvent required by one part of drug [4, 7]. The inference noted after observation are represented in Table (3). All these results are made based on standard given in Indian Pharmacopoeia.

2.2. Formulation of microencapsulated particles

A microencapsulated drug polymer particle (Olopatadine+Eudragit 100) was prepared by microencapsulation method [2]. Formulation of drug polymer microencapsulation was done by the batch process; 100 mg of polymer

Table 8. Interpretation (Polymer)

S. NO.	Functional group	Peak	Type of vibration	Intensity
1	C-H(alkene)	2872.01	Stretch	Strong
2	C-H(alkyne)	3273.2	Stretch	Strong
3	C-O	1271.09	Stretch	Strong
4	C-N	1151	Stretch	Medium-weak
5	C=O	1728.22	Stretch	Strong

Table 9. Particle size range

S.No.	Particle	Size range
1	2d	300
2	3d	250
3	4d	500
4	5d	200
5	6d	350
6	7d	350
7	8d	200
8	9d	100
9	10 d	350
10	11d	300

Avg size of particle = 300µm

Table 10. Observations of Taste evaluation test

S.No.	Tasteless	Slightly bitter	Bitter	Very bitter
1	✓	-	-	-
2	✓	-	-	-
3	✓	-	-	-
4	✓	-	-	-
5	✓	-	-	-
6	✓	-	-	-
7	✓	-	-	-
8	✓	-	-	-
9	✓	-	-	-
10	✓	-	-	-

(eudragit 100) was placed in a beaker containing 10 mL of HCl and allowed to swell for a definite period. Accurately weighed amount of Olptadine (as per 1: 10 and 1: 20 drug polymer ratio) was added and stirred for desired period of time. The mixture was filtered and residue was washed with deionized water. Filtrate was analyzed by U.V. spectrophotometer at 301 nm for the unbound drug and percentage drug was calculated [8].

2.3. Characterization of Microparticles

2.3.1. Particle size analysis and Morphology

The particle size was determined using Light Microscopy .The surface morphology of the pure Olptadine crystals and coated Olptadine granules was also examined. The samples were attached to aluminium stubs with double side adhesive carbon tape then gold coated with a sputter coater and examined sing a scanning electron microscope (Jeol 5200, scanning electron microscopy - SEM)[9].

Table 11. Observations of studies performed

S. No.	Parameters	Result
1	% drug entrapment	34.2% & 45.7%
2	% yield	72.72%
3	% drug content	4.28%

Table 12. Observations of Preformulation studies

S.No.	Parameter	Result
1	Bulk density	0.5±0.017 g/ml
2	Tapped density	0.57±0.015 g/ml
3	Carrs index	18.02
4	Hausner ratio	1.4
5	Angle of repose	29.05±1.11

Table 13. Formula for Mouth Dissolving Tablet (MDTb)

S.No.	Ingredients	F1(optimized formulation)
1	Sodium starch glycolate	7.2mg
2	Magnesium stearate	2.16mg
3	Talc	1.24mg
4	Mannitol	84mg
5	Drug polymer complex	30mg
Total weight		**124mg**

Table 14. Result for Post Compression Parameter

S.No.	Parameters	Results
1	Friability (%)	1.05
2	Hardness(kg/cm)	3
3	Thickness (mm)	2±4
4	Weight variation	106.3± 1.4
5	Disintegration time	31 secs

2.3.2. Entrapment efficiency

The percentage of drug incorporated was determined by research centrifuge of the drug loaded oloptadine at 800 rpm for 10 min and the supernatant was separated. The pellet obtained was washed twice with water and dissolved in methanol followed by estimation of the drug in UV spectrophotometer at 301nm [10-11].

2.3.3. Bitter taste masking of micro particles

Taste evaluation the optimum drug polymer complexes were subjected to taste evaluation. Taste evaluation was performed by testing the samples on 20 male volunteers in the age group 22–28 years [12-14]. Each volunteer held encapsulated microparticles equivalent to 25 mg in the mouth for 15 s and then spit out. The scale used was (a) 0-tasteless, (b) 1-slightly bitter, (c) 2-bitter, and (d) 3-very bitter.

