WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL RESEARCH

Review Article

2025
Volume: 02
Issue: 07
Page: 09-19

FORMULATION AND EVALUATION OF IMMEDIATE RELEASE TABLETS OF DOPAMINE ANTAGONIST

***[1]MALOTH ASHOK, [2]BANOTH PUJITHA, [3]YETTI PAVANI, [4]SRAVANI KOILAMUDI, and [5]DR. SAMBASIVA RAO (M. PHARM Phd)**

KHAMMAM COLLEGE OF PHARMACY.

Received: 21 April 2025 **Revised: 12 May 2025** **Accepted: 01 June 2025**

Corresponding Author: MALOTH ASHOK
Address: KHAMMAM COLLEGE OF PHARMACY.
Email ID: malothashoknaik766@gmail.com,

ABSTRACT

This study presents the formulation and evaluation of an immediate-release tablet of metoclopramide hydrochloride, a dopamine D_2 receptor antagonist widely used for the management of nausea, vomiting. The primary objective was to develop a tablet that ensures rapid disintegration and dissolution, enhancing the onset of therapeutic action. Formulation development involved direct compression and wet granulation techniques using excipients such as starch, lactose, propyl paraben, methyl paraben, talc, magnesium stearate and disintegrants like sodium starch glycolate The tablets were evaluated for physical parameters including hardness, friability, weight variation, disintegration time, and in vitro drug release. Among the formulations, the batch containing as a superdisintegrant sodium starch glycolate exhibited the best performance, with a disintegration time under 2 minutes and over 85% drug release within 30 minutes. The drug-excipient compatibility was confirmed through FTIR analysis, and the optimized batch showed acceptable stability under accelerated conditions. The study concludes that an effective immediate-release tablet of metoclopramide can be formulated with optimal disintegration and release profiles suitable for rapid relief of gastrointestinal symptoms.

KEYWORDS: Immediate release Tablets, Meclopramide.

INTRODUCTION

Immediate Release (IR) Tablets are oral solid dosage forms designed to disintegrate and release the active pharmaceutical ingredient (API) rapidly after administration**.**

Figure: 1

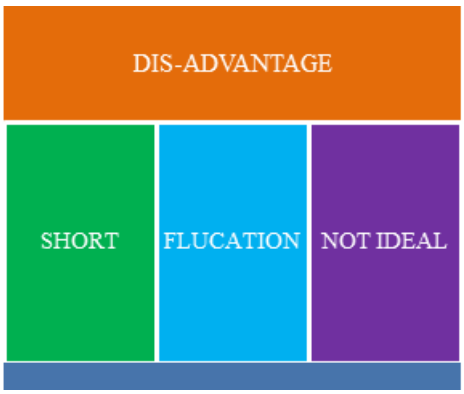


Figure: 2

Dopamine antagonists are drugs that bind to dopamine receptors (mainly D2 receptors) and inhibit the physiological actions of dopamine, either centrally (in the brain) or peripherally (in other tissues). Dopamine antagonists are frequently formulated as immediate release tablets to ensure a rapid onset of action**,** especially in conditions where fast symptom control is critical**.** Here's a breakdown of the reasons Example: Metoclopramide

MATERIAL METHODS:

Metoclopramide Hydrochloride, Starch, Lactose, Methyl paraben, Propyl paraben, Talc, Magnesium Stearate, Sodium starch glycolate

Tablet Compression Machine, Friability Tester, Tablet Hardness Tester, Bulk density apparatus, Dissolution Apparatus

Formulation:

Pre-Compression Parameters in Tablet Formulation

Parameter	Description	Purpose
1. Bulk Density	Mass of powder per unit volume without tapping	Indicates how well the powder fills the die cavity
2. Tapped Density	Density after mechanical tapping	Assesses flow properties and compressibility
3. Compressibility Index (Carr's Index)	$\frac{\text{Tapped-bulk}}{\text{bulk}}$ X 100	Measures flowability
4. Hauser's Ratio	$\frac{\text{Tapped density}}{}$	Flow indicator (values >1.25 indicate poor

