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Formulation and Evaluation of Domperidone Orodispersible Tablet

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ABSTRACT

In the present study, an attempt has been made to design and develop domperidone orodispersible tablet using a combination of SR microspheres and IR solid dispersion of domperidone into an orally disintegrating tablet using direct compression method and sodium starch glycolate, crosspovidone. Domperidone helps in gastric emptying and decreases small bowel passing time by increasing esophageal and gastric peristalsis and also by lowering esophageal spincter pressure. Domperidone sustained release orodispersible tablet prepared and evaluated for parameters like hardness, disintegration time, weight variation, friability, and Invitro dispersion time. The hardness of the tablet was in the range of 2+-0.5kg/cm2,disintegration time 11=-15 sec. The formulation was optimized using 2 factorial designs. The concentration of super disintegrant selected as the dependent variable, and disintegration time was selected as dependent variable. Sodium starch glycolate and crosspovidone at 3% concentration give disintegration time 11=-15 sec with 46% release at the end of 1 hr and 94% at the end of 2 hrs.

INTRODUCTION:

Sustained-release tablets and capsules are commonly taken only once or twicedaily, compared with counterpart that may have to be taken three or four times daily to achieve the same therapeutic effect.

Typically, sustained-release products provide an immediate release of drug that promptly produces the desired therapeutic effect followed by gradual release of additional amounts of drug to maintain this effect over a predetermined period. The sustained plasma drug levels provided by sustained release products often eliminate the need for night dosing. The basic idea of a sustained or controlled drug delivery system is to optimize the Biopharmaceutics, Pharmacokinetic and Pharmacodynamics properties of a drug in such a way that its utility is maximized through reduction in side effect, cure and control of condition in the shortest possible time by using optimum quantity of drug, in practically possible dosage form. Domperidone is selected as the model drug which comes under anti-emetic class. Domperidone is optimized suits for preparation of ODT as it has longer half-life and in case of vomiting it is required. Quick release. This drug is effective in all categories i.e. pediatrics, adults, geriatrics. Domperidone blocks the action of dopamine. It has strong affinities for the D2 and D3 dopamine receptors, which are found in the chemoreceptor trigger zone (CTZ) located just outside the "Blood-brain" This is the correct term to refer to the barrier between the blood vessels and the brain tissue. Barrier, which regulates nausea and vomiting.

1.1. Sustained release (SR) delivery

1.1.1. Advantages: [1-9]

1. Patient Compliance:
2. Reduced 'seesaw' fluctuation:
3. Reduced total dose:
4. Improved efficiency in treatment:
5. Economy:

1.1.2. Disadvantages: [1-9]

1. Dose dumping:
2. Dose adjustment:
3. *In Vitro* – *In Vivo* correlation is poor:
4. Patient variation:

1.1.3 Classification of sustained release[10]

Depending upon the manner of release the controlled release system isclassified as follows:

- Continuous release systems
- Continuous release and delayed transit
- Delayed release systems

Continuous release systems are further classified into dissolution controlled, diffusion controlled and dissolution controlled release systems.

Further they are classified into matrix and reservoir types.

1.2 Overview of orally disintegrating tablet (ODT):-

ODT provides an attractive alternative to conventional solid oral dosage forms. ODT is a solid dosage form that disintegrates or dissolves in the mouth without aid of water within 60 sec or less. The US Food and Drug Administration Center and drug evaluation and Research Centre (CDER) define in the orange book an ODT as "A solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds when placed upon the tongue".

The European Pharmacopoeia defines the term "orodisperse" as a tablet thatcan be placed in the mouth where it disperses rapidly before swallowing

ODT is known by various names such as "fast-melting, fast-dissolving, mouth disintegrating or orodisperse tablet".

1.2.1 Mechanism of ODTs[12]

ODTs involve the following mechanisms to achieve the desired fast-dissolving characteristics.

1. Water must quickly enter into the tablet matrix to cause rapid disintegration and instantaneous dissolution of the tablet.

2. Incorporation of an appropriate disintegrating agent or highly water-soluble excipients in the tablet formulation.

3. There are some under-mentioned mechanisms by which the tablet is broken down into smaller particles and then subsequently result in a solution or suspension of the drug. The mechanisms are-

- The high swell ability of disintegration
- Chemical reaction
- Capillary action

1.2.2 Drug selection criteria [12-16]

The ideal characteristics of a drug for oral dispersible tablet include [6]

- Have the ability to diffuse and partition into the epithelium of the upper GIT.
- Small to moderate molecular weight.
- Low dose drugs preferably less than 20mg.
- Short half-life and frequent dosing drugs are unsuitable for ODT.
- Very bitter or unacceptable taste and odour drugs are unsuitable for ODT.

