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Research Article

Formulation And Evaluation Of Mouth Dissolving Tablet Of Prochlorperzine Maleate

Arun Kumar Pandey*., Pavan Kumar Rawat.,C.K.Tyagi.,Sunil Shah.

Department of Pharmaceutics

Sri SatyaSai University of Technology and Medical Sciences, Sehore, Madhya pradesh.

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Abstract

Rapidly disintegrating oral tablet are gaining popularity over conventional tablets due to their convenience in administration and suitability for patients having dysphagia. Moreoverno water is required for swallowing the tablets and hence suitable for geriatric, pediatric and traveling patients. Superdisintegrants like 4 % & 8 % (Croscarmellose Sodium, Crospovidone and sodium starch glycolate), Binder (Povidone K-30), Diluent (Starlac) along with sweetening agent (aspartame) were used in the formulation of tablets by direct compression technique. The granules were evaluated for angle of repose, bulk density, tapped density, carr's index and hausner's ratio. The tablets were evaluated for hardness, friability, water absorption ratio, in-vitro disintegration time (DT) and *in vitro* drug release. In-vitro release studies were performed using USP XXIII apparatus-2 (paddle method) in 900ml of pH 1.2 at 50rpm. Maximum % drug release (97.82 %) and minimum disintegration time (23.67 second) were observed with formulation F3 comprising of crospovidone prepared by direct compression technique.

Key words: Prochlorperzine maleate, Croscarmellose Sodium, Crospovidone, Sodium starch glycolate.

INTRODUCTION

Formulation of a convenient dosage form for administration, by considering swallowing difficulty and poor patient compliance, leads to development of rapidly disintegrating oral tablets. This are also called mouth dissolving, mouth disintegrating and fast melt system. This disintegrates in the mouth in seconds without chewing and the need of water which is advantageous mainly for pediatrics, geriatrics and patients having difficulty in swallowing tablets and capsules[1]. Prochlorperzine maleate is a H2 receptor antagonist[2]. A thiazole ring containing H2 blocker which binds tightly to H2 receptors and exhibits longer duration of action despite a elimination[3]. Prochlorperzine maleate after oral administration has an onset of effect within 1 hr and inhibition of gastric secretion is present for the next 10-12 hrs[4]. Elimination is by renal and metabolic route. It is therefore important to decrease the dose of the drug for patient with kidney or renal failure[2,4]. Prochlorperzine maleate not only decrease both basal, food-stimulated acid secretion by 90% or more but also promotes healing of duodenal ulcer[5,6].Disintegrant plays a major role in the disintegration and dissolution of rapidly disintegrating oral tablets. Superdisintegrants provide quick disintegration due to combined effect of swelling and water absorption. Due to swelling of Superdisintegrants, the wetted surface of the carrier increases, this promotes the wettability and dispersibility of the system thus enhancing the disintegration and dissolution[7].In the present study an attempt had been made to prepare rapidly disintegrating oral tablets of Prochlorperzine maleate in the oral cavity with enhanced dissolution rate and hence improved patient compliance. The basic approach used in the development of rapidly disintegrating oral tablets is the use of superdisintegrants like croscarmellose sodium and crosspovidone and Sodium starch glyolate which provide instantane-

ous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva. These systems may offer superior profile with potential mucosal absorption, thus increase the drug bioavailability [8].

Materials and Method:

Prochlorperzine maleate obtained as gift sanplefromShreya Life sciences Pt. Ltd. Aurangabad.Other chemicals were used in study were of analytical grade and were purchased from Loba Chemicals Mumbai.

Method:

Rapidly disintegrating oral tablets of Prochlorperzine maleate were prepared by direct compression method according to the formula given intable. All the ingredients were passed through 40 mesh sieve separately. The drug and diluents was mixed by small portion of both each time and blending it to get a uniform mixture kept aside. Then magnesium stearate was passed from 60 mesh sieve then mixed with above mixture.Prepared blend was compressed (6.35mm FFBE Punchbreakline on one side and plain on other side) using Cadmach Machine.