	Bulk density	flow)
5. Angle of Repose	Angle formed by powder cone	Assesses flow characteristics
6. Moisture Content	Measured via LOD or Karl Fischer titration	Prevents sticking or degradation during compression
7. Particle Size Distribution	Measured via sieve analysis or laser diffraction	Influences flow, uniformity, and dissolution
8. Flow Rate	Rate at which powder flows through an orifice	Essential for die filling consistency
9. Blend Uniformity	Assesses drug content uniformity in the powder blend	Ensures dose accuracy
10. Lubrication Efficiency	Evaluates the effectiveness of lubricants like Mg stearate	Affects tablet ejection and integrity

ANGLE OF REPOSE

Procedure: The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The angle of repose was calculated using the following formula:

- Tan θ = h / r Tan θ = Angle of repose
- h = Height of the pile,

  r = Radius of the cone base

- the angle of repose of powder it calculated without the added of glidants
- The glidants selected is talc
- The concentration are 1%,2%,3% ,4% and 5%
- Add the gradient is low concentration to the powder and mix it
- Estimate the angle of repose which blent in the trails 1
- Calculated the angle of repose average
- Repeat the same procedure for the concentration of glidants

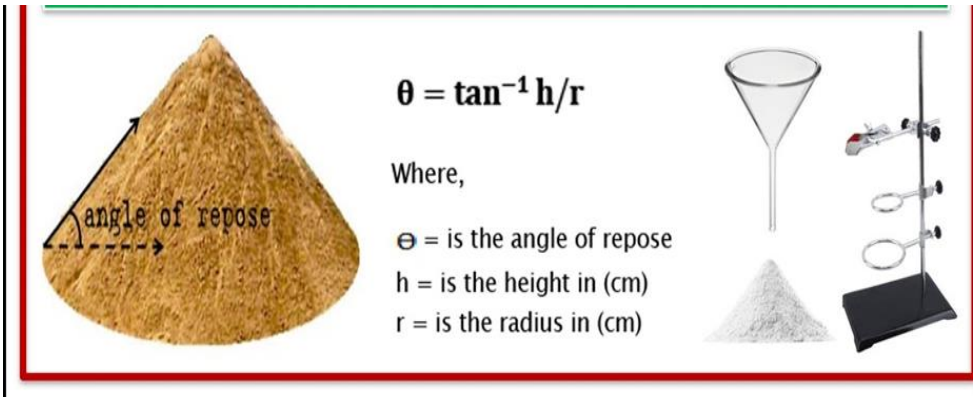


Figure: 3

- **Tapped density procedure**

- Take about 50 to 100 grams of the powder.
- Record the weight (m) accurately.
- Gently fill the 100 mL cylinder with the powder.
- Do not shake or tap during filling.
- Note the bulk volume (V_0) of the powder (in mL).
- Place the cylinder on the tapped density tester.
- Tap 500 times, and then check the volume.
- Tap another 750 times (total 1250) and check again.
- If volume changes <2 mL between readings, stop

1. PHARMACOPOEIAL TESTS

1. Content of active ingredient.

2. Uniformity of weight.

3. Uniformity of content.

4. Uniformity of container contents.

5. Disintegration.

6. Dissolution.

7. Uniformity of dispersion (for dispersible tablets only).

The first four standards are designed to control the amount of active drug in the tablet and the number of tablets in a pack while the last three control the ability of the drug to be released from the tablet.

3. **Uniformity of content**: In this test, ten tablets are assayed individually by the method specified in the individual monograph or by means of any other suitable analytical method. The tablets comply if not more than one tablet is outside the range of 85% to 115% of the average value or if none of the tablets are outside the 85% to 115% range but none outside the 75%-125% limits, then a further 20 tablets are assayed. This test is not applicable to coated tablets other than film coated tablets and to tablets that are required to comply with the test for content uniformity of active ingredients.

