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FORMULATION AND EVALUATION OF MOUTH DISSOLVING DRUG DELIVERY SYSTEM OF PANTOPRAZOLE SODIUM

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ABSTRACT: Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, selfmedication, pain avoidance and most importantly the patient compliance. Fast dissolving drug delivery system offers a solution for those patients having difficulty in swallowing tablet. In the present study, an attempt has been made to formulate fast dissolving tablets of Pantoprazole Sodium Sesquihydrate using superdisintegrants such as Croscarmellose sodium (Ac-Di-Sol), Sodium starch glycolate (Explotab) and Crosspovidone by direct compression technique. The prepared tablets were evaluated for hardness, friability, wetting time, weight variation, *in vitro* disintegration time and *in vitro* dissolution study. The hardness of the tablets was in the range of 3.0 - 4.0 Kg/cm². The percentage friability of the tablets was less than one. Weight variation test results showed that the tablets were deviating from the average weight within the permissible limits of ±7.5 %. Drug content uniformity study results showed the uniform dispersion of the drug throughout the formulation i.e. 98.54% to 101.23%. Tablets containing Crosspovidone (F9) showed better disintegrating character along with the rapid release (99.83% drug within 4 minutes). No appreciable difference was found between the formulations containing other two superdisintegrants. Crosspovidone was found to be better suited for the formulation of mouth dissolving tablet of Pantoprazole Sodium Sesquihydrate compared to other superdisintegrarnts used in thestudy.

Keywords: *Mouth-dissolving tablets, Pantoprazole Sodium Sesquihydrate, Superdisintegrants*

INTRODUCTION

Solid dosage forms and capsules are most popular and preferred drug delivery system because they have a high patient compliance. Many patient find difficulty to swallow tablet and hard gelatin capsules, consequently they do not take medication as prescribed. It is estimated that 50% of the population is affected by this problem which result high incidence of non-compliance and ineffective therapy1. The difficulty is experienced in particular by pediatric and geriatric patients, but it is applicable to people who are ill in bed and those active working patients who are busy or traveling, mentally ill, developmentally disable and patients who are uncooperative. To overcome this problem fast dissolving tablet is prepared2. Pantoprazole Sodium Sesquihydrate inhibits the H^+/K^+-ATPase (PP).With the view to all the above information, an attempt had been made to develop a rapidly disintegrating Pantoprazole Sodium Sesquihydrate mouth dissolving tablets of which disintegrate in the oral cavity without the need of water within a matter of seconds. This will lead to the formation of suspension / solution form which can be easily swallowed, thereby improving dissolution rate and bioavailability of drug and onset of pharmacological action.

II MATERIALS AND METHODS

Materials

Pantoprazole Sodium Sesquihydrate was obtained as gift sample from Vama Pharma Ltd., Nagpur, India, Crospovidone, Croscarmellose sodium, Sodium starch glycolate and aspartame were gifted sample from Vama pharma, Nagpur,India, Lactose and Magnesium stearate were procured from S.D Fine Chemicals, Mumbai, India, were used and all other chemicals/solvents used were analytical grade.

Method

Formulation of mouth dissolving tablets of Pantoprazole sodium sesquihydrate

Tablet each containing 20 mg Pantoprazole sodium sesquihydrate were prepared as per composition given in Table1. The drug and excipients were passed through sieve (#80) to ensure the better mixing. Microcrystalline Cellulose was used as a direct compressible vehicle. Super disintegrates like Sodium Starch Glycolate, Crospovidone and Croscarmellose Sodium were used in different ratios. The powder was compressed using Rimek compression machine equipped with 8 mm round punch by direct compression technique. A minimum of 50 tablets was prepared for eachbatch.

Table 1: Formulation using different superdisintegrants

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10*
Pantoprazole Sodium sesqu.	20	20	20	20	20	20	20	20	20	20
Sodium Starch Glycolate	5	-	-	10	-	-	15	-	-	-
Crosscarmellose Sodium	-	5	-	-	10	-	-	15	-	-
Crosspovidone	-	-	5	-	-	10	-	-	15	-
Microcrystalline Cellulose	21	21	21	21	21	21	21	21	21	21
Aspartame	5	5	5	5	5	5	5	5	5	5
Mg-stearate	2	2	2	2	2	2	2	2	2	2
Pearlitol SD 200	145	145	145	140	140	140	135	135	135	150
Orange flavor	2	2	2	2	2	2	2	2	2	2
Total weight of Tablet = 200mg										

F10*- Control batch

Pre Compression Parameters Angle of Repose

Angle of repose was determined using funnel method4. The blend was poured through funnel that can be raised Vertically until a maximum cone height(h) was obtained. Radius of the heap was measured and angle of repose was calculated using the formula

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

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 (ρb) was determined by pouring the blend into a graduated cylinder4. The bulk volume (Vb) and weight of powder (M) was determined. The bulk density was calculated using the formula,

$$\rho b = \frac{M}{Vt}$$

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 (ρb) 4 were calculated using the following formula

$$\rho t = \frac{M}{Vt}$$

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 index4 (I), which is calculated by using the following formula,

Weight Variation

Twenty tablets from each formulation were selected at a random and average weight was determined. Then individual tablets were weighed and was compared with average weight [4].

Friability

Friability of the tablets4 was determined using Veego Friabilator. This device subjects the tablets to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. Pre weighed sample of tablets was placed in the friabilator and were subjected to100 revolutions. Tablets were de dusted using a soft muslin cloth and reweighed. The friability (f) was given by theformula,

Friability (f) = (1 -W0) x 100W

Where W0 is weight of the tablets before the test and W is the weight of the tablet after the test.

***In vitro* Disintegration time**

The disintegration time for all formulations was carried out using tablet disintegration test apparatus. Six tablets were placed individually in each tube of disintegration test apparatus and discs were placed. The water was maintained at a temperature of 37°±2°C and time taken for the entire tablet to disintegrate completely was noted7.

Drug content

Five tablets were powdered and the blend equivalent to 100 mg of Pantoprazole sodium sesquihydrate was weighed and dissolved in suitable quantity of distilled water. The solution was filtered, suitably diluted and the drug content was analyzed spectrophotometrically at 293nm.Each sample was analyzed in triplicate.

***In vitro* Dissolution studies**9

In vitro dissolution studies for all the fabricated tablets was carried out by using USP Type II apparatus (USP XXIII Dissolution Test Apparatus) at 50 rmp in 900 ml of phosphate buffer pH 6.8, maintained at 37±0.5ºC. 5 ml aliquot was withdrawn at the specified time intervals, filtered through Whatmann filter paper and assayed spectrophotometrically at 239nm using Shimadzu 1700 Spectrophotometer. An equal volume of fresh medium, which was pre warmed at 37^0C was replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test. Dissolution studies were performed in triplicate.

Stability study[10,11]

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity, light and enables recommended storage conditions, re-test periods and shelf lives to be established. ICH specifies the length of study and storage conditions:

- Accelerated testing 40°C ±2 °C / 75 % RH ± 5 % for 6 months. Tablets were evaluated for hardness, weight variation, friability, content uniformity, disintegration and drug release.

III RESULTS ANDDISCUSSION

Ten formulations of Pantoprazole sodium sesquihydrate were prepared with concentration of three superdisintegrants: Sodium Starch glycolate, Croscarmellose sodium, Crospovidone and microcrystalline cellulose were used as a

direct compressible vehicle. For each formulation, blend of drug and excipients were prepared and evaluated for various parameters as explained earlier. The powder blend was compressed using direct compression technique. Bulk density was found in the range of 0.3876-0.4345 g/cm3 and the tapped density between 0.4152-0.4896 g/cm3 (Table II). Using these two density data Hausner's ratio and Carr's index was calculated. The powder blend of all the formulations had Hausner's ratio of 1.15 or less indicating good flowability. The Carr's index was found less than15% and the compressibility - flowability correlation data indicated a fairly good flowability of the blend. The good flowability of blend was also evidenced with angle of repose (range of 26.99 – 32.15), which is below 40.0 indicating good flowability. (Table 2).