Precompression Studies:

Angle of Repose (Θ) [9]:

The frictional forces in a loose powder can be measured by the angle of repose. It is an indicative of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane.

$$\Theta = \tan^{-1}(h/r)$$

Where,**Θ** is the angle of repose, h is the height in cms, r is the radius in cms.

Method:

The powder mixture was allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of powder formed. Care was taken to see that the powder particles slip androll over each other through the sides of the funnel. Relationship between angle of repose and powder flow property.

Bulk density: [10].

Bulk density is the ratio between a mass of granules and its bulk volume. It is expressed by gm/cc.

Method:

A bulk density (g/ml) is determined by pouring presieved (40-mesh) bulk drug in to a graduated cylinder via a large funnel and measuring the volume and weight.

$$\text{Bulk Density} = \frac{\text{Mass of powder (M)}}{\text{Bulk volume of the powder (V)}}$$

Tapped Density

Tapped density is the ratio between mass of granules and volume of the granules after tapping; it is expressed by gm/cc.

Method:

Tapped density is determined by placing a graduated cylinder containing a known mass of drug or formulation on a mechanical tapper apparatus, which is operated for a fixed number of taps (100) until the powder bed volume has reached a minimum.

$$\text{Tapped Density} = \frac{\text{Weight of powder}}{\text{Tapped volume of the powder}}$$

Carr's index[11]:

This was measured for the property of a powder to be compressed; as such they are measured for relative importance of interparticulate interactions. Carr's index was calculated by following equation-

$$\text{Carr}'\text{s index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Hausner ratio:

Hausner ratio was calculated by following equationHausner's ratio $= \frac{\text{Tapped density } (\rho\text{Bmax})}{\text{Bulk density } (\rho\text{Bmin})}$

Where, (ρBmax) = tapped density, (ρBmin) = bulk density.

Table no.1: **Composition of Rapidly disintegrating oral tablets of Prochlorperzine maleate (Weight in mg)**

Sr.No	Ingredients (mg/tab)	F_1	F_2	F_3	F_4	F_5	F_6
1	Prochlorperzine Maleate	5.0	5.0	5.0	5.0	5.0	5.0
2	Mannitol (Pearlitol SD 200)	27.0	27.0	27.0	27.0	27.0	27.0
3	Microcrystalline Cellulose PH102	54.45	54.45	54.45	54.45	54.45	54.45
2	Croscarmellose Sodium	10	20	-	-	-	-
3	Crospovidone	-	-	10	20	-	-
4	Sodium starch Glycolate	-	-	-	-	10	20
5	Povidone K-30	2	2	2	2	2	2
6	Starlac	209	199	209	199	209	199
7	Aspartame	5	5	5	5	5	5
8	Magnesium Stearate	4	4	4	4	4	4
	Total weight	250	250	250	250	250	250

Postcompression Studies:

Tablet description[10]:

The general appearance of a tablet, its visual identity and overall "elegance", is essential for consumer acceptance.

Thickness and diameter:

The thickness of individual tablets was measured with a micrometer, which permits accurate measurement and provides information on the variation between tablets. The tablet thickness should be controlled within a ± 5% variation of a standard value.

Hardness:

Tablet requiresa certain amount of strength, or hardness and resistance to friability, withstand mechanical shock of handling in manufacture, packaging, and shipping. Tablet hardness is also called as *crushing strength*. Monsanto hardness tester was used to check the hardness of the tablets.