1.2.3 Ideal Properties of ODTs [14-16]

They should -

- Not require water to swallow and should dissolve or disintegratein the mouth within a few

seconds.

- Allow high drug loading.
- Be compatible with taste masking and other excipients.
- Have a pleasing mouth feel.
- Leave minimal or no residue in the mouth after oral administration.
- Have sufficient strength to withstand the rigors of the manufacturing process and not make post-manufacturing handling.very difficult.
- Exhibit low sensitivity to environmental conditions such as humidity and temperature.
- Be adaptable and amenable to existing processing and packaging machinery.
- Allow the manufacture of tablets using conventional processing and packaging.
- Be commercially viable requiring equipment of low cost for manufacturing.

1.2.4 Advantages [14-16]

- Easy to administer to patient who has difficulty swallowing such as pediatric, geriatric, bedridden, stroke victim and institutionalized patient (especially for mentally retarded and psychiatric patients).
- Pre-gastric absorption leads to increased bioavailability/ rapid absorption of drugs from mouth, pharynx and oesophagus as saliva passes down to stomach, also avoids hepatic metabolism.
- Convenient for administration to travelling patients and busy people who do not have accesses to water.
- Excellent mouths feel property produced by use of flavours and sweeteners help to change the perception of “medication as bitter pill” especially in pediatric population.
- Fast disintegration of tablets leads to quick dissolution and rapid absorption which may produce a rapid onset of action.

- ODTs offer all the advantages of solid dosage forms and liquiddosage forms.
- Convenience of administration and accurate dosing compared toliquids.

1.2.5 Technologies used for manufacturing of orally disintegrating tablets [13, 17-28]

A. Conventional technology

B. Patented technology

A. Conventional technology:-

- Freeze drying or lyophilization
- Direct compression
- Molding
- Mass extrusion
- Melt granulation
- Phase transition process
- Sublimation

B. Patented technology:-

- Zydis technology
- Orasolv technology
- Wow tab technology
- Cotton candy technology
- Oraquick technology
- Nanocrystal technology
- Shearform technology

- Pharma burst technology
- Frosta technology

1.2.6 Evaluation of ODT's[11-13]

A. Evaluation of blends before compression

- Compressibility index
- Hausner's ratio
- Tapped density
- Bulk density
- Angle of repose

B. Evaluation of Tablets:

- Hardness
- Friability
- Weight variation:
- Wetting time
- Disintegration test
- Dissolution test

1.3 MATERIAL AND METHOD:

Material:

The list of materials used in the present investigation is given below in Table No 1 List of instruments used is given in Table No. 2.

Table No 1.3.1 List of materials

Sr.no	Material	Source
1.	Domperidone (DMP) IP,BP	Cadila pharmaceuticls
2.	Polyethylene glycol 400	Loba chemie
3.	Methanol AR grade	Loba chemie
4.	Potassium dihydrogenPhosphate AR grade	Loba chemie
5.	Methanol HPLC grade	Pallav chemicals
6.	Ethylcellulose	Evonik
7.	Gellucire 50/13	Gateffose
8.	Pearlitol SD 200	Roquette pharma
9.	Avicel PH 102	DFE pharma
10.	Sodium starch glycolate	DFE pharma
11.	Crospovidone	DFE pharma
12.	Talc	Signet
13.	Magnesium Stearate	Loba chemie
14.	Light Liquid paraffin	Loba chemie
15.	Ethanol	Arihant enterprises
16.	Dichloromethane AR grade	Loba chemie
17.	Conc. HCL	Pallav chemicals
18.	n-hexane AR grade	Loba chemie
19.	Sodium hydroxide ARgrade	Loba chemie
20.	HPLC water	Merck

Table No 1.3.2 List of Instruments

Sr.no	Equipment name	Manufacturer
1.	UV Spectrophotometer	Shimadzu
2.	FTIR	Shimadzu
3.	Electronic weighing balance	Premier psp 600
4.	HPLC	Shimadzu
5.	PH meter	DBK instruments
6.	Magnetic stirrer	Remi enterprises
7.	Vacuum filter	Jsil
8.	Stability chamber	Oscar
9.	Heating mantle	Remi enterprises
10.	Dissolution apparatus	Labindia DS 8000
11.	Mechanical stirrer	Remi
12.	Friability apparatus USP	Veego
13.	Hardness tester	Monsanto hardnesstester
14.	Bulk density apparatus	Dolphin

Methods:

The domperidone ODT was formulated from a combination of SR microspheres and IR solid dispersion. The combination of sodium starch glycolate and crosspovidone was used to achieve the desired disintegration time.

