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Formulation and Evaluation of Mouth Dissolving Tablet of Propranolol HCl Using Different Superdisintegrant

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ABSTRACT

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes. United State Food and Drug Administration (FDA) defined ODT as "a solid dosage form containing medicinal substance or active ingredients which disintegrate rapidly usually within a matter of second when placed upon the tongue. Propranolol is a nonselective beta-adrenergic blocker and is almost completely absorbed following oral administration. However , most of drug is undergoes high first-pass metabolism by the liver and on average, only about 25% of propranolol reaches the systemic circulation. The present study investigated to development of novel fast dissolving tablet of Propranolol HCL which was by first pass metabolism, provide rapid onset of action and increasing the bioavailability of the drug. The fast dissolving tablets were prepared by Direct compression method by using different superdisintegrant like Crosspovidone, crosscarmellose sodium, sodium starch glycolate etc. The advantage of this formulation is such that in case of hypertension attack patient can take the drug without the usage of water. Therefore the main objective of the present work is to develop orodispersible tablets of Propranolol hydrochloride to improve bioavailability, disintegration time, dissolution efficacy and patient compliance.

Keywords: Superdisintegrants, Orodispersible tablets, Disintegration time, Direct compression, Propranolol hydrochloride

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INTRODUCTION

Drug delivery through oral route is one of the most common and widely acceptable route through all over world and best route of administration since decades.

Mouth dissolving tablet:

Mouth dissolving tablets (MDT) are single unit dosage form that dissolve or disintegrate quickly in mouth with the help of saliva and without the need of water. As these drugs are quickly dissolve or disintegrate hence it readily available for absorption improving its bioavailability and onset of action.

Since it is absorb from oral mucosal membrane directly into the systemic circulation, hence it avoids the first pass metabolism thus reduce the dose size and side effect of drug.[1,2]

The FDT formulation is defined by the Food And Drug Administration (FDA) as "a solid dosage form medicinal substances which disintegrate rapidly, usually within a matter of seconds, when placed upon the tongue".However most of the patient like geriatric and pediatric patient feels some difficulty to swallow the conventional tablets, which may lead poor patient compliance. To overcome this problem and weakness the researcher and scientist have developed the innovative drug delivery system which is known as oral disintegrating tablet.[3,4]

Propranolol:

It is a non-selective beta blocker, that is, it blocks the action of epinephrine and nor epinephrine on both β_1- and β_2-adrenergic receptors. It has little intrinsic sympathomimetic activity (ISA) but has strong membrane stabilizing activity. It is mainly used in treatment of Hypertension, supraventricular, tachyarrhythmias, Ventricular arrhythmias, pheochromocytoma, thyrotoxicosis, vascular headache. Propranolol is almost white powder which is soluble in water and in ethanol, slightly soluble in ethanol, practically insoluble in ether. The oral bioavliabilty of drug is 26%.

Advantage of MDT[5,6,7,8,9,10]

1. No need of water to administration.
2. Convenience of administration and accurate dosing as compared to liquids.
3. Rapid dissolution and absorption of drug, which may produce quick onset of action
4. Suitable of pediatric and geriatric patient and also for those who has swallowing problem.
5. First pass metabolism is reduced, offering improved bioavailability and reduce dose size and side effect.
6. Pre-gastric absorption increased the bioavailability.

MATERIALS AND METHOD:

Material

Propranolol was obtained as gift sample from Cipla Pvt. Ltd. Mumbai. Crosscarmellose sodium, Sodium starch glycolate were gift sample from Signet Chemical Corporation Mumbai. All other ingredients were used of pharmaceutical grade.

Method

Propranolol is prepared by Direct Compression Method. Each tablet containing 20 mg Propranolol Hydrochloride were prepared as per composition given in table. The drug and excipients were passed through sieve (80) to ensure better mixing. Microcrystalline Cellulose was used as a direct compressible vehicle. Superdisintegrant like Crosspovidone, Cross carmellose sodium, and Sodium starch glycolate were used in different ratios. To the blended powder finally talc and magnesium stearate were added. The powder was compressed using Rimek compression machine equipped with 8mm round punch by direct compression technique. A minimum of 40 tablets were prepared for each batch.

PREFORMULATION STUDIES

Angle of Repose:

Angle of repose was determined using funnel method. The blend was poured through funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and angle of repose was calculated using the formula[11]

$$\mathbf{Tan\ \theta = h/r}$$

$$\mathbf{\theta = tan^{-1}h/r}$$

Where, θ is the angle of repose, h is height of pile; r is radius of the base of pile.