Friability:

The friability of the tablets was measured in a Roche friabilator (Camp-bell Electronics,

Mumbai, India).Tablets of a known weight (W0) or a sample of tablets are dedusted in a drum for a fixedtime (100 revolutions)and weighed (W) again. Percentage friability was calculated from theloss in weight as given in equation asbelow. The weight loss should not be more than 1%w/w[12].

$$\% \text{ Friability} = (W0-W)/ W0 \times 100$$

Weight Variation Test

To study weight variation, 20 tablets of each formulation were weighed using an electronic

balance (Electro lab, India), and the test was performed

according to the official method.[13]

Determination of drug content[14]:

Twenty tablets from each formulation were crushed. Thepowder equivalent to 100mg of Prochlorperzine maleate was weighed and dissolved in acidic buffer pH 1.2 in 100mlstandard flasks. From this, suitable dilution was preparedand the solution was analyzed at 265nm using UV doublebeam spectrophotometer using pH 1.2 asblank.

Disintegration Test[15]:

Disintegration of rapidly disintegrating oral tablets is achieved in the mouth owing to the action of saliva; however amount of saliva in the mouth is limited. A modified method was used to determine disintegration time of the tablets. A cylindrical vessel was used in which 10 mesh a screen was placed in such a way that only 2 ml of disintegrating medium would be placed below the sieve. To determine disintegration time, 6 ml of phosphate buffer (pH 6.8), was placed inside the vessel in such a way that 4 ml of the media was below the sieve

and 2 ml above the sieve. Tablet was placed on the sieve and the whole assembly was then placed on a shaker. The time at which all the particles pass through the sieve was taken as a disintegration time of the tablet.

Wetting time[5]:

The wetting time of the tablets can be measured using a simple procedure. Five circular tissue papers of 10 cm diameter were placed in a petri dish with a 10 cm diameter. Six ml of phosphate buffer (pH 6.8) containing eosin, a water soluble dye, was added to Petri dish. A tablet was carefully placed on the surface of the tissue paper. The time required for phosphate buffer (pH 6.8) to reach upper surface of the tablet was noted as

the wetting time.

Water absorption ratio:

A piece of tissue paper folded twice was placed in a small petri dish containing 6 ml of phosphate buffer (pH 6.8). 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 indicated with R, which is calculated by using the below mentioned equation.

$R = (Wa - Wb) / Wa \times 100$

Where, Wa = weight of tablet after water absorption

Wb = weight of tablet before water absorption.

Resultsand Discussion:

Table no.2: Calibration values of Prochlorperzine maleate in acidic buffer (pH 1.2)

Sl. No.	Concentration (µg/ml)	Absorbance
0	0	0.000
1	5	0.181 ± 0.01
2	10	0.358 ± 0.01
3	15	0.521 ± 0.02
4	20	0.706 ± 0.01
5	25	0.889 ± 0.02

As UV spectrophotometric method was selected for quality control purposes, the $\lambda_{max}$was found to be 265 nmfrom UV spectrum of Prochlorperzine maleate in pH 1.2 acidic buffer as shown in above figure. The data obtained i.e. absorbance versus concentration were linearly regressed and the slope was found to be 0.035 and regression coefficient being 0.999.

Compatibility Study:

Standard calibration curve of Prochlorperzine maleate

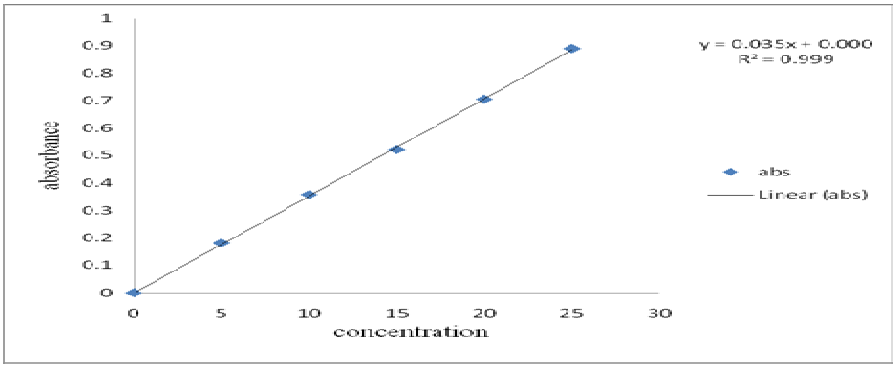
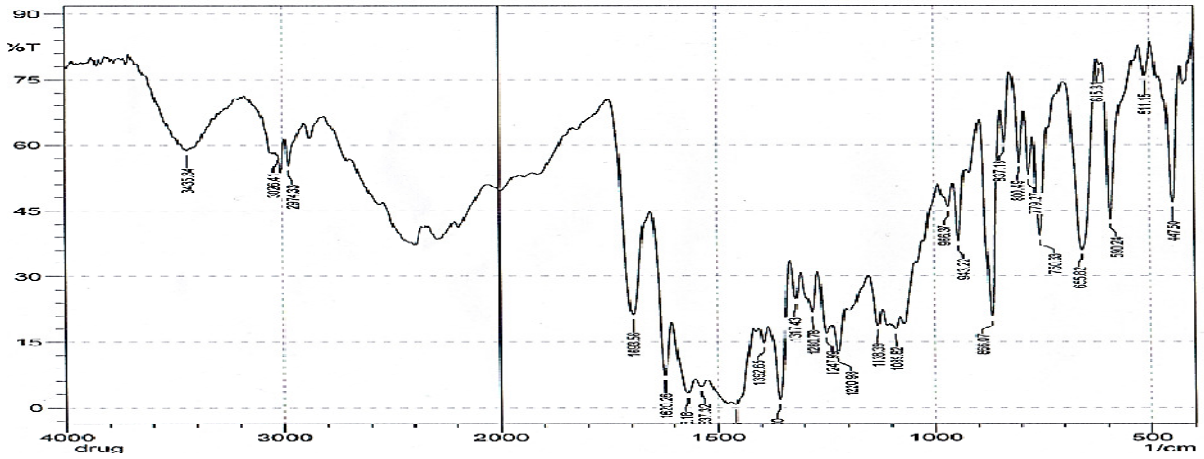


Fig.no.1: Standard calibration curve of Prochlorperzine maleate

IR data of Drug : Prochlorperzine maleate



IR data ofDrug :Superdisintegrants (CroscarmelloseSodium:Crospovidone:SSG)

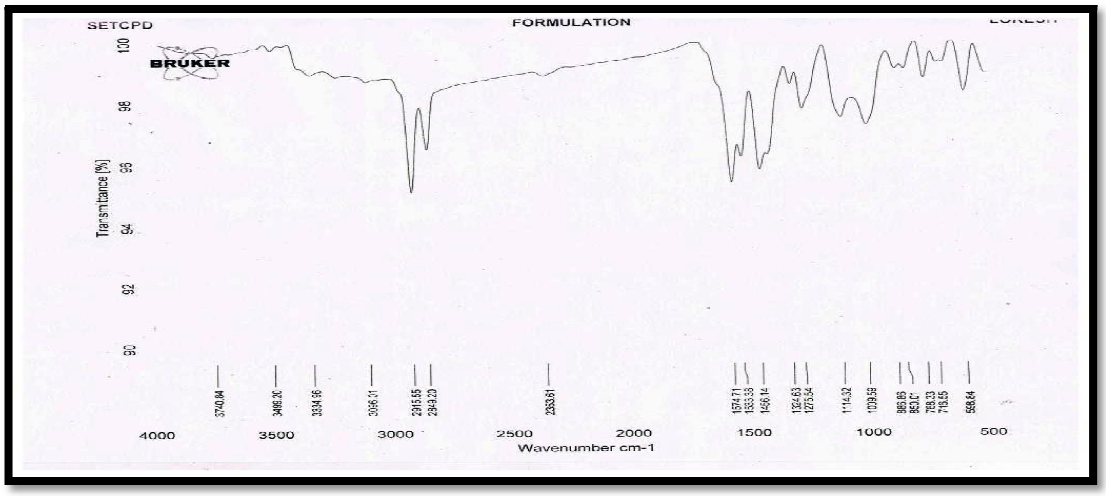


Fig.no.2: Superdisintegrants (CroscarmelloseSodium:Crospovidone:SSG)