Tablets were prepared using direct compression technique. Thickness of the tablets was measured by screw gauge by picking tablets randomly from all the batches. The mean thickness was (n=3) almost uniform in all the formulations and values ranged from 4.32 ± 0.01 mm to4.38±0.03mm.Thestandarddeviationvaluesindicatedthatallthef ormulationswerewithintherange. Since the powder material was free flowing, tablets were obtained of uniform weight due to uniform die fill, with acceptable weight variations as per pharmaceutical specifications. The drug content was found in the range of 98.07– 99.01 % (acceptable limit) and the hardness of the tablets between 3.0 –4.0 kg/cm2 (Table III). Friability of the tablets was found below 1 % indicating a good mechanical resistance of tablets. Wetting time is closely related to the inner structure of the tablet. This showed that wetting process was very rapid in almost all formulations. This may be due to ability of swelling and also capacity of water absorption and causes swelling. The *in-vitro* dispersion time is measured by the time taken to undergo uniform dispersion. Rapid dispersion within few minutes was observed in all the formulations. The results showed that tablet containing Crospovidone having low dispersion time as compare to other superdisintegrants. The dispersion time increases as the concentration of superdisintegrants increases (Table 3and4).

Table 2: Result of evaluation of blends for various parameters

Formulation	Parameter				
	Bulk Density	Tapped Density	Carr's Index	Hausner's Ratio	Angle of Repose
F1	0.3896	0.4152	6.165	1.065	29.10
F2	0.4219	0.4456	5.318	1.056	27.90
F3	0.4265	0.4585	6.979	1.075	29.46
F4	0.3899	0.4514	13.624	1.157	28.66
F5	0.4198	0.4500	6.711	1.071	29.26
F6	0.4156	0.4521	8.073	1.087	29.95
F7	0.4269	0.4801	11.081	1.124	26.99
F8	0.4345	0.4756	8.641	1.094	29.32
F9	0.4235	0.4896	13.500	1.156	32.15
F10	0.3876	0.4690	17.461	1.219	33.11

Table 3: Evaluation parameters and results of formulation batches (F1-F5)

Parameter	F1	F2	F3	F4	F5
Average wt.(g)*	202.80 ±0.66	203.36±0.88	204.36±1.56	205.09±0.78	202.22±0.56
Diameter (mm)**	8.06	8.06	8.06	8.06	8.04
Thickness (mm)**	4.32±0.02	4.36±0.03	4.34±0.07	4.36±0.05	4.38±0.03
Hardness(kg/cm^2)**	3±0.65	3±0.52	2.7±0.21	2.8±0.11	3±0.65
Friability (%)***	0.22±0.06	0.26±0.05	0.25±0.08	0.22±0.12	0.23±0.04
Wetting Time(sec)**	36±1.18	38±1.06	44±0.76	46±0.40	45±1.24
Water Absorption ratio (%)**	33.69± 0.85	32.10±1.94	32.38± 1.90	31.75±1.22	36.77±0.76
Disintegration Time(sec)**	46±0.81	41±0.89	37±1.03	48±1.17	44±0.81
Drug content (%)*	98.10 ± 1.02	97.65 ±0.98	98.07±2.16	98.63±1.35	97.13±1.84

*Mean ± S.D.(n=20), **Mean ± S.D.(n=6), and ***Mean ± S.D. (n=33)

Table 4: Evaluation parameters and result of formulation (F6-F10)