Bulk Density:

Apparent bulk density (Db) was determined by pouring the blend into a graduated cylinder. The bulk volume (Vb) and weight of powder (M) was determined. The bulk density was calculated using the formula[11]

$$\mathbf{Db = M/Vb}$$

Tapped Density:

The measuring cylinder containing known mass of blend was tapped for a fixed time. The minimum volume (Vt) occupied in the cylinder and weight (M) of the blend was measured. The tapped density (Dt) was calculated using the following formula[11]

$$\mathbf{Dt= M/Vt}$$

Carr's Compressibility Index:

The simplest way of measurement of free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by compressibility. The

compressibility index of the granules was determined by Carr's compressibility index, which is calculated by using the following formula[11]

$$I = Dt-Db/Dt\times100$$

Hausner Ratio:

Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following formula[11]

$$\text{Hausner ratio} = Dt/Db$$

Where Dt is tapped density and Dd is bulk density.

Lower Haunser ratio (< 1.25) indicates better flow properties than higher ones6 (>1.25).

EVALUATION OF THE TABLETS:

Weight variation:

The tablets were selected randomly from each formulation and weighed individually to check for weight variation. The U.S Pharmacopoeia allows a little variation in the weight of a tablet. The following percentage deviation in weight variation is allowed.

Table 1. Percentage deviation in weight variation (USP)

Average weight of a tablet	Percentage deviation
130mg or less	10
More than 130mg and less than 324 mg	7.5
324 mg or more	5

Uniformity in thickness: [12]

The crown thickness of individual tablet may be measured with a **vernier calliper**, which permits accurate measurements and provides information on the variation between tablets. Other technique employed in production control involves placing 5 or 10 tablets in a holding tray, where their total crown thickness may be measured with a sliding caliper scale. The tablet thickness was measured using screw gauge.

Hardness test: [12]

Tablets require a certain amount of strength, or hardness and resistance to friability, to withstand mechanical shocks of handling in manufacture, packaging and shipping. The hardness of the tablets was determined using **Monsanto Hardness tester**. It is expressed in Kg/cm2. Three tablets were randomly picked from each formulation and the mean and standard deviation values were calculated.

Friability test: [12]

It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition. The friability of tablets was

determined by using Roche friabilator. It is expressed in percentage (%).

Four tablets were initially weighed (W initial) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions.The tablets were weighed again (W final). The percentage friability was then calculated by,

$$F = W_{initial} - W_{final} / W_{initial} \times 100$$

% Friability of the tablets less than 1% is considered acceptable.

Wetting time: [12]

The method was applied to measure tablet wetting time. A piece of tissue paper folded twice was placed in a small petridish (i.d. = 6.5 cm) containing 10 ml of water, a tablet was placed on the paper, and the time for complete wetting was measured. Three trials for each batch were performed and standard deviation was also determined.

Water absorption ratio: [12]

A piece of tissue paper folded twice was placed in a small petridish containing 6ml of water. A tablet was put on the paper and time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R was determined using following equation.

$$R = 100 (W_a - W_b)/W_b$$

Where,W b = weight of tablet before absorption

W a = weight of tablet after absorption

Three tablets from each formulation were performed and standered deviation was also determined.

***In vitro* disintegration time:** [12]

The process of breakdown of a tablet into smaller particles is called as disintegration. The in-vitro disintegration time of a tablet was determined using disintegration test apparatus as per I.P. specifications.

I.P. Specifications: Place one tablet in each of the 6 tubes of the basket and run the apparatus using simulated gastric pH 6.8 maintained at 37°C ± 2°C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the distilled maintained at 37°C ± 2°C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded.

***In vitro* dissolution studies:**[12]

Dissolution rate was studied by using USP type-II apparatus (USP XXIII Dissolution Test Apparatus at 50 rpm) using 900ml of phosphate buffer pH (6.8) as dissolution medium. Temperature of the dissolution medium was maintained at 37±0.5°C; aliquot of dissolution

medium was withdrawn at every 5 minute interval and filtered. The absorbance of filtered solution was measured by UV spectrophotometric method at 239 nm and concentration of the drug was determined from standard calibration curve.