Table no.3: Principal absorption peaks of different groups found in IR

Sl. No	Drug/ Super-disin-tegrants Name	Principal absorption peaks of different groups found in IR Absorption spectrum, wavelength in cm^{-1}						
		NH			CH	SO_2		SN
		Stretch (amide)	Asymme-tric (SO_2)	Symmetric (SO_2)	Stretch	Asymm-etric	Symm-etric	Stretch
1	Standard	3500-3100	3500-3100	3500-3100	3000-2850	1375-1300	1350-1140	850-915
2	Drug:Super-disintegrants	3499.20	3334.96	3229.25	3096.01	1324.63	1114.32	886.86

Table no.4: Evaluation of Precompression parameters of rapidly disintegrating oral tablets containing Prochlorperzine maleate; values as mean ± S.D, n=3

Formulation code	Mean Angle of repose* ± S.D.	Mean bulk density * (g/cm^3) ± S.D	Mean Tapped density* (g/cm^3) ± S.D.	Carr's Index* (%) ± S.D	Hausner's Ratio* ± S.D
F1	23.53±0.63	0.64± 0.002	0.76±0.006	15.72±0.02	1.19±0.0006
F2	26.21±1.25	0.60±0.003	0.71 ±0.005	15.08±0.19	1.18±0.003
F3	24.7±1.30	0.61± 0.002	0.72±0.003	15.17±0.06	1.18±0.001
F4	26.13 ±0.97	0.61±0.002	0.73 ±0.002	15.32±0.04	1.18±0.0006
F5	26.52±0.86	0.58±0.002	0.72 ±0.002	18.64±0.03	1.23±0.0006
F6	26.99±2.31	0.61± 0.003	0.75 ±0.005	18.79±0.08	1.23±0.001

Table no.5:Evaluation of postcompression parameters of rapidly disintegrating oral tablets containing Prochlorperzine maleate. F= Formulation values as mean ± S.D, n=3

'F' code	Hardness (Kg/cm^2)	Thickness (mm)	Friability (%)	Weight Variation		Content of drug uniformity (%)
				Mg	%	
F1	4.35±0.13	5.52 ±0.15	0.58±0.001	250.4±0.001	0.16	97.82±0.42
F2	4.37±0.08	5.52±0.01	0.57 ±0.001	250.45 ±0.001	0.18	98.65±0.22
F3	4.35±0.22	5.52 ±0.01	0.52 ±0.001	250.2 ±0.002	0.08	99.29±0.28
F4	4.33±0.20	5.52±0.01	0.54 ±0.002	250.45 ±0.001	0.18	101.02±1.26
F5	4.43±0.12	5.52±0.02	0.58 ±0.001	249.95 ±0.002	0.09	99.33±0.94
F6	4.43±0.06	5.52 ±0.02	0.55 ±0.001	250.1 ±0.002	0.04	99.12±0.22

Evaluation of Precompression parameters of rapidly disintegrating oral tablets containing Prochlorperzine maleate.

The IR spectra of drug:superdisintegrants showed principal peaks at 3499.20 cm^{-1}(N-H (amide) Stretching), 3334.96 cm^{-1}(N-H (SO_2) Asymmetric Stretching), 3229.25 cm^{-11} (N-H (SO_2) Symmetric Stretching), 3096.01 cm^{-}(C-H Stretching), 1324.63 cm^{-1}(SO_2 Asymmetric Stretching), 1114.32 cm^{-1} (SO_2 Symmetric Stretching) and 886.86 cm^{-1} (S-N stretching). From the results, it was concluded that there was no interference in the functional groups as the principle peaks of the Prochlorperzine maleate were found to be unaltered in the spectra of the drug-polymer physical mixture.