Table no-1.3.3 Results from the Combination of SR microspheres and IR solid dispersion of DMP into an orally disintegrating tablet

Ingredients	O1	O2	O3	O4
DMP MS(mg)	54	54	54	54
DM P Solid dispersion (mg)	43	43	43	43
Avicel PH 102(mg)	67.48	67.48	67.48	59.98
Pearlitol® SD 200(mg)	22.49	22.49	22.49	19.99
Talc (mg)	2	2	2	2
Ma magnesium stearate (mg)	1	1	1	1
Sodium starch glycolate(mg)	-	-	10	10
Crossprovidone(mg)	10	-	-	10
Crosscarmellose sodium(mg)	-	10		-
Sucralose (mg)	0.015	0.015	0.015	0.015
Strawberry flavor(mg)	0.01	0.01	0.01	0.01
Total(mg)	200	200	200	200
Disintegration time	90-95sec	100-103sec	120-123sec	11-15sec
Hardness	2±0.5kg/cm^2	2±0.5kg/cm^2	2±0.5kg/cm^2	2±0.5kg/cm^2

- Batch O4 gives the desired disintegration time of 11-15 sec.

• As seen from the result, batch O4 produced the desired disintegration time of 11-15 sec. so the combination of SSG and crospovidone was finalized as a super disintegrant blend for formulation which was subjected to further optimization.

Table NO -1.3.4 ANOVA for disintegration time of DMP ODT

Source	Sum of Squares	df	Mean square	F- value	p-value Prob>F	
MODEL	54.92	3	18.31	12.92	0.0020	
A:-CONC. OF SSG	30.08	1	30.08	21.24	0.0017	
B:-CONC.OFCROSPOVIDONE	24.08	1	24.08	17.00	0.0033	
AB	0.75	1	0.75	0.53	0.4876	**SIGNIFICANTT**
Pure Error	11.33	8	1.2	-	-	
Corr Total	66.25	11	-	-	-	

1.4 Characterisation and evaluation of DMP ODT:-Results from the evaluation of the optimized batch are given in table no--1.4.1 and the dissolution profile of DMP ODT is given below in Figure no-1.4.1.

Table no 1.4.1-Results from evaluation of DMP ODT

Sr.no	Parameter	Comment
1.	Diameter	8±0.1 mm
2.	Hardness	2±0.5 kg/cm^2
3.	Disintegration time	11±15sec
4.	Wetting time	25±4 sec
5.	Weight variation	Passes
6.	Assay	90 ± 1.458 %
7.	Friability	0.6±1%
8.	*In vitro* dispersion time	11±13sec
9.	% release at end of 1 hrs % Release at end 24 hrs	46% 94%

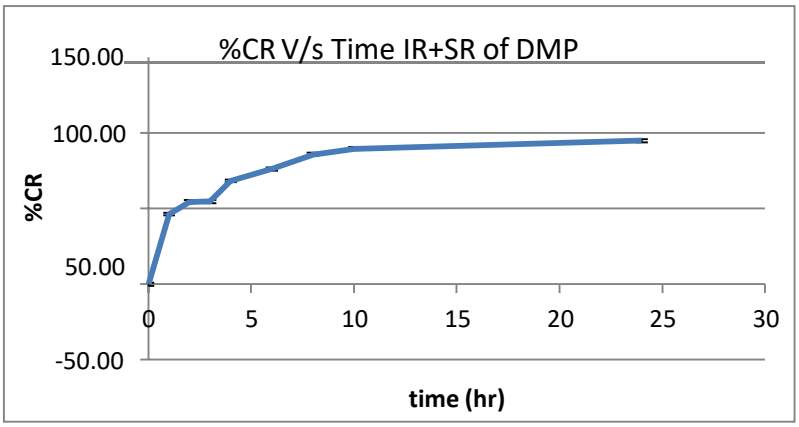

Figure no-1.4.1 Dissolution profile of DMP solid ODT

DMP ODT formulations were presented in succession to 6 healthy volunteers and the subjects were told to decide how much they liked or disliked the taste of the product and grittiness of product to mark the scales accordingly as shown in figure no.1. 4. 2 and 1.4.3.