RESULTS AND DISCUSSION

Propranolol Hydrochloride tablets were prepared by direct compression method. Nine formulations were with three different superdisintegrants. Each was used in three different concentrations (3%, 4% and 5%) Table no.3 shows the data obtained from the pre-compression evaluation of tablets. All batches of the tablets were evaluated for various pre and post compression parameters. Pre-compression parameters like angle of repose, bulk density , tapped density , hausner ratio, compressibility index and post compression parameters such as hardness, friability, wetting time, disintegration time , and dissolution were evaluated. Post compression parameters are reported in table no.4. All above properties and value were near to standard limit. All the tablets maintained hardness in the range 3.1-3.5kg/cm. The loss in total weight of the tablets due to friability was in the range of 0.21-0.48%. The drug content in different formulation was highly uniform and in the range of 98.32-99.96%. Wetting time is used as an indicator of the ease of tablet disintegration and found to be 39-61sec. The result in vitro disintegration were within the prescribe limit and comply with the criteria for orally disintegrating tablets, the value were with 22-58sec. The cumulative % of drug release increased as the time increases upto 5min with increased in the concentration of superdisintegrants. Among all formulations, F6 (contains 5% crsspovidone) formulation considered as better as it gives disintegration time 26 sec which fulfill official requirement (less than 30 sec as per USFDAGuideline) for orodispersible tablets and also it shows highest drug release 97.15 at 5 minute s compared to the other formulations.

Table 2: Composition of mouth dissolving tablet of Propranolol.

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Propranolol hydrochloride	20	20	20	20	20	20	20	20	20
Sodium starch glycolate	6	8	10	-	-	-	-	-	-
Crosspovidone	-	-	-	6	8	10	-	-	-
Cross carmellose sodium	-	-	-	-	-	-	6	8	10
Aspartame	10	10	10	10	10	10	10	10	10
Magnesium stearate	4	4	4	4	4	4	4	4	4
Talc	8	8	8	8	8	8	8	8	8
Microcystalline cellulose	50	50	50	50	50	50	50	50	50
Lactose	102	100	98	102	100	98	102	100	98
Total	200	200	200	200	200	200	200	200	200

Table 3: Evaluation of powder blend

Formulation code	Angle of repose (θ) (θ) (±sd) (n=3)	Compressibility (±sd) (n=3)	Hausner ratio (n=3)
F1	19.78±0.19	15.18+0.13	1.17+0.11
F2	22.32±0.21	16.71+0.16	1.19+0.09
F3	21.55±0.10	15.72+0.12	1.18+0.15
F4	18.15±0.33	17.21+0.10	1.15+0.12
F5	20.22±0.18	16.12+0.09	1.20+0.11
F6	15.92±0.90	14.52+0.18	1.14+0.08
F7	19.02+0.18	15.53+0.16	1.20+0.15
F8	20.24+0.11	16.84+0.11	1.21+0.09
F9	15.78+0.22	12.82+0.13	1.18+0.12

Table 4: Evaluation of propranolol mouth dissolving tablet

Formulation	Hardness Kg/cm^2 (n=3)	Friability % (n=6)	Drug content % (n=10)	Disintegration time Sec (n=6)	Wetting time Sec (n=3)	Weight variation n=20
F1	3.2±0.11	0.33	99.78±1.50	45	55	200.53±1.62
F2	3.1±0.12	0.21	98.72±0.88	48	57	201.23±2.23
F3	3.4±0.14	0.28	99.52±1.50	57	61	199.72±2.17
F4	3.2±0.17	0.48	99.90±0.52	41	58	200.53±2.42
F5	3.5±0.12	0.26	99.96±0.82	32	46	201.13±1.34
F6	3.3±0.08	0.36	98.95±0.38	26	39	201.51±0.08
F7	3.4±0.12	0.34	99.12±0.62	39	49	201.53±1.80
F8	3.5±0.17	0.28	98.72±0.34	28	43	200.23±2.80
F9	3.2±0.16	0.36	98.32±0.62	29	45	201.12±1.32

Table 5: In-vitro drug release of prepared propranolol fast dissolving tablet

Time in min	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	28.12	32.29	35.48	42.54	46.49	48.18	40.40	43.34	46.54
2	43.17	46.47	48.37	52.51	57.57	61.83	51.27	57.28	65.21
3	62.65	68.34	65.49	61.63	65.69	68.41	63.38	71.72	78.72
4	80.87	78.58	76.71	84.49	85.34	79.64	82.71	87.98	91.34
5	83.34	81.28	79.13	86.78	88.23	97.15	87.46	94.63	93.12