Disintegration test: This test determines whether tablets disintegrate within the prescribed time when placed in a liquid medium under the prescribed experimental conditions. The test is not applicable for modified release tablets and tablets for use in the mouth. Tablets for

which the dissolution test is prescribed in the individual monograph are not required to comply with this test. The apparatus used for the test consists of a basket rack assembly supporting six glass tubes of specified dimensions, each tube being closed at the lower end by a screen of 2 mm nominal aperture. For the test, one tablet is placed in each of six tubes and if specified, a disc is added to each tube

The tubes are raised and lowered (28-32 times per minute) in a bath of fluid maintained at 37=2°C contained in a suitable vessel, preferably a 1000 ml beaker. The fluid is water unless otherwise specified and for most uncoated tablets, the permitted disintegration time is 15minutes. Tablets are said to have disintegrated if no fragment (other than fragments of coating) remains on the screen or, if particles remain, they are soft without a un wetted core. If one or two tablets fail to disintegrate, the test is repeated on 12 additional tablets. Not less than 16 of the total of 18 tablets tested should disintegrate.

The test is modified slightly for tablets other than uncoated tablets. For film coated tablets, the specified disintegration time is 30 minutes while for other coated tablets, it is 60 minutes. If coated tablets other than film-coated tablets fail to disintegrate in water, the same may be replaced with 0.1M hydrochloric acid. Enteric coated tablets should not disintegrate in 120 minutes when tested using 0.1M hydrochloric acid as the fluid medium and should disintegrate within 60 minutes when subsequently tested in mixed phosphate buffer PH 6.8. Dispersible and soluble tablets must disintegrate in water at 24° to 26° within three minutes, and effervescent tablets must disintegrate within five minutes when tested in cold water at 20°-30° contained in a 250ml beaker.

6. DISSOLUTION TEST

The Indian pharmacopoeia permits two types of apparatus, the paddle apparatus and the rotating basket apparatus for dissolution testing of tablets. The basket apparatus consists of a cylindrical steel basket into which the tablet to be tested is placed. The assembly is then immersed in the dissolution fluid contained in a cylindrical glass vessel and rotated at the specified speed. The quantity and type of dissolution fluid to be used is specified in the individual monographs and has to be maintained between 36.5° and 37.5° C. When using the paddle apparatus, the tablet is allowed to sink to the bottom of the vessel prior to the rotation of the paddle. A suitable device such as a wire or glass helix may be used to prevent floatation of tablets. Aliquot samples of the dissolution medium are withdrawn at specified intervals and analyzed for the drug content. Except in the case of single sampling, an equal

volume of the dissolution medium is immediately replaced to the vessel. The amount of the drug dissolved is calculated as percentage of the labelled claim. The test is carried out in stages, the acceptance criteria for the test being as specified in Table 15.2. If the results do not conform to the requirements at stage S1, testing is continued with additional tablets through stages S2 and S3 unless the result conform at stage S2.

UNIFORMITY OF DISPERSION:

S. No	Ingredi ents (in mg)	Formulations								
		F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F**	**F9**
1	Metoclopramid e Hydrochloride	10	10	10	10	10	10	**10**	10	10
2	Starch	54.2	59.2	64.2	54.2	59.	64.2	**54.2**	52.2	64.2
3	Lactose	29.5	24.5	19.5	30	4.5	19.2	**29**	24	
4	Methyl paraben sodium	0.18	0.18	0.18	0.18	0.18	0.18	**0.18**	0.18	0.18
5	Propyl paraben sodium	0.12	0.12	0.12	0.12	0.12	0.12	**0.12**	0.12	0.12
6	Starch for paste	4	4	4	4	4	4	**4**	4	4
7	Talc	1	1	1				**1**	1	1
8	Magnesium stearate	1	1	1	1	1	1	**1**	1	1
9	Sodium starch glycolate				0.5	1	1.5	**0.5**	1	1.5
10	Total weight (in mg)	100	100	100	100	100	100	**100**	100	100

This test is applicable only to dispersible tablets and evaluates the uniformity of the dispersed particles. For the test, two tablets are placed in 100ml of water and stirred gently until the dispersion is complete. A smooth dispersion should be obtained which should pass through a sieve screen with a nominal mesh aperture of 710 µm (sieve number 22).

