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Formulation development and Characterization of Orodispersible Tablets of Pantoprazole Sodium

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ABSTRACT: Aim: This study aims to develop orally disintegrating tablets (ODTs) containing pantoprazole as a representative proton pump inhibitor (PPI) via the direct compression method. **Method:** ODT formulations were designed using the direct compression technique, with pre-compression parameters such as bulk density, tapped density, angle of repose, Carr's Index, and Hausner's ratio being assessed. The formulated ODTs underwent evaluation for characteristics including colour, shape, hardness, friability, tablet thickness, weight variation, drug content uniformity, in-vitro dispersion time, and in-vitro dissolution rate. Drug-excipient interaction studies were conducted using Fourier-transform infrared spectroscopy (FTIR), and short-term accelerated stability studies were performed to assess the selected formulations' stability. **Result:** The ODTs prepared exhibited rapid disintegration and immediate release properties, meeting the desired criteria for patient compliance. **Conclusion:** The direct compression method proved effective in formulating ODTs containing pantoprazole as a PPI, demonstrating quick disintegration and immediate release properties.

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INTRODUCTION:

Orodispersible Tablets [1] (ODTs) represent a significant advancement in pharmaceutical dosage [2] forms, designed to provide convenