EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 4
Issue: 11
520-527
Year: 2017

FORMULATION DEVELOPMENT AND EVALUATION OF ETORICOXIB ORAL DISINTEGRATION TABLET

S. R. Senthilkumar*, N. Venkatesan, R. Ramprasad, Nilsha Anil, J. Amutha Iswarya Devi and R. Subish

Arulmigu Kalasalingam College of Pharmacy, Anand Nagar, Krishanan Koil.

***Corresponding Author: S. R. Senthilkumar**

Arulmigu Kalasalingam College of Pharmacy, Anand Nagar, Krishanan Koil.

Article Received on 10/09/2017 **Article Revised on 01/10/2017** **Article Accepted on 22/10/2017**

ABSTRACT

Etoricoxib has some of the ideal characteristics required for an orally disintegrating tablet.[1,2,3] There were some challenges faced during this formulation development. The aims of the present research were to mask the bitter taste of etoricoxib and to formulate orally disintegrating tablets of taste masked drug.[4] Taste masking was performed by ion resin complexation etoricoxib with suitableresin indone 294.[5] Disintegration time was effectively reduced by adding disintegrating agents such as crospovidone and croscarmellose sodium.[6] The increasing the concentration of tartaric acid the ph level was change and it also reduced the bitter teats.[7] The resultant ODT tablets were then evaluated for particle size and in vitro taste masking. The tablets prepared were evaluated for weight variation, thickness, hardness, friability, drug content, water content, in vitro disintegration time and in vitro drug release of etoricoxib.[8]

KEYWORDS: Etoricoxib has some etoricoxib with suitableresin indone etoricoxib.

INTRODUCTION

The oral route of administration is considered as the most widely accepted route because of its convenience of self administration, compactness and easy manufacturing.[9] But the most evident drawback of the commonly used oral dosage forms like tablets and capsules is difficulty in swallowing, leading to patients incompliance particularly in case of pediatric and geriatric patients , but it also applies to people who are ill in bed and to those active working patients who are busy or traveling, especially those who have no access to water.[10,11,12] Over a decade, the demand for development of orally disintegrating tablets (ODTs) has enormously increased as it has significant impact on the patient compliance.[13,14,15] Orally disintegrating tablets are appreciated by a significant segment of populations particularly who have difficulty in swallowing.[16,17] It has been reported that Dysphagia (difficulty in swallowing) is common among all age groups and more specific with pediatric, geriatric population along with institutionalized patients, psychiatric patients and patients with nausea, vomiting, and motion sickness complications.[18] ODTs with good taste and flavor increase the acceptability of bitter drugs by various groups of population. This dosage form combines the advantages of dry and liquid formulation.[19] Some novel ODT technology allow high drug loading, have an acceptable taste, offer a pleasant mouth felling, leaving minimal residue in the mouth after oral administration.[20] ODT have been investigated for their potential in improving bioavailability of poorly soluble drug through enhancing the dissolution profile of the drug and hepatic metabolism drugs.[21]

METHODS AND MATERIALS

Pre-formulation testing is an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. It is the first step in the rationale development of dosage forms. Pre-formulation studies yield necessary knowledge to develop suitable formulation. It gives information needed to define the nature of drug substance and provide a dosage form. Hence, the following pre-formulation studies were performed for the obtained sample of drug.[22]

(i)Drug – excipients compatibility (ii) FTIR drug – excipients compatibility (iii) Particle size distribution (iv) Angle of repose (v) Bulk density (vi) Tapped density (vii) Compressibility index (viii) (Hausner's ratio (ix) Solubility studies (x) Loss on drying.[23]

Preparation of complex: The preparation is done by ion exchange resin complex technique. The drug and the resin (indion294) are taken in the ratio of 1:3.

Resin activation process: The resin activation process is nothing but the soaking of resin in water. The resin soaked for 45 minutes in water and the resin swells.

pH adjustment: The P^H of activated resin is adjusted to 3-4 by using tartaric acid. The tartaric acid used as the buffering agent.

Stirring process: The P^H adjusted resin and drug are mixed in a same beaker with mechanical stirrer for 8 hours in 1000 rpm. After completion of stirring (8 hours). Then the drug resin complex is set aside stably for 12 hours. Two layers get separated. The upper layer (supernatant fluid) is water and the lower layer (suspansoide) is drug resin complex.[24]

Post formulation study

(i) Weight variation test (ii) Hardness (iii) Thickness (iv) Friability (v) Disintegration time (vi) Assay (vi) Dissolution study.[25]

RESULT AND DISCUSSION

Fourier Transform-Infrared spectroscopy

Drug excipient compatibility was analyzed using FT-IR. FT-IR was done using Perkin-Elmer spectrum. All the samples were mixed properly with KBr in 1:3 ratios and were made into pellets. Those pellets were analyzed. Each KBr disc was scanned over a wave number region of 4000-400 cm-1 using FT-IR Spectrophotometer.

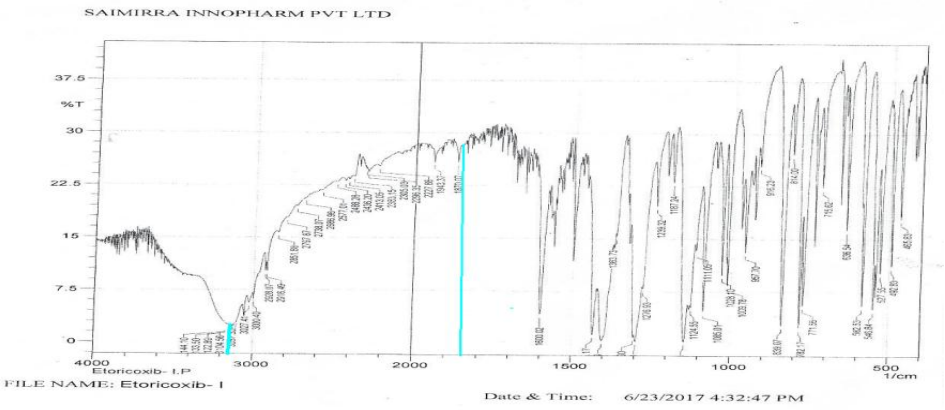

Figure 1: FTIR Spectrum of etoricoxib pure drug.

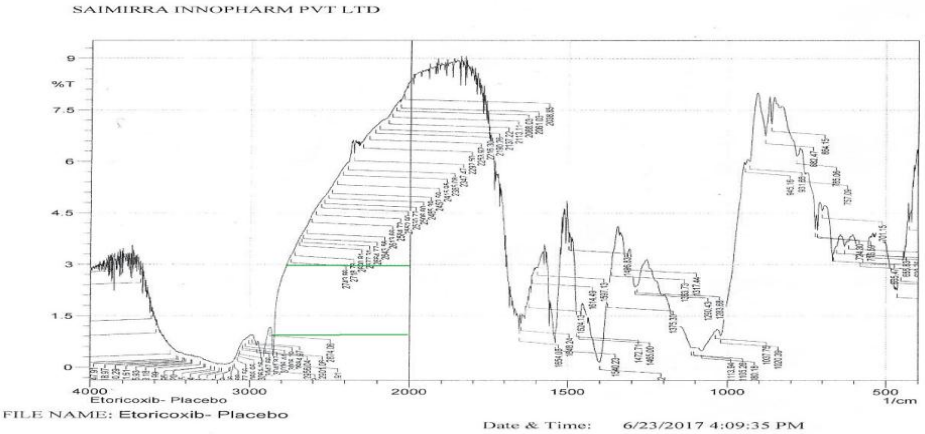

Figure 2: FTIR Spectrum of placeboc (WITHOUT API).

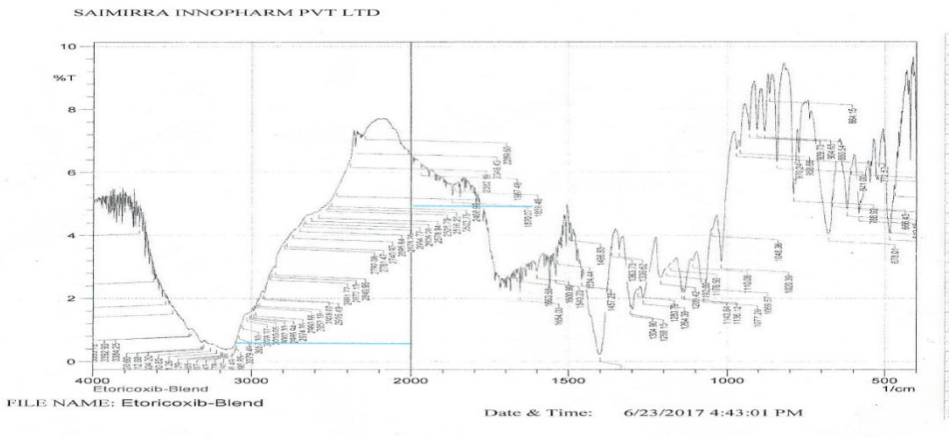

Figure 3: FTIR Spectrum of etoricoxib blend.

FT-IR on the selected formulation was prepared with different polymer and excipients combination. The spectrum peak point of the formulation were similar with that of pure etoricoxib, it clearly indicates that there is no polymer interaction.

Table No. 1: Particle size.

S. No.	Ingredient	Sieve number	Particle size
1	Etoricoxib	20	0.850
2	Excipients	40	0.425

PARTICLE SIZE DETERMINATION

The particle size determined by using sieving method.

Table No. 2: Flow properties of etoricoxib.

S. No.	Angle of repose Mean ± SEM	Bulk density Mean ± SEM	Tapped density Mean ± SEM	*Carr"s* Index Mean ± SEM	Hausner's Ratio Mean ± SEM
1	22.62	0.64	0.63	14.51	1.22
2	22.91	0.60	0.65	14.41	1.24
3	23.95	0.63	0.67	14.74	1.26
	23.16 ± 0.403	0.62 ± 0.01	0.66 ± 0.011	14.55 ± 0.097	1.24±0.01

Table No. 3: Evaluation flow properties of blend.

Formulation code	Evaluation parameter					
	Angle of repose	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Compressibility Index (%)	Hausners ratio	Flowability
EDI 1	25.15	0.571	0.699	14.64	1.17	Excellent
EDI 2	26.35	0.586	0.684	14.32	1.16	Excellent
EDI 3	24.21	0.579	0.674	14.09	1.20	Fair
ETI 1	28.65	0.568	0.667	14.84	1.17	Excellent
ETI 2	23.95	0.578	0.678	14.74	1.18	Excellent
ETI 3	27.84	0.588	0.688	17.53	1.23	Fair

Compressibility index**,** Angle of repose, Bulk density. Tapped density and hausner ratio of trial batches were computed and found that all blends possess good flow properties and hence suitable for direct compression of blends into tablets.

Table No. 4: complex formation.

S. No.	Formulation	Observation/pH	Drug Complexsation %	Taste
1	DRC-1 120mg=60mg	pH-9.2, Separation layer. No complex formation	-	Bitter
2	DRC-2 145mg=60mg	pH-5.2, no separation complex is formed	85.6%	Bitter
3	DRC-3 170mg=60mg	pH-3.5, no separation. Complex is formed	99.2%	Slightly bitter
4	DRC-4 230mg=60mg	pH-3.68, no separation. Complex is formed	99.38%	Slightly bitter
5	DRC-5 290mg=60mg	pH-3.85, no separation. Complex is formed	99.82%	Bland taste
6	DRC-6 290mg=60mg	pH-3.56, no separation. Complex is formed	78.87%	Bitter

Table No. 5: Calibration curve.