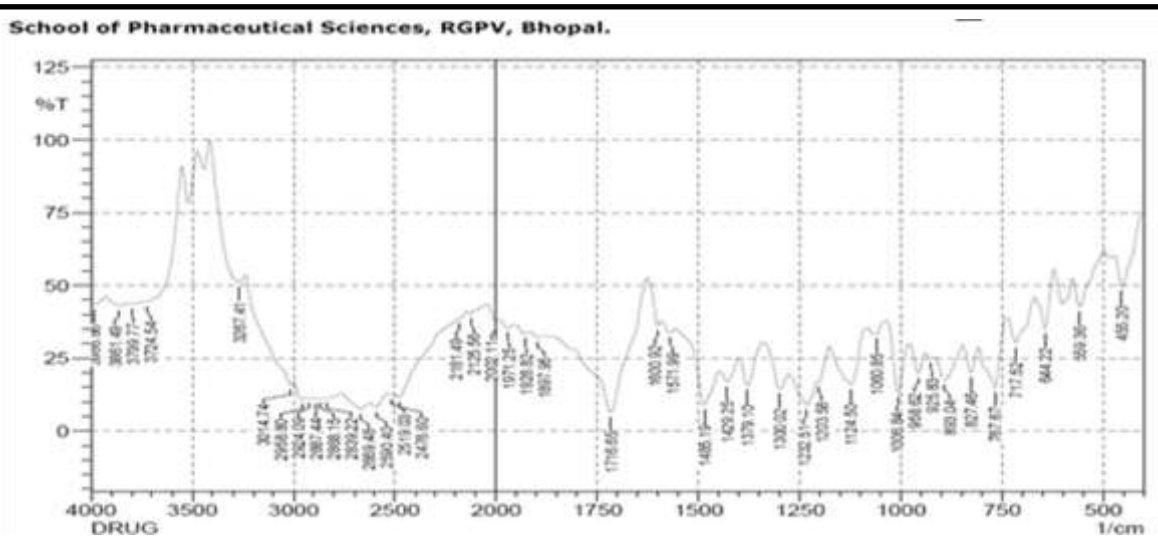

Figure 1. FTIR spectrum of Oloptadine

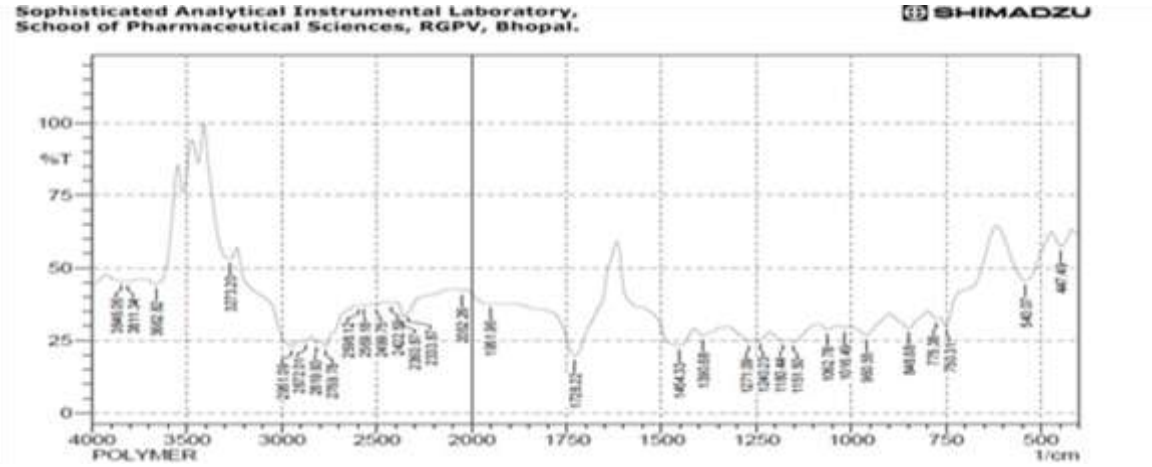

Figure 2. FTIR spectrum of microencapsulated particles

2.4. Preparation of MDTb

Fast disintegrating tablets of Olptadine was prepared by direct compression method [15]. 20] The main composition of tablet was the microencapsulated particles which consist of drug and the polymers, diluents, super disintegrates and sweeteners. Firstly, the particles along with additional excipients was screened through 40# and uniformly mixed together. Talc and magnesium stearate was screened through 80# and blended with initial mixture. Powder thus obtained was compressed into Tablets on an 8-station single punch rotary tablet compression machine.