Parameter	F6	F7	F8	F9	F10
Average wt.(g)*	201.36±1.76	201.95±1.03	202.22±0.56	205.09±0.78	203.07±0.21
Diameter (mm)**	8.06	8.06	8.06	8.04	8.04
Thickness (mm)**	4.36± 0.05	4.34±0.07	4.32±0.02	4.32±0.05	4.34± 0.04
Hardness (kg/cm^2)**	3±0.52	3±0.65	3±0.52	2.7±0.21	2.8±0.11
Friability (%)***	0.25±0.08	0.25±0.08	0.26±0.05	0.27±0.13	0.23± 0.04
Wetting Time(sec)**	38 ±1.06	38 ±1.06	36 ±1.18	36 ±0.68	34 ±1.09
Water Absorption ratio (%)**	29.98±1.43	32.10±1.94	29.98±1.43	32.38±1.90	32.18±1.34
Disintegration Time(sec)**	44±0.76	39±0.45	41±0.89	37±1.03	36 ±1.76
Drug content (%)*	98.62±1.67	97.07 ±1.45	98.47 ±1.07	99.01±1.45	98.13±1.45

*Mean ± S.D.(n=20), **Mean ± S.D.(n=6), and ***Mean ± S.D. (n=33)

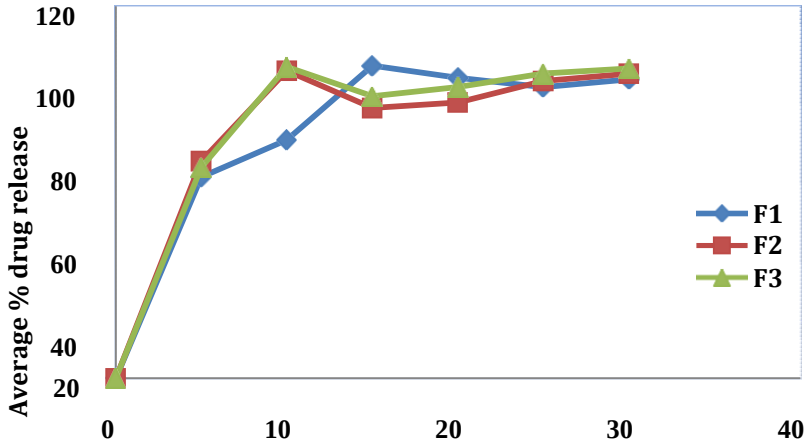

Figure 1: comparative dissolution profile of pantoprazole sodium tablets containing different superdisintegrants F1, F2, F3.

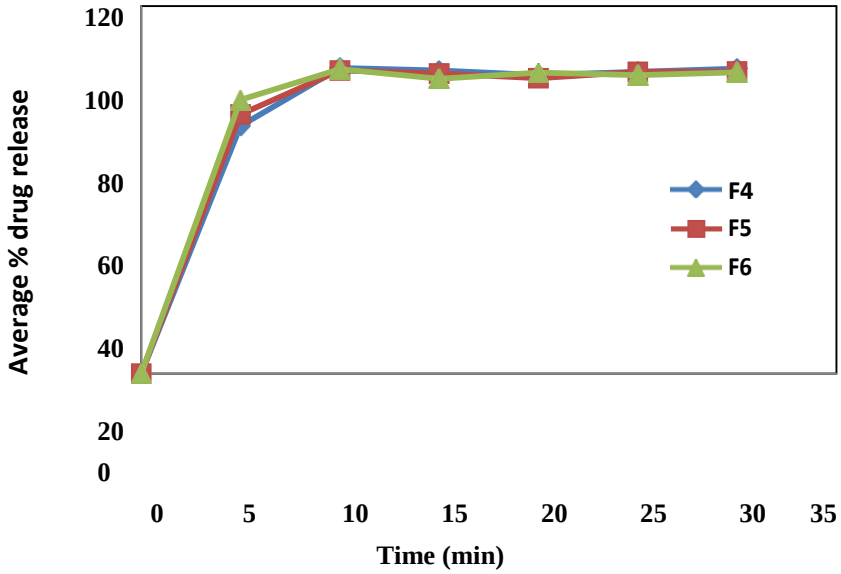

Figure2: comparative dissolution profile of pantoprazole sodium tablets containing different superdisintegrants F4, F5, F6.