The values of angle of repose were found to be in the range of $23^0.53'$ ± 0.63 and $26^0.99'$ ± 2.31. All the formulations prepared by direct compression methods showed the angle of repose less than 30^0, which reveals good flow property. Bulk density was found in the range of 0.58 ±0.002 to 0.64 ± 0.002 g/cm^3 and the tapped density between 0.71 ± 0.005 to 0.76 ± 0.006 g/cm^3. Using above two density data, Hausner's ratio and compressibility index were calculated. The powder blends of all formulations with Hausner's ratio <1.25 indicated better flow properties. The compressibility index was found between 15.08 ± 0.19 to 18.79 ± 0.08% and the compressibility-flowabilty correlation data indicated an excellent flowability of all powder blends. When the % compressibility ranges from 5 to 16, the materials have acceptable flow property and packing ability. There was better compressibility observed with crospovidone in comparison to sodium starch glycolate and croscarmellose sodium attributing to its smaller particle size.

Evaluation of postcompression parameters of rapidly disintegrating oral tablets containing Prochlorperzine maleate.

The hardness of all the tablets prepared by direct compression methods was maintained within the 4.33 ± 0.20 kg/cm^2 to 4.43 ± 0.12 kg/cm^2. The mean thickness was (n=3) almost uniform in all the for-

mulations and values ranged from 5.52 ± 0.01 mm to 5.52 ± 0.15 mm. The friability of all the tablets prepared by direct compression methods was within 0.52 % to 0.58 %. The formulations F-1 and F-5 showed slightly higher than the other. The weight variation of all the tablets was found between 249.95 ± 0.002 to 250.45 ± 0.002 mg. The percent drug content of formulations F1, F2, F3, F4, F5 and F6 was found to be 97.82%, 98.65%, 99.29%, 101.02%, 99.33% and 99.11% respectively. All the formulation parameters are within pharmacopeial limit.

The *in-vitro* wetting time was found to be in the range of 47.33 ± 1.15 to 119.33 ± 1.15 seconds. Percent water absorption ratio for all formulations was found to be in the range of 43.97 ± 0.04 to 66.56 ± 0.01%. Formulations with crospovidone exhibited quicker wetting time and higher percent water absorption ratio when compared to sodium starch glycolate and croscarmellosesodium.Disintegration time as per Indian Pharmacopeia for all the formulation was found to be within 60 seconds, which was well within Indian Pharmacopeial limit (Indian Pharmacopeial limit is 180 seconds). The lowest disintegration time was seen for formulation F3 which shows 23.33 seconds followed by formulation F4 which was 27.66 seconds in which crospovidone was the superdisintegrant used. It indicated that crospovidone was a better superdisintegrant followed by sodium starch glycolate and croscarmellose sodium. As crospovidone rapidly exhibits high capillary activity and pronounced hydration capacity when compared to the latter two.

***In-vitro* dissolution studies:**

All the six formulations were subjected for *in-vitro* dissolution studies using tablet dissolution tester USP XXIII apparatus type – 2 (paddle). The dissolution medium 1.2 pH acidic buffer was used to study the drug release. The samples were withdrawn at different intervals of time and analyzed at 265nm using UV spectrophotometer.

Percent Drug release profile of Prochlorperzine maleate rapidly disintegrating oral tablets (Formulation F1-F6).

The maximum percentage cumulative drug release after 10 min. of the formulations F1, F2, F3, F4, F5 and F6 was found to be 93.96, 92.67, 96.53, 97.82, 96.53 and95.24% respectively as shown intable no.6.

From the graph R^2 values of F1, F2, F3, F4, F5 and F6 was found to be 0.965, 0.979, 0.970, 0.975, 0.968 and 0.986 which is higher as compared to zero order kinetic. Hence we can say that drug release follows first order kinetic.