2.5. Characterization of MDTb

2.5.1. Thickness variation

Tablet thickness can be measured using a simple procedure. Five tablets were taken and their thickness was measured using Vernier calipers. The thickness was measured by placing tablet between two arms of the Vernier calipers [16-17].

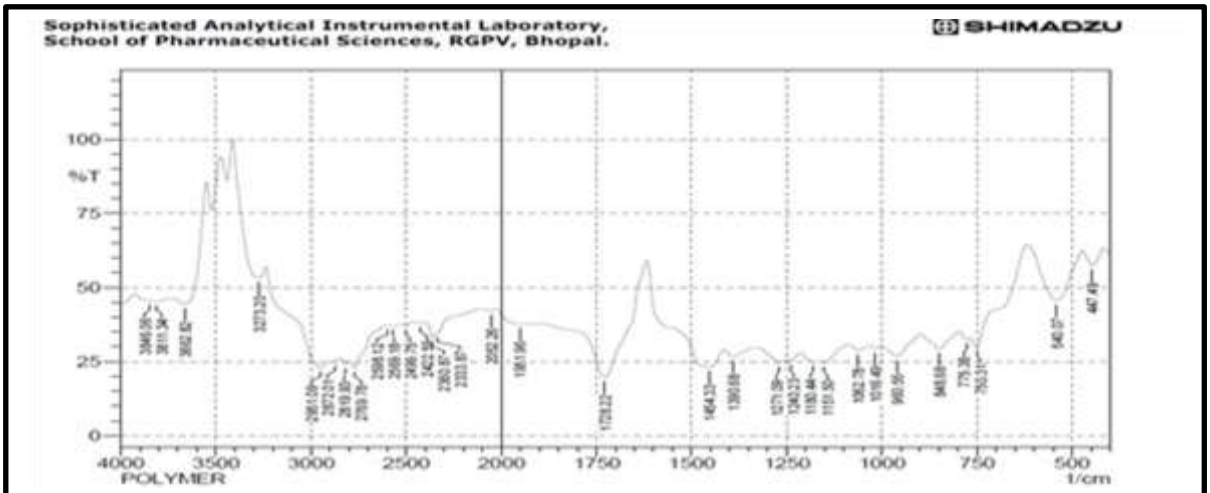

Figure 3. FTIR Spectrum of polymer (Eudragit e100)

2.5.2. Hardness test

Hardness or crushing strength of the tested orally disintegrating tablet formulations was measured using the dial hardness tester (Monsanto hardness tester) [17].

2.5.3. Friability test

The friability of the sample was for 20 orally disintegrating tablets measured utilizing a USP type Roche friabilator [18]. Pre-weighed tablets were placed in a plastic chambered friabilator attached to a motor revolving at a speed of 25 rpm for 4 min. The tablets were then de-dusted, reweighed, and percentage weight loss (friability) was calculated by equation: -

% Friability = w_0 - w/ w_0 * 100

w_0 = initial weight of 20 tablets,

w = weight of 20 tablets after 100 revolutions

3. RESULTS AND DISCUSSION

3.1. Physical and physiological characterization: Solubility

The solubility of oloptadine drug was determined in different solvent at room temperature. The solubility of drug was determined on the basis of approximate volume of solvent required by one part of drug. The inference noted after observation are represented in Table (3) [19, 20].

3.2. Melting point

The melting point of sample of oloptadine was determined as per procedure given in materials and methods part. The melting point of the drug was found in a specified range and the results are illustrated in Table (4).