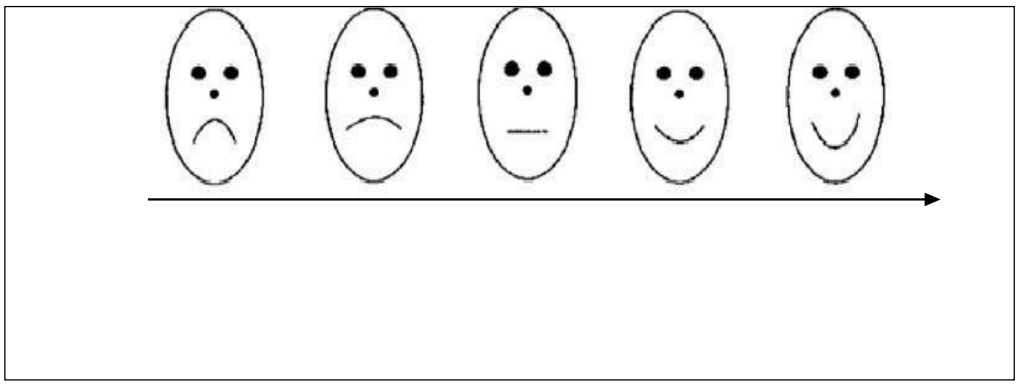

Figure no1.4.2 scale for the assessment of taste

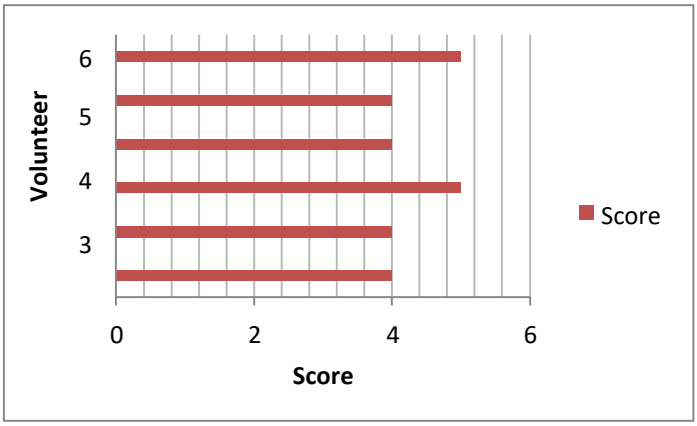

Figure no-1.4.3 subjective taste evaluation

Based on scores given by the volunteers as shown in figure no- 1.4.3, it was concluded that 66.66 % of volunteers rated it as very good and 33.33 % rated it as like extremely. The results indicated an acceptable taste of formulation, Also the formulation showed a good moth feel with no grittiness.

Table No-1.4.2 Mouth Feel Evaluation

Subject no	Grittiness felt (yes/no)
1.	No
2.	No
3.	No
4.	No
5.	No
6.	No

As seen from the results DMP ODT formulation compiled with desired criteria for friability, and disintegration time, however hardness was required to be set on a lower scale Also the drug release of ODT tablet was as expected with 46% release in 60 min and notless than 90% release in 24 hrs.

1.5 *In vitro* release kinetics

The DMP release data were fitted using the mathematical models and the linear regression was assessed. Table No -1.5.1 reports the results of the kinetic parameters (release rate constants and determination coefficients (R^2) applied to the data. The criteria for selectingthe most suitable mathematical model was established to be the highest value of R^2.

Table No -1.5.1 Kinetic parameters obtained after fitting the drug release data of DMP with five mathematical models

Mathematical Model	**Correlationcoefficient (R^2)**	**Diffusion release exponent (n)**
Zero-order	0.697	
First order	0.981	
Higuchi model	0.885	
Korsmeyer-Peppas model	0.719	**1.292**
Hixson-Crowell cuberoot law	0.903	

The *in vitro* release profile was applied to various kinetic models in order to find out the mechanism of drug release. The best fit model with the highest correlation coefficient was showed first order model as given in table no-1.5.1 The rate constants were calculated from the slope of respective plots. The data obtained was also put in Korsmeyer-Peppas model in order to find n value diffusion exponent, which describes the drug release mechanism. The value of 'n' was found to be 1.292 indicating that drug release was followed by anomalous (non-fiction) diffusion. First order equation describes release is dependent on the drug concentration.