2. NON-PHARMACOPOEIAL TESTS

A wide variety of non-pharmacopoeia tests are applied to tablets, both as in-process controls and as part of quality assurance programmers. Tests like individual tablet weights, thickness and diameters are routinely measured. Other non-pharmacopoeia tests include:

HARDNESS: Hardness or crushing strength is a measure of the mechanical strength of the tablet. The test measures the compressional force which, when applied diametrically to the tablet, just causes it to fracture. A number of commercial instruments are available for measurement of the same and these works on similar principles.

Examples include Monsanto and strong Cobb hardness testers. A moving plunger presses on the edge of the tablet, which is held either vertically or horizontally, and the applied force is measured by a suitable means. In the Monsanto hardness tester, the force is applied via a screw-driven spring and the force required to break the tablet is directly read from the

calibrated scale. In case of Pfizer tester, the tablet is placed between the jaws of the tester and a gripping action transfers the force to the tablet

The reading is read from the pressure dial fitted with the apparatus. It has been shown that the rate at which force is applied can affect the measured value of the crushing strength, and so more accurate results are obtained if the force is applied at a uniform rate by mechanical or electromechanical means rather than manually. Examples in this category include Schleuniger, CT40 and Eureka testers

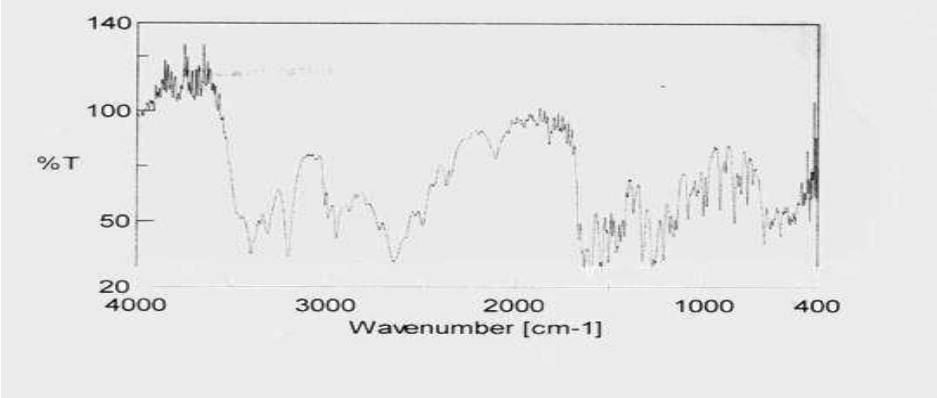
FRIABILITY: Friability test is performed to assess the resistance of the tablet to abrasion and shock which may be encountered during handling and transportation. The most common equipment used for the test is the Roche Friabilator. It consists of a circular plastic chamber divided into 2 to 3 compartments. The chamber is made to rotate at a speed of 25 rpm. With each rotation the tablets drop from a height of 15cm. Weighed samples of tablets are placed in the chamber and subjected to a standardised level of agitation, usually 100 revolutions and are weighed again. Friability is expressed as percentage weight loss and should normally be less than 1% w/w.