3.3. FTIR Spectrocopy

The FTIR studies of drug, formulation and polymer has been mentioned in Graph 1, 2 and 3 along with interpretation (Table 6-8) respectively. The FTIR Spectra of pure drug showed the peaks at wave numbers (cm-1) which correspond to the functional groups present in the structure of the drug. Infra-red spectra of drug and polymer mixture showed matching peaks with the drug spectra. The

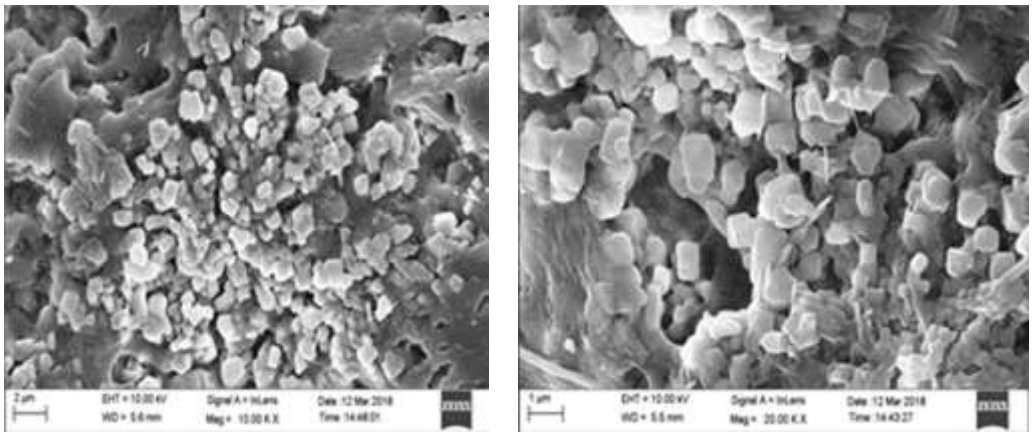

Image 1. SEM analysis

characteristics peak of the drug was also seen in the spectra of formulations [21].

3.4. Particles size range of polymer

Particle size analysis by light microscope (ocular and stage micrometer) was done to analysis 100 particle. The particle size was found in the expected range and the average of particle size=300µm, as shown in the table (9).

3.5. Taste evaluation studies

As per the procedure taste evaluation studies were carried out and the taste which was observed was tasteless and the observations are illustrated in Table (10).

Image 2. Mouth Dissolving Tablet of Olopatadine Hydrochloride

3.6. Pre-formulation studies

Percent drug entrapment, percentage yield and percent drug content was determined for the micro-particles and their results have been illustrated in Table (11-12). All the blends were evaluated for angle of repose, lies in 29.05, this show that the flow ability was fair to good. Compressibility index calculated found to be in the range of 18.02 which was within the acceptable limit, the hausner ratio computed lies between 1.4 this shows free flowing property of all granules. The blends passed the test as per limits mentioned in USP [22-23].

3.7. Post Compression Parameter

The post compression test like hardness, friability, weight variation and disintegration was done as per USP and the results of Tablets obtained was found within specified range which are illustrated in Table (14).

The encapsulated drug polymer particles with different component ratio exhibited, significant taste masking as confirmed in the taste

assessment by volunteer. Percentage drug entrapment in encapsulated drug polymer particles was found 34.2-45.2% with drug polymer ratio of 1:10 and 1:20 there observed significant difference. Number of particles (eudragit 100) increased at high concentration and drug entrapment was increased then lower concentration of particles (eudragit 100).

It was revealed the drug and polymer ratio and their combination had significant influence on taste masking. FTIR shows no interaction between drug and polymer. All the blends were evaluated for angle of repose, lies in 29.05, this show that the flowability was fair to good. Thus, it is evident that the taste masking and mouth dissolving tablet formulation of oloptadine can be developed using microencapsulation method without use of organic solvent. The formulation procedure is simple and does not lengthy procedure and use of several pharmaceutical excipients. Mouth dissolving tablet were prepared successfully by direct compression method using eudragit e100 polymer.

4. CONCLUSION

Oloptadine is a antihistaminic drug, is used as treat allergic reaction but taste and odor is very bitter therefor use of polymer (eudragit e100) for taste masking of drug & formulate mouth dissolving tablet. It was shown that effective taste masking with eudragit E 100 was achieved for oloptadine drug by (precipitation method) microencapsulation technique were successfully obtained. New pharmaceutical method used for taste masking is green synthesis which was designed to facilitate taste masking process, regulating compliance, inexpensive & eco-friendly.

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6. CONFLICT OF INTEREST

The authors have declared that there is no conflict of interest.