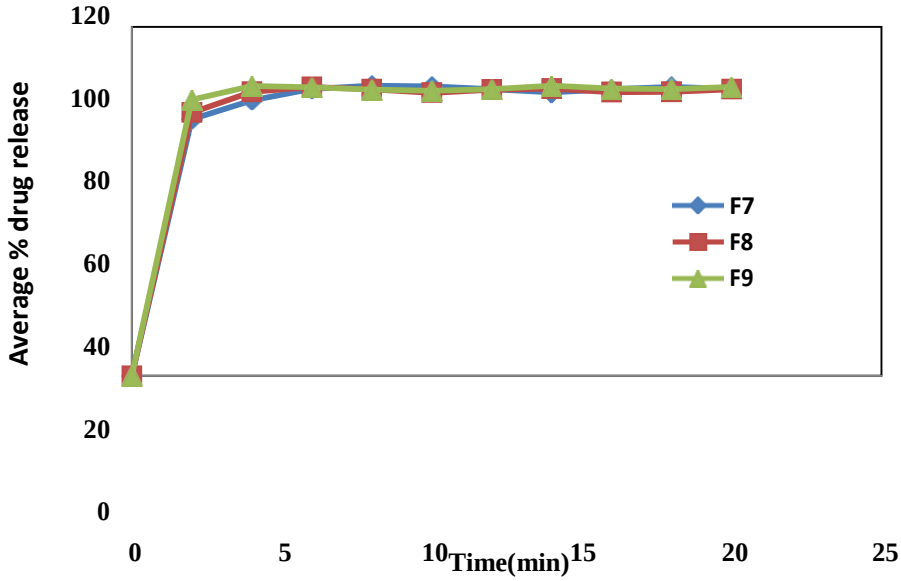

Figure 3: comparative dissolution profile of pantoprazole sodium tablets containing different superdisintegrants F7, F8, F9.

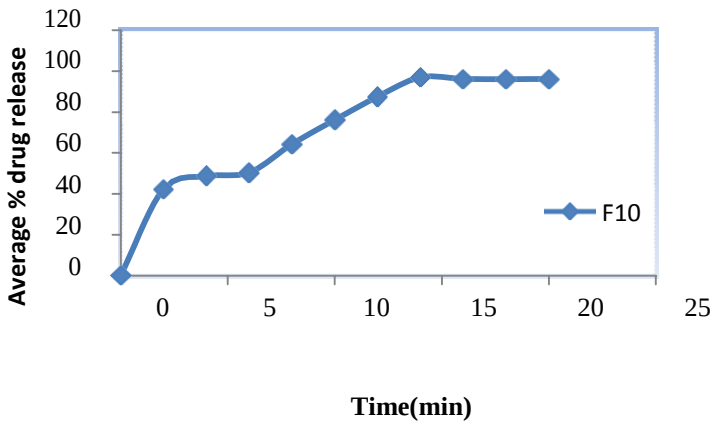

Figure 4: Dissolution profile of control batch (F10)

The in vitro disintegration time of the tablets was found to be less than 60 sec. All the formulations showed enhanced dissolution rate as compared to Pantoprazole sodium sesquihydrate without superdisintegrants. The maximum increase in the dissolution rate was observed with crospovidone amongst the three superdisintegrants. The order of enhancement of the dissolution rate with various superdisintegrants found to be Crospovidone >Cross carmellose>Sodium starch glycolate. Stability study shows no significant changes in values during one- month study (Figure 1,2,3,4)

IV CONCLUSION

1. It was concluded that mouth dissolving tablets of Pantoprazole sodium sesquihydrate can be successfully prepared by direct compression technique using selected superdisintegrants for the better patient compliance and effective therapy.

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