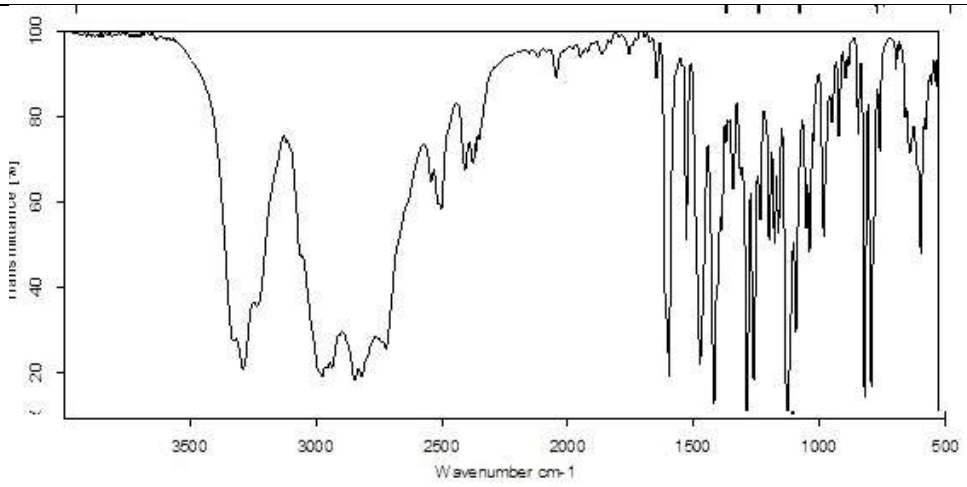

Figure 1:FTIR Spectra of Propranolol HCl

DRUG EXCIPIENT INTERACTION STUDY:

FTIR was used to identify if there is any drug excipient interaction. FTIR studies were performed on drug, polymer and optimized formulation. Samples were analyzed by the potassium bromide pellet method in an IR spectrophotometer (Shimadzu, FTIR 8700) in the region between 3500-500 cm–1.

CONCLUSION

The present work efforts have been made to prepare mouth dissolving tablet of Propranolol HCl with the help of three different superdisintegrants like Sodium starch glycolate, Crosspovidone and Crosscarmellose sodium in 3%, 4% , 5% respectively by Direct compression method. Nine formulations were prepared (F1 to F9) in which F6 formulation shows highest percentage release and 26 sec disintegration which is under standard limit.

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REFERENCE:

1. Subal, C Basak. Melt in mouth tablet. An innovative technology for convenience. Pharmabiz. Com. 2008;11.
2. Segale, L et al. Preformulation study of fast melting tablets. Biopharmaceutics and Pharmaceutical Technology , Geneva, 2006;27-30.
1. 3.R. Chang, R. Couch. A review of fast dissolving tablets. Pharma Tech. 2000;52-58.
3. Y.Bi, H. Sunda, Y. Yonezawa, K. Dayo. Preparation and evaluation of a compressed tablet rapidly disintegrating in oral cavity. Chem Pharm Bull. 1996;44:2121-2127..
2. 5.L.H. Rddy , B. Ghosh and Rajneesh. Fast Dissolving Drug Delivery System: A Review of Literature. Indian J Pharm Sci 2002;64(4):331-336.
3. 6.W. Habib, R.Khankari and J. Hont z. Fast Dissolving Drug Delivery System: Critical Review In Therapeutics. Drug Carrier Systems 2002;17(1):61-72.
4. 7. R. Bradoo, S. Shahani, S. Poojary, B. Deewan, and S. Sudarshan. Fast Dissolving Drug Delivery Systems. JAMA India 2001;4(10):27-31.
5. 8.SS Birander, ST Bhagwati and IJ Kuppasad. Fast Dissolving Drug Delivery Systems: A Brief Overview. The International Journal of Pharmacology.2006;4(2).
6. 9. S. Bhaskaran, GV Narmada. Rapid Dissolving Tablet A Novel Dosage Form. Indian Pharmacist. 2002;1;9-12.

7. 10. PV Devrajan and SP Gore. Melt In Mouth Tablets: Innovative Oral Drug Delivery System. Express Pharma Pulse 2002;7(1):16.
8. 11. Marshall K, LachmanN, LibermanHA,The theory and practice of industrial pharmacy:(3rd Edition) Varghese Publishing House, Mumbai, 1987, 66-69.
9. 12. P.V. Swamy et al, Orodispersible tablets of Carbamazepine prepared by direct compression method using 32 full factorial design. J. Pharm. Sci. 2008; 7 (1):1-5.