S. No.	Concentration (µg)	Absorbance
1	0	0
2	5	0.218
3	10	0.406
4	15	0.624
5	20	0.848

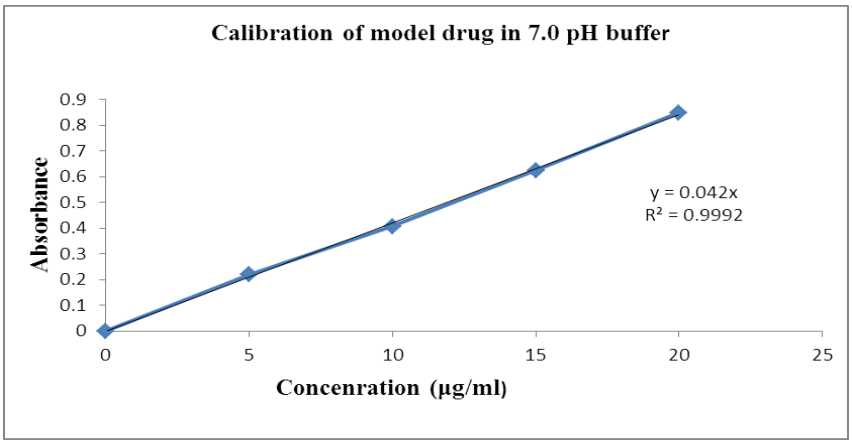

Figure 3: Calibration curve.

The ƛ max of etoricoxib was found to be 240 nm. The linear equation was y = 0.042 x (x=concentration µg/ml). Different standard concentration and their absorbance was shown in the table. Regression value of calibration curve is 0.999. A graph of Absorbance Vs Concentration was found to be linear indicating its compliance with beer's law.

Table No. 6: Weight VariationTest.

S. No.	Formulation	Weight variation (mg) (Mean±SEM)	Average thickness (mm) Mean ± SEM	Average hardness (kg/cm^2) Mean ± SEM	Friability
1	EDI 1	403±0.96	3.5 ± 0.09	4.3 ± 0.12	0.5%
2	EDI 2	402±0.71	3.7 ± 0.08	4.1± 0.11	0.7%
3	EDI 3	403±0.32	3.8 ± 0.09	4.2± 0.09	0.6%
4	ETI 1	404±0.55	3.9 ± 0.08	4.3± 0.12	0.8%
5	ETI 2	401±0.39	3.8 ± 0.10	4.5± 0.08	0.6%
6	ETI 3	402±0.62	3.9 ± 0.09	4.4± 0.10	0.9%

All values are expressed as mean ± SEM for twenty determinations

Table No. 7: Drug content.

S No.	Formulation	Drug content uniformity (%)
1	EDI 1	91.20%
2	EDI 2	91.67%
3	EDI 3	93.80%
4	ETI 1	94.40%
5	ETI 2	96.23%
6	ETI 3	95.33%

Table No. 8: Disintegration test.

S. No.	Disintegration test (sec) EDI 1	Disintegration test (sec) EDI 2	Disintegration test (sec) EDI 3	Disintegration test (sec) ETI 1	Disintegration test (sec) ETI 2	Disintegration test (sec) ETI 3
1	52	53	48	44	39	45
2	55	53	45	43	39	48
3	52	55	47	45	38	47
4	49	54	50	44	35	50
	52 ± 0.05	54± 0.03	48 ± 0.05	44 ± 0.02	37 ± 0.03	47 ± 0.03

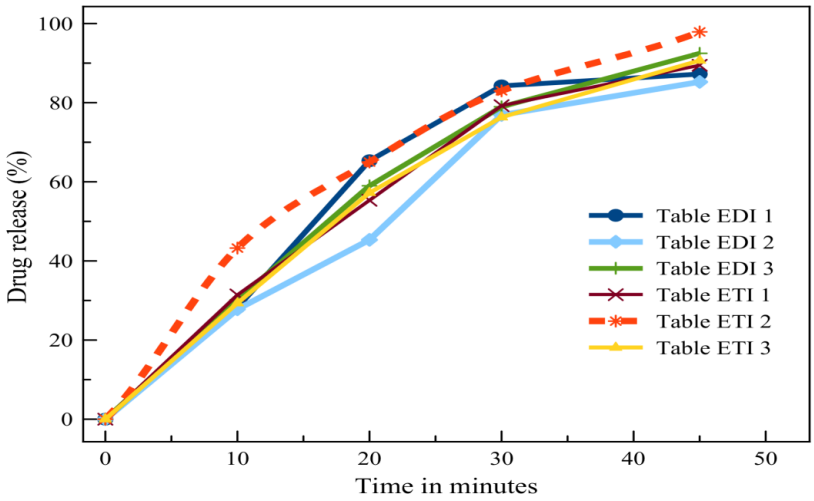

Figure 4: Disintegration test.

From the above data it was found that when Cros povidone and croscarmellose sodium was used in the formulation (ETI 2), the %drug release was found to be 97.89% at 45 mins time point.

Table No. 9: Comparison study of formulation tablet and marketed tablet.

Time	Dissolution test (conc/time) EDI 1	Dissolution test (conc/time) EDI 2	Dissolution test (conc/time) EDI 3	Dissolution test (conc/time) ETI 1	Dissolution test (conc/time) ETI 2	Dissolution test (conc/time) ETI 3	Dissolution test (conc/time) Marketed sample
	0	0	0	0	0	0	0
10	28.25	27.78	30.21	31.41	43.25	29.33	25.22
20	65.33	45.33	58.99	55.33	64.99	57.22	58.99
30	84.24	76.88	78.96	79.25	82.99	76.33	82.99
45	87.23	85.25	92.47	89.45	97.89	90.66	91.55

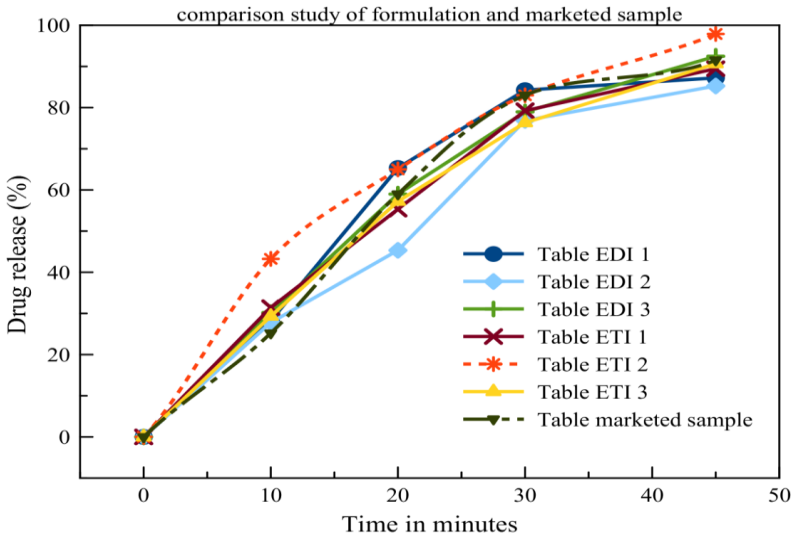

Figure 5: Dissolution test.

Table No. 10: Results of different parameters used for Accelerated Stability study data of selected ODT formulations subjected to study as per ICH guidelines (3month at 40°C ± 2°C and 75%RH ± 5% RH). At predetermined time intervals of 30, 60 and 90 days.