1.6 Stability Studies:

The results of stability batch kept at 30℃± 2℃/65% RH ± 5%RH and 40℃ ± 2℃/75% RH ± 5% RH are given below in Table No. 1.6.1and 1.6.2.

Table no 1.6.1 The results of stability batch kept at 30℃± 2℃/65% RH ± 5% RH

Interval (days)	% CR atthe end of 2hrs.	% CR atthe end of 24hrs.	Disintegration time (sec)	Assay(%)	Hardness kg/cm^2
0	47.32	94.95	12	96.23	2.5
15	46.20	96.23	13	97.53	2
30	47.85	92.33	12	97.75	2.5
60	46.87	96.28	12	98.52	2.5
90	46.10	96.22	13	97.23	2

Table no:-1.6.2 The results of stability batch kept at 40℃ ± 2℃/75% RH ± 5% RH

Interval (days)	% CR atthe end of 2hrs.	% CR atthe end of 24hrs.	Disintegration time (sec)	Assay(%)	Hardness kg/cm^2
0	46.23	94.87	13	96.52	2
15	46.85	99.28	12	98.74	2.5
30	46.23	96.28	12	97.58	2.5
60	46.89	97.32	11	96.23	2.5
90	46.15	94.89	11	96.21	2.

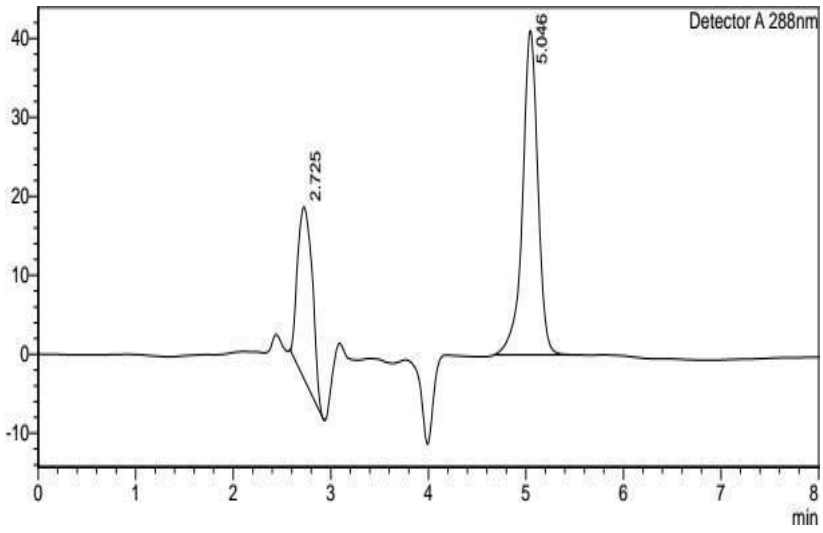

Figure No-1.6.1 standard peak of DMP10ug/ml

Retention time -6.0min Total peak area- 448234

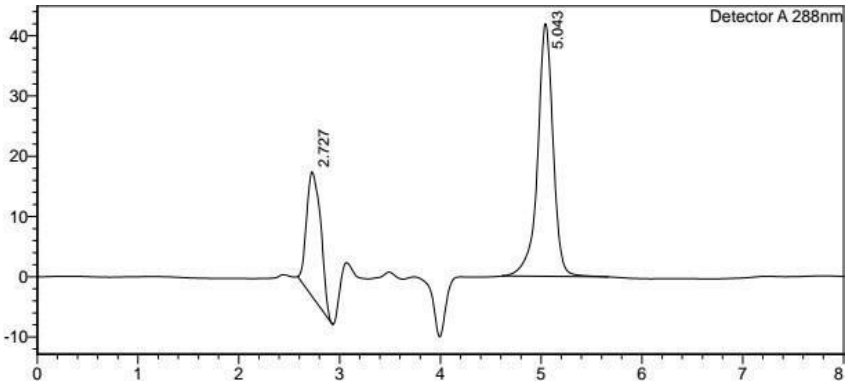

Figure No-1.6.2 DMP assay on 0th day

Retention time -6.0min Total peak area- 432584

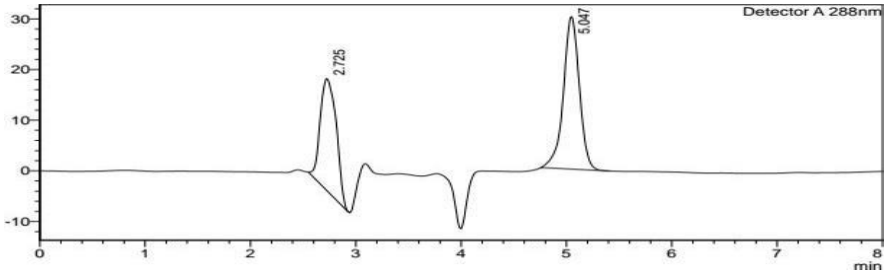

Figure No-1.6.3 DMP assay at 40℃ ± 2℃/75% RH ± 5% RH at the end of 3 months

Retention time -6.0min Total peak area- 42487

- As seen from Table no-1.6.1 and 1.6.2 and figure no-1.6.2 and 1.6.3 the formulation was found to be stable over 3months when kept at 30℃± 2℃/65% RH ± 5% RH and 40℃ ± 2℃/75% RH ±5% RH as per ICH conditions of stability studies.

- However, real-time stability studies at 25℃ ± 2℃/60% RH ± 5% RH for one year are requiredto be done to assign shelf life to the product.

- Thus stable, patient-compliant ODT formulation of DMP was successfully formulated with acceptable hardness, low friability , low disintegration time of 11-15sec and desired drug release of 46% in 1hr and not less than 90% in 24hrs.

RESULT AND DISCUSSION