Table no. 6: Formulation parameters with in pharmacopeial limit. F= Formulation values as mean ± S.D, n=3

F code	Wetting time (sec)	Water absorptionn ratio (%)	Disintegration time (sec)
F1	80.66 ±1.52	49.33 ±0.01	51.66 ±1.52
F2	119.33 ±1.15	43.97 ±0.04	54.33 ±2.08
F3	47.33 ±1.15	61.90±0.01	23.33 ±0.57
F4	51±1.73	66.56±0.01	27.66 ±0.57
F5	74.33 ±1.15	52.65±0.01	42.33 ±1.52
F6	110.33 ± 1.15	47.83±0.01	46.66 ±0.57

Fig no.3: Zero order comparative dissolution profile of rapidly disintegrating tablets of Prochlorperzine maleate in acidic buffer (pH 1.2) for formulation F1-F6.

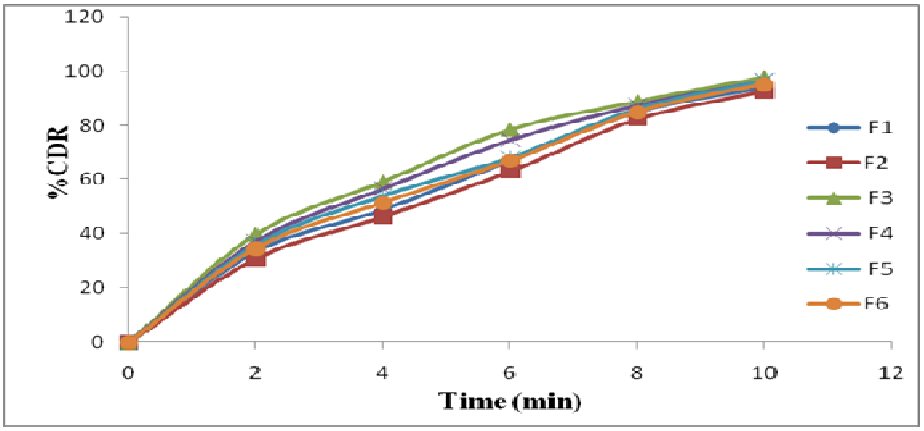
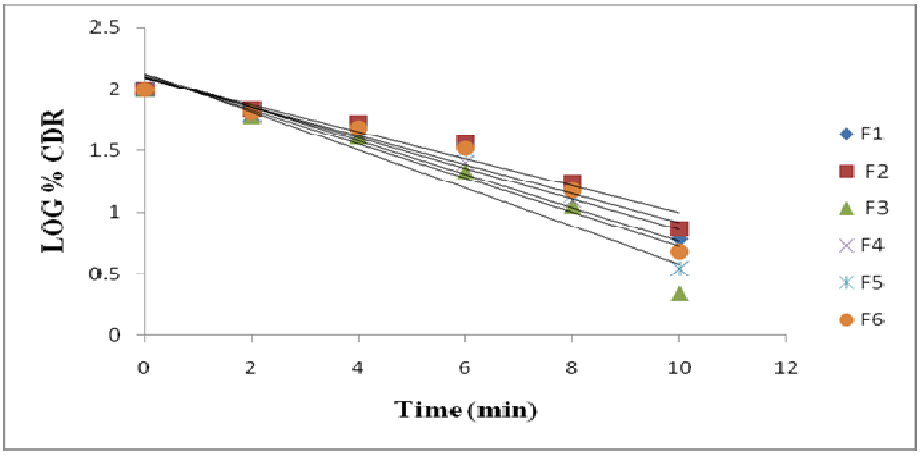


Fig no.4: First order rate kinetic release study for Formulation F1-F6.