Formulation of Metoclopramide Hydrochloride Tablets

Characterization of Drug

Test	**Specification**	**Result**
Colour	White	Confirms
Odour	Odourless	Confirms
Physical State	Crystalline Powder	Confirms
Melting point	182^0C-185^0C	183^0C
Thin Layer Chromatography	Test Preparation is more intense than Standard Preparation	Confirms
pH of Water Solution	4.5- 6.5	Confirms

The FTIR Spectrum of Metoclopramide Hydrochloride



Spectral assignment of metoclopramide hydrochloride

S. No	Functional Group	Frequency (cm^{-1})
1	C=O	1600
2	O-H, N-H	3200, 3300,3340, 3400,3460.
3	NH (Amide)	1540
4	C-O	1270
5	C-Cl	700

Pre-compression parameters

Parameters	Bulk Density (g/cm^3)	Tapped density (g/cm^3)	Carr's Index (%)	Angle of Repose (θ)	Hausner Ratio
F1	0.59	0.75	12	25.25	1.2
F2	0.63	0.73	13.69	26.27	1.15
F3	0.61	0.71	14.08	27.32	1.16
F4	0.60	0.70	13.79	26.65	1.16
F5	0.62	0.71	12.67	28.42	1.14
F6	0.64	0.74	13.51	29.96	1.15
F7	0.63	0.72	12.5	25.07	1.14
F8	0.66	0.76	13.15	26.56	1.15
F9	0.64	0.75	14.66	27.60	1.17

Particle size determination of Metoclopramide hydrochloride

Sieve No	Microns	Wt of drug + sieve (g)	Wt of the drug retained (g)	% of drug retained	Cumulative% of drug (µ) retained
#18	1000	389.7	3.7	18.5	18.5
#50	297	360	16	80	98.5
#70	210	331.3	0.3	1.5	100
#120	125	340	0	0	0
#140	105	338	0	0	0
#170	88	325	0	0	0
#200	74	320	0	0	0
#200 Pass		460	0	0	0
			20	100	

Evaluation of Post Compression Parameter							
Formulation Code	Hardness (kg/cm^2)	Friability (%)	Weight variation Test (%) ±S.D	Uniformity of Drug Content (%) ± S.D	Thickness of Tablets	Wetting Time (Seconds)	Disintegration Time (sec)
F1	3.7	0.69	102.3±0.15	98.94±0.25	2.7	36	42±0.73
F2	3.9	0.71	101.2±0.66	99.46±0.24	2.7	39	51±0.58
F3	4.2	0.68	98.9±0.301	99.65±0.33	2.7	45	55±0.65

F4	3.6	0.71	100.6±0.23	99.45±0.12	2.7	38	34±0.59
F5	3.5	0.74	102.1±0.18	99.25±0.31	2.7	40	41±0.85
F6	4.1	0.72	101.3±0.26	99.52±0.06	2.8	43	45±0.71
F7	3.7	0.69	101.6±0.22	99.86±0.39	2.7	35	30±0.64
F8	3.9	0.71	99.5±0.18	99.78±0.35	2.7	39	32±0.48
F9	4.1	0.70	100.8±0.21	99.42±0.14	2.8	42	35±0.40