Days	Formulation	Colour and Odour	pH	Wight variation test	Friability test	Hardness test	Thickness test	Disintegration test (sec)	Assay	Solubility	Dissolution test
0 Day	EDI -1	Yellow	6.7	404	0.96%	No change	4.4%	39	95.82%	No change	Good
	EDI-2	Yellow	6.4	405	1.01%	No change	4.5%	37	96.21%	No change	Good
	EDI-3	Yellow	6.8	403	1.5%	No change	4.5%	38	97.11%	No change	Good
	ETI-1	Yellow	6.6	402	1.5%	No change	4.3%	40	96.01%	No change	Good
	ETI-2	Yellow	6.3	401	0.9%	No change	4.2%	36	95.22%	No change	Good
	ETI-3	Yellow	6.2	405	1.2%	No change	4.4%	38	94.43%	No change	Good
30 Days	EDI -1	Yellow	6.6	405	1.01%	No change	4.5%	39	95.21%	No change	Good
	EDI-2	Yellow	6.3	403	1.5%	No change	4.2%	39	94.19%	No change	Good
	EDI-3	Yellow	6.7	402	0.9%	No change	4.3%	38	95.15%	No change	Good
	ETI-1	Yellow	6.4	404	1.01%	No change	4.4%	40	96.10%	No change	Good
	ETI-2	Yellow	6.5	405	1.5%	No change	4.5%	39	95.32%	No change	Good
	ETI-3	Yellow	6.4	404		No change	4.3%	39	95.21%	No change	Good
60 Days	EDI -1	Yellow	6.6	404	1.01%	No change	4.4%	37	94.82%	No change	Good
	EDI-2	Yellow	6.0	403	0.9%	No change	4.6%	37	96.37%	No change	Good
	EDI-3	Yellow	6.3	405	1.5%	No change	4.2%	36	96.23%	No change	Good
	ETI-1	Yellow	5.9	401	0.9%	No change	4.1%	38	94.19%	No change	Good
	ETI-2	Yellow	6.7	403	1.01%	No change	4.2%	36	96.23%	No change	Good
	ETI-3	Yellow	6.2	403	0.9%	No change	4.4%	39		No change	Good
90 Days	EDI -1	Yellow	6.5	405	1.5%	No change	4.4%	40	93.21%	No change	Good
	EDI-2	Yellow	5.9	406	0.9%	No change	4.2%	38	94.7%	No change	Good
	EDI-3	Yellow	6.2	405	1.01%	No change	4.1%	38	96.58%	No change	Good
	ETI-1	Yellow	5.9	403	1.5%	No change	4.3%	39	95.19%	No change	Good
	ETI-2	Yellow	6.4	404	0.9%	No change	4.4%	39	94.34%	No change	Good
	ETI-3	Yellow	6.5	403	1.5%	No change	4.1%	38	94.22%	No change	Good

CONCLUSION

Etoricoxib orally disintegration tablet were prepared by using polacrilin potassium (Indion 294) ion exchange resin complexation technique.

The evaluation results of all six batches were found to be satisfactory within limit and the disintegration time was quite good than synthetic super disintegrants such as Cros povidone and croscarmellose sodium. The synthetic disintegratant creates hydrodynamic pressure when comes in contacts with saliva and disintegrates the tablets within few seconds by swelling

The results of etoricoxib ODTs evaluation of different batches were done. The weight variation of 400mg tablets was found maximum up to ± 1.2% RSD. Hardness was found to be within 3.0 to 4.0 kg/cm2 which limit friability within 0.7% only. As the combination of super disintegratant conc decrease with same ratio the formulation ETI 2 gave 96.54% drug release at 45 mins time point,. The drug Contents was found to be within limits and all tablets were passing the dispersion test. The FT-IR study shows that there was no interaction between the drug and the polymer. Acc stability study was carried out for 3 month they was no change absorbed before and after storage periods.