- The present study was undertaken with an aim to formulate and evaluate Orodispersible tablets of Domperidone using direct compression method with a combination of SR microspheres and IR solid dispersion.

- While formulating ODT of domperidone various trials were carried out using different superdisintegrants namely crosscarmellose sodium, sodium starch glycolate and crosspovidone to achieve disintegration time of less than 30 sec but individually none of them have given the desired disintegration time so the combination of sodium starch glycolate and crosspovidone was used to achieve desired disintegration time of 11 to 15 sec.

- The result from the combination of SR microspheres and IR solid dispersion of domperidone showed a disintegration time of 6-8 sec among the O1, O2, O3, and O4, batch O4 produced the desired result.

- The domperidone ODT was evaluated for various parameters, the hardness of the tablet is 2=-2.5kg/cm2, disintegration time 11=-15 sec, friability 0.6=-1%, In vitro dispersion time 11=-13 sec and % release at the end of 1 hr was 46% and at end of 24 hrs was 94%. The domperidone.

- ODT formulations were presented to 6 healthy volunteers and the subjects told to decide the taste of the product and grittiness based on scores given 66.66% of individuals rated it very good and 33.33% rated like extremely.

- Stability studies were carried out of the optimized batch by keeping the product at

conditions as per ICH guidelines at 30c=-2c/65%RH=-5%RH and 40c=-2c/75%RH=-5%RH for 3 months. Thus the formulations were found to be stable over given conditions of storage.

- Thus patient patient-compliant orodispersible tablet [ODT] of domperidone was successfully formulated for once-a-day administration.

CONCLUSION:

Domperidone requires quick action for relieving emesis so it is suitable for orodispersible tablets. The study results reveal that O4 formulation exhibits faster disintegration i.e. 6-8 sec.

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REFERENCES:

(1) Lachman L, L. H. and K. J. L. The Theory of Practice of Industrial pharmacy,3rd Edn, Varghese Publishing House Bombay; 2002.
(2) Khar R.K., V. S. P. Targeted and Controlled Drug Delivery-Novel Carrier system,1 st Edn,2002,CBS publications,1-50.
(3) Jain N.K. Controlled and Novel Drug Delivery, CBS Publication 2002, 1-2,676-698.
(4) Gilbert B., Modern Pharmaceutics, 4th Edition, 501-513,
(5) R., M. 2005, Design and Evaluation of 1 and 3 Layer Matrices of Verapamil for Sustained Release, AAPS Pharm Sci Tech; 6(4) Article 7.
(6) Chien Y.W. Novel Drug Delivery System, IInd Edn, Revised and Expanded 1982, 12, 139-140.
(7) Aulton M.E. Hand Book of Pharamaceutics, Edition 2001, 291-295.
(8) Thomas W., J. R. Controlled- Release Drug-Delivery Systems, Chapter-47 in Remington: The Science and Practice of Pharmacy, 20th Edition, Vol-1, 903.
(9) Bramhankar D.M. and Jaiswal S.B. 1995, Biopharmaceutics and Pharmacokinetics. A Treatise, Vallabh Prakashan, 1 St Edn, 335-337, 347- 352.
(10) Remington, The Science andPractice of Pharmacy, 20th Edn, vol.I, 903-913.
(11) Hallouard, F.; Mehenni, L.; Lahiani-Skiba, M.; Anouar, Y.; Skiba, M. Solid Dispersions for Oral Administration: An Overview of the Methods for Their Preparation. Curr. Pharm. Des. 2016, 22 (32), 4942–4958.
(12) Nagar, P.; Singh, K.; Chauhan, I.; Verma, M.; Yasir, M.; Khan, a; Sharma, R.; Gupta, N. Orally Disintegrating Tablets: Formulation, Preparation Techniques and Evaluation. J. Appl. Pharm. Sci. 2011, 1 (4), 35–45.
(13) Pandey, P. Dahiya, M. Oral Disintegrating Tablets: A Review. Int. J. Pharma Res. Rev. IJPRR 2016, 5 (51), 50–62.
(14) Velmurugan, S.; Vinushitha, S. Oral Disintegrating Tablets: An Overview. Int. J. Chem.Pharm. Sci. 2010, 1 (2), 1–12.
(15) Nayak, A. K.; Manna, K. Current Developments in Orally Disintegrating Tablet Technology. J. Pharma Educ. Res. 2011, 2 (1), 21–34.

(16) Mizumoto, T.; Masuda, Y.; Yamamoto, T.; Yonemochi, E.; Terada, K. Formulation Design of a Novel Fast-Disintegrating Tablet. Int. J. Pharm. 2005, 306 (1–2), 83–90.
(17) Shukla, D.; Chakraborty, S.; Singh, S.; Mishra, B. Mouth Dissolving Tablets II: An Overview of Evaluation Techniques. Scientia Pharmaceutica. 2009, pp 327–341.
(18) Deshmukh, V. N. Mouth Dissolving Drug Delivery System: A Review. Int. J. Pharm Tech Res. 2012, 4 (1), 412–421.
(19) Mizumoto, T.; Masuda, Y.; Yamamoto, T.; Yonemochi, E.; Terada, K. Formulation Design of a Novel Fast-Disintegrating Tablet. Int. J. Pharm. 2005, 306 (1–2), 83–90.
(20) Shukla, D.; Chakraborty, S.; Singh, S.; Mishra, B. Mouth Dissolving Tablets II: An Overview of Evaluation Techniques. Scientia Pharmaceutica. 2009, pp 327–341.
(21) Rathod, S.; Phansekar, M.; Bhagwan, A.; Surve, G. A Review on Mouth Dissolving Tablets. Indian Drugs. 2013, pp 5–14.
(22) Parakh, S. R.; Gothoskar, A. V. A Review of Mouth Dissolving Tablet Technologies. Pharm. Technol. 2003, 27 (11), 92–100.
(23) Fernandes Tavares, D. F.; Espada García, J. I.; Martín Sabroso, C.; Gil Alegre, M. E.; Torres Suárez, A. I. Disintegrating Tablets: Therapeutic Advantages and ExaminationTechnologies. Ars Pharm. 2009, 50 (3).
(24) Divya, P.; Nagaraja, T. S.; Yogananda, R.; Pharmacy, S. J. M. C. An Over View on Patented Technologies of Orodispersible Tablets. Int. J. Drug Discov. Herb. Res. 2013,3 (1), 556–564.
(25) N., S.; L., G.; P., K. Orally Disintegrating Tablets: A Review. International Journal of Advances in Pharmaceutical Research. 2012, pp 1222–1228.
(26) Pfister, W. R. .; Ghosh, T. K. Orally Disintegrating Tablets, Products, Technologies, and Development Issues. Pharm. Technol. 2006, 29 (10), 136–150.
(27) S., K.; S.K.R., G. Fast Dissolving Tablets (FDTs): Current Status, New Market Opportunities, Recent Advances in Manufacturing Technologies and Future Prospects. Int. J. Pharm. Pharm. Sci. 2014, 6 (7), 22–35.
(28) Deshmukh, V. N. Mouth Dissolving Drug Delivery System: A Review. Int. J. PharmTech Res. 2012, 4 (1), 412–421.