Summary and Conclusion:

In the present work, an attempt was made to develop rapidly disintegrating oral tablets of Prochlorperzine maleate. From the above results it was concluded that, the *in-vitro* disintegration, wetting time parameters revealed that croscarmellose sodium, crospovidone, sodium starch glycolate, alone and withstarlac, acts as superdisintegrants and water absorption ratio also reveals good absorptivity in all the formulations. *In-vitro* dissolution studies revealed a maximum drug release up to 97.82% within a period of 10 minutes thus increase in the bioavailability of the drug. Thus, rapidly disintegrating oral tablets will surely enhance the patient compliance, low dosing, rapid onset of action, increased bioavailability and less side effects.

Based on the experimental data and the results obtained the formulation of a rapidly disintegrating oral dosage form of Prochlorperzine maleate an H_2 receptor antagonistic drug as envisaged in the research objectives have been achieved successfully.

References:

1. Halakatti P.K, Shaista O, Gulgannavar R.S, PatwariP.K.Formulation and evaluation of mouth disintegrating tablets of Prochlorperzine maleate by using to hibiscus rosa- sinensis mucilage and treated agar. Int J Res Ayurveda Pharm 2010 Nov-Dec 1(2):497-505.
2. David E. Golan, Armen H. Tashjian, EthrinJ.Armstrong and April W. Armstrong. Principles of pharmacology. The pathophysiologic basis of drug therapy. Wolters Kluwer (India) Pvt. Ltd, New Delhi, 2nd edition, 2008, 815.
3. Tripathi. Essential of medical pharmacology. Jaypee brothers, New Delhi. 4th edition, 2000, 633.

4. Charles R. Craig and Robert E. Stitzel. Modern pharmacology with clinical applications. Little,Brown and company, New York. 5th edition, 1997, 514.
5. Rang HP, Dale MM, Ritter JM, Moore PK, Pharmacology 5th ed. New Delhi. Churchill Livingstone; 2003;.229,370.
6. Sathoskar R.S, Bhandarkar and Nirmala N. Rege. Pharmacology and pharmacotherapeutics, popular prakashan, Mumbai, 2005, 620.
7. Shailesh Sharma, GoswamiJ.P, Rajinibala, Nimrata Seth and Gupta G.D. Mouth dissolving tablet: A review, Pharma buzz, 2009, 30-40.
8. Patil A, Aman T, Nithin B.B, Abhilash P, Turga M, Kulkarni S. Formulation and evaluation of mouth dissolving tablets of montelukast sodium. Res J Pharm Bio ChemSci, 2011 Jul- Sept 2(3):268-74.
9. Bhowmik D, Chiranjib B, Krishnakanth, Pankaj, Chandira RM. Fast dissolving tablet: an overview. J chem pharm Res 2009;1(1):163-177.
10. Lachman L, Lieberman HA, Kanig JL. The theory and practice of industrial pharmacy. 3rd ed. Mumbai: Varghese Publishing House, 1987;71,183,316,296-97.
11. Lakade SH, Bhalekar MR. Formulation and evaluation of sustained release matrix tablet of anti-anginal drug, influence of combination of hydrophobic and hydrophlic matrix former. Res J Pharm Tech 2008 oct-dec;1(4):410-13.
12. Lachman.L, Liberman.A, Kinig J.L. The theory and practice of industrial Pharmacy, 4th edition, Varghese publishing house, Bombay.1991:67-68.
13. Krishanaiah YS, Development of colon target oral guar gum matrix tablet of Albendazole for the treatment of Helminthiasis. Indian J. Pharm. Sci. 2003; 65 (4):378-85.
14. Siji R, Shanmuganathan S, Raja ST, Senthil Kumar SR, Thanga AT. Formulation and evaluation of mouth dissolving Prochlorperzine maleate tablet. Int J Chem Tech Res 2009 Oct-Dec;1(4):1251-56.
15. Khinchi MP, Gupta MK, Bhandari A, Sharma N, Agarwal D. Design and development of orally disintegrating tablets of Prochlorperzine maleate prepared by direct compression method using different super-disintegrants. J Appl Pharm Sci 2011;01(01):50-58.