REFFERANCE

1. Arun A, Amrish C. Fast drug delivery systems: a review. Pharm Lett, 2010; 2(2): 350-61.
2. Nayak AK, Manna K. Current developments in orally disintegrating tablet technology. Journal of Pharmaceutical Education and Research, 2011 Jun 1; 2(1): 21.
3. Dobetti L. Fast-melting tablets: Developments and technologies. Pharm Technol Eur, 2000 Sep; 12(9): 32-42.
4. Hirani, Jaysukh J., Dhaval A. Rathod, and Kantilal R. Vadalia. "Orally disintegrating tablets: a review." Tropical journal of pharmaceutical research, 2009; 8(2).
5. Patra, S., Samantaray, R., Pattnaik, S. and Barik, B.B., Taste masking of Etoricoxib by using ion-exchange resin. Pharmaceutical development and technology, 2010; 15(5): 511-517.
6. Manivannan R. Oral disintegrating tablets: A future compaction. Drug Invention Today, 2009 Nov 1; 1(1): 61-5.
7. Sahoo S, Mishra B, Biswal PK, Panda O, Mahapatra SK, Jana GK. Fast Dissolving Tablet: As a potential drug delivery system. Drug invention today, 2010 Feb 1; 2(2).
8. Manivannan R. Oral disintegrating tablets: A future compaction. Drug Invention Today, 2009 Nov 1; 1(1): 61-5.
9. Patil SC. Formulation and evaluation of oral disintegrating tablet of lornoxicam. International Journal of Pharmaceutical & Biological Archive, 2011; 2(5).
10. Dressman JB, Amidon GL, Reppas C, Shah VP. Dissolution testing as a prognostic tool for oral drug absorption: immediate release dosage forms. Pharmaceutical research, 1998 Jan 1; 15(1): 11-22.
11. Merisko-Liversidge EM, Liversidge GG. Drug nanoparticles: formulating poorly water-soluble compounds. Toxicologic pathology, 2008 Jan; 36(1): 43-8.
12. Ma JK, Barros E, Bock R, Christou P, Dale PJ, Dix PJ, Fischer R, Irwin J, Mahoney R, Pezzotti M, Schillberg S. Molecular farming for new drugs and vaccines. EMBO reports, 2005 Jul 1; 6(7): 593-9.
13. Sahoo S, Mishra B, Biswal PK, Panda O, Mahapatra SK, Jana GK. Fast Dissolving Tablet: As a potential drug delivery system. Drug invention today, 2010 Feb 1; 2(2).
14. RoshanRai R, Chirra P, Thanda V. Fast dissolving tablets: A novel approch to drug delivery–A Review. International journal of preclinical and pharmaceutical research, 2012; 3(1): 23-32.
15. Sreenivas SA, Dandagi PM, Gadad AP, Godbole AM, Hiremath SP, Mastiholimath VS, Bhagawati ST. Orodispersible tablets: New-fangled drug delivery system-A review. Indian Journal of Pharmaceutical Education, 2005 Oct; 39(4): 177.
16. Manivannan R. Oral disintegrating tablets: A future compaction. Drug Invention Today, 2009 Nov 1; 1(1): 61-5.
17. Tripathi KD. Essentials of medical pharmacology. JP Medical Ltd, 2013 Sep 30.
18. Valleri M, Mura P, Maestrelli F, Cirri M, Ballerini R. Development and evaluation of glyburide fast dissolving tablets using solid dispersion technique. Drug Dev Ind Pharm, 2004; 30(5): 525-34.
19. Awasthi R, Sharma G, Dua K, Kulkarni GT. Fast disintegrating drug delivery systems: A review with special emphasis on fast disintegrating tablets. Journal of Chronotherapy and Drug Delivery, 2013; 4(1): 15-30.
20. Sreenivas SA, Dandagi PM, Gadad AP, Godbloe AM, Hiremath SP, Mastiholimath VS. Orodispersible tablets: New-fangled drug delivery systems – A review. Indian J Pharm Educ Res, 2005; 39(4): 177-181.
21. Wagh MA, Kothawade DP, Salunkhe KS, Chavan NV, Daga VR. Techniques used in orally disintegrating drug delivery system. International journal of drug delivery, 2010 Apr 1; 2(2).
22. Panchal Dhavalkumar M, Ajaykumar T, Priyam S. A review on orodispersible tablets–a novel formulation for oral drug delivery system and its future prospective. IAJPR, 2013; 3(5): 4149-68.
23. US Department of Health and Human Services FDA Center for Drug Evaluation and Research, US Department of Health and Human Services FDA Center for Biologics Evaluation and Research, US Department of Health and Human Services FDA Center for Devices and Radiological Health. Guidance for industry: patient-reported outcome measures: use in medical product development to

support labeling claims: draft guidance. Health and Quality of Life Outcomes, 2006 Dec; 4: 1-20.
24. Mali SS, Jadhav SB, Bharkad VB, VS MJ, Kapse GR, Hadbe NB. An Overview on Fast Disintegrating Tablets. Pharma Science Monitor, 2014 Apr 2; 5.
25. Das D. *Development and evaluation of high porous mouth dissolving tablets containing lamotrigine complexation* (Doctoral dissertation, RGUHS).