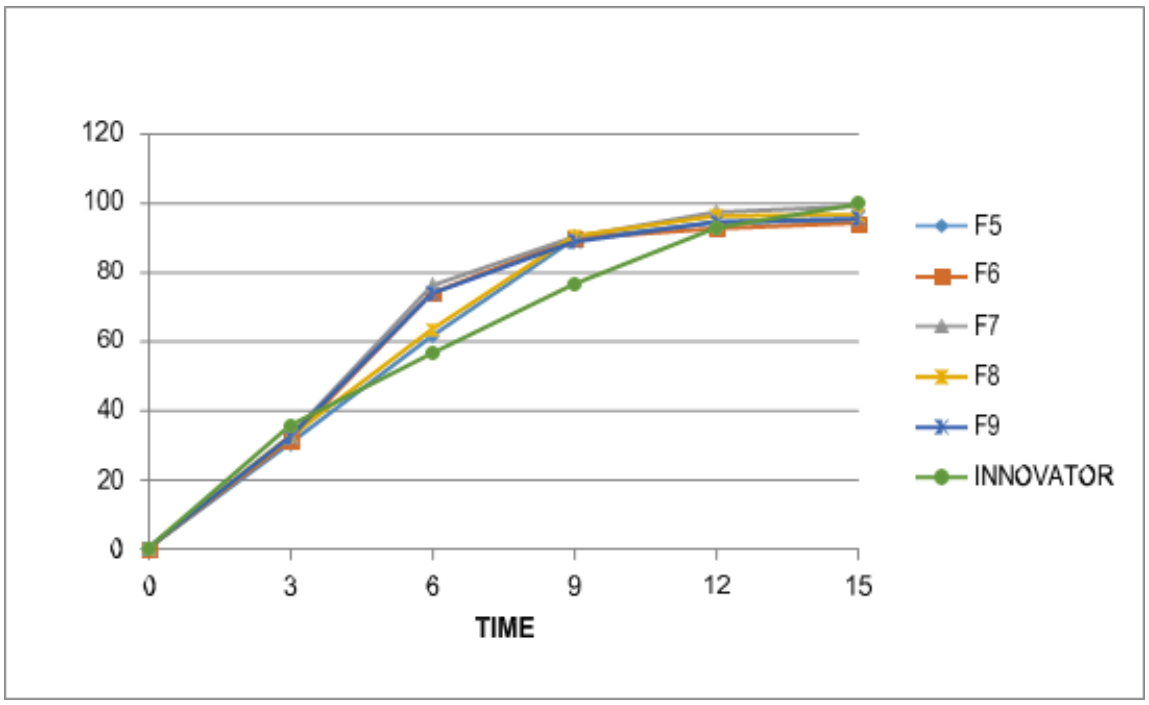
Drug Release Study

In-vitro Drug release profile of various formulation and innovator

Time (Min)	Formulation					
	F5	F6	F7	F8	F9	Innovator
3	30.24	31.11	32.46	32.24	32.18	35.50
6	61.18	73.56	76.11	63.18	73.56	56.40
9	89.12	89.38	90.18	90.12	88.56	76.40
12	93.92	92.18	97.34	95.92	94.24	92.68
15	94.42	93.76	99.10	96.26	95.16	99.58

Stability studies of optimized formulation F7 at 25^0C/ 60% RH.

S. No	Evaluation Parameters	Observation		
		Initial	1 Month	2 Months
1	Physical Appearance	White	White	White
2	Weight variation (%)	101.6±0.22	101.9±0.22	101.9±0.22
3	Friability (%)	0.69	0.71	0.71
4	Thickness (mm)	2.7±0.051	2.7±0.046	2.7±0.056
5	Hardness (kg/cm^2)	3.70±0.18	3.68±0.27	3.68±0.29
6	Disintegeration Time (sec)	30±0.64	28±0.54	28±0.59
8	Drug content (%)	99.86±0.25	99.85±0.15	99.85±0.23



Stability studies of optimized formulationF7 at 40^0C/ 75% RH.

S. No	Evaluation Parameters	Observation		
		Initial	1 Month	2 Months
1	Physical Appearance	White	White	White
2	Weight variation (%)	101.6±0.22	101.8±0.35	101.8±0.22
3	Friability (%)	0.69	0.71	0.72
4	Thickness (mm)	2.7±0.053	2.7±0.42	2.7±0.048
5	Hardness (kg/cm^2)	3.70±0.21	3.65±0.26	3.65±0.29
6	Disintegeration Time (sec)	30±0.62	28±0.54	28±0.60
7	Drug content (%)	99.86±0.28	99.86±0.35	99.85±0.39

Stability study of In-vitro dissolution of optimized formulation

Time (Min)	Cumulative% Drug Release			
	Stored at 25^0C Temperature		Stored at 40^0C Temperature	
	After 1 Month	After 2 Months	After 1 Month	After 2 Months
3	31.42	31.08	31.38	30.96
6	74.85	74.52	74.45	74.36
9	89.18	88.98	88.84	88.53
12	96.34	96.12	96.38	95.97
15	98.98	98.97	98.94	98.91

Comparison of Formulated and Marketed Tablets

Sl. No	Parameters	F7	Marketed Tablet
1	Average weight of Tablet(mg)	101.6±0.22	140±0.58
2	Hardness (kg/cm2)	3.7±0.16	3.9±0.21
3	Friability (%)	0.69	0.26
4	Wetting Time (%) ±S.D	35±0.64	32±0.58
5	Uniformity of Drug Content (%) ± S.D	99.86±0.32	99.80±0.28
6	Disintegration Time (sec) ± S.D	30±0.62	25±0.53
7	Thickness(mm)	2.7±0.043	2.2±0.064
8	Drug Release (%)	99.58	99.10

CONCLUSION

The Present study was conducted to formulate and evaluate the immediate release tablet of Metoclopramide hydrochloride. Pre-formulation study was carried out initially with study of selection of super disintegrants was done and different formulations were prepared using sodium starch glycolate and starch as disintegrants. Immediate release tablet of Metoclopramide hydrochloride was prepared by wet granulation method. The tablet disintegrated rapidly and has an acceptable friability and hardness. *In vitro* drug release from the tablets shows significantly improved drug dissolution. Hence it could be concluded that the super disintegrant based on immediate release tablet of Metoclopramide hydrochloride would be quite effective in emesis, providing quick onset of action on administration.

1. REFERENCES

1. Alfred N Martin, Patrick J Sinko: Martins Physical pharmacy and pharmaceutical science: physical chemical and bio pharmaceutical Principles in the pharmaceutical science (Lippincott Williams and Wilkins): Sixth Edition.
2. GS Banker; NR Anderson, Tablets in: The theory and practice of industrial pharmacy 3rdEd. Varghese publishing house, Mumbai, 1987; 314-324.
3. EL Parrot. Compression in pharmaceutical dosage form, tablets. Marcel Dekker Inc. New York, 1990; 2: 153-182.
4. Lehman, HA Liberman, L.J. Kanig, theory and practice of industrial pharmacy 3rd Ed.vargese publication house, Mumbai, 1990; 293-294; 329-335.
5. Ansel's Pharmaceutical dosage form and Drug Delivery systems. Ninth Edition.
6. Anisul Quardir, Karl Kolter 2006. A comparative study of current Super disintegrant's, pharmaceutical technology.
7. Shyamala, B. & Narmada, G. Y. Rapid dissolving tablets: A novel dosage form, The Indian Pharmacist, 2002; 13: 9–12.
8. Parikh DM. Theory of Granulation, Handbook of Pharmaceutical Granulation Technology. 2nd Ed., 2005: 7-33.
9. Chien YW. Novel drug delivery systems. Marcel Dekker Inc. 2nd Ed., 1992; 139-40.
10. Leah E, Appel DT, Friesen JE, Byers MD, Crew BC, Hancock SJ, Schadtle. Immediate release dosage forms containing solid drug dispersion. United States Patent No. 424465; 2002.
11. T Gosh; AGosh. Int. J. of Phar. and Phar Sci., 2011; 3(1): 43-49.
12. R Margret;B Jayakar; APasupathi;BL Maurya.J. of pharm. Res., 2009; 2(6): 1039-1041.
13. S Sahoo; B Mishra; P Biswal; O Pand; S Mahapatra; G Jana. Drug invention today, 2010; 2: 130-133.
14. LH Reddy; BR Gosh.Int. J of Pharma Sci., 2002; 331-336
15. A Review on New Generation Orodispersible Tablets and Its Future Prospective, Tanmoy Ghosh, Amitava Ghosh and Devi Prasad, International Journal of Pharmacy and Pharmaceutical Sciences, 2011; 3(1): 1491.

Debjit Bhowmik, Chiranjib.B, Krishnakanth, Pankaj, R. Margret Chandira