7. SOURCE/S OF FUNDING

No source of funding

8. REFERENCES

1. Gandhi A. (2012), Mouth dissolving tablets, A new venture in modern formulation technology, JPharm Int ;1(8):2277-7695.
2. Shaikh TH, Bhaise SD, Ligade DM, Patil MVK, Patankar RD. (2012), Formulation and evaluation of mouth dissolving tablet of metformines. Int J Res Pharm; **3(*6*)**:15-20.
3. Drewnowski and C Gomez-Carneros (2000), Bitter taste, phytonutrients and the consumer: a Review. Am. J. Clin. Natur;**72(*6*)**:1424-1435.

4. Cervellati C. A(2012), qnmr approach for bitterness phenotyping and qtl identification in an f1 apricot progeny. J. Biotechnol;**159(*4*)**: 312–319.
5. Rodgers S, Busch J, H. Peters, Christ-hazelhof E (2005), Building a tree of knowledge: analysis of bitter molecules. Chem. Senses ;**30(*7*)**:547–57.
6. Pronin AN, Tang H, Connor J, Keung W.(2004), Identification of ligands for two human bitter taste 2r receptors. Chem. Senses; **289(*36*)**: 583–593.
7. Kermani F.(2012), Patient compliance: sweetening the pill (google ebook). Vol.9 (gower publishing, ltd.
8. Liew KB, Peh K, Kok and Tan YTF(2013), Orally disintegrating dosage forms: breakthrough solution for non-compliance. Int. J. Pharm. Pharm. Sci.; **5(*4*)**: 4–8.
9. Chandrashekar J, Hoon MA, Ryba NJP, Zuker CS.(2006), The receptors and cells for mammalian taste. Nature ; 444: 288–94.
10. Zhang Y, Hoon MA, Chandrashrkar J.(2003), Coding of sweet, bitter, and umami tastes. Cell ; **112 (*3*)**: 293–301.
11. Behrens M, Brackhoff A, Bufe B, Kunh C.(2004), The human taste receptor htas2r14 responds to a variety of different bitter compounds. Biochem. Biophys. Res. Commun.;**319 (*2*)**: 479–485.
12. Dhakane K.(2011), A noval approach for taste masking techniques and evaluations in pharmaceutical: an updated review. Asian j. Biomed. Pharm. Sci.; **1**: 40–47.
13. Tomchik SM, Berg S, Kim JW, Chaudhari N Roper SD. (2007), Breadth of tuning and taste coding in mammalian taste buds. J. Neurosci.; **27(*40*)**: 10840–10848.
14. Smith DV, Margolskee RF(2006), Making sense of taste. Sci. Am.; 16: 84–92.
15. 20 Sajal JK, Uday SR, Surendra V.(2008), Taste masking in pharmaceutical. J Pharm Res;**1(*2*)**.
16. Amelian A, Winnicka K.(2017), Polymer in pharmaceutical taste masking application. PRZET ORSTWU POLIMEROW; **12(*1*)**:25-32.
17. Alison A, Keatinga J, Sotoa B,. Tuleua C, Forbesc C, Zhaod M. (2017), Solid state characterisation and taste masking efficiency evaluation of polymer based extrudates of isoniazid for paediatric administration. International journal of pharmaceutics; **536(*2*)**: 553–572.
18. Malik K, Arora G, Singh I.(2011), Taste masked microspheres of ofloxacin: formulation and evaluation of orodispersible tablets. Sci pharm.;**79(*3*)**: 653–672
19. Bogner RH, Wilkosz MF.(2002), Fast dissolving tablets: new dosage convenience for patients. U.S Pharmacist.; **27(*3*)**:34-43.
20. Bhise K, Shaikh S, Bora S.(2008), Taste mask, design and evaluation of an oral formulation using ion exchange resin as drug carrier.pharm sci tech. ;**9(*2*)**:557-562.
21. Patra S, Sahoo R, Panda RK, Himasankar K, Barik BB.(2010), In vitro evaluation of domperidone mouth dissolving tablets. Indian J Pharma Sci.**72(*6*)**:822-825
22. Upmanya N, Shah K, Porwal PK, Gokhul TS.(2016), Degradation kinetics of oloptadine HCL using a validated UV-AUC method. J Anal Pharm Res;**2(*2*)**:00016.

23. Arora P, Arora SA. (2013), Orodispersible tablets. Int J Res Dev Pharm L Sci ;**2(*2*)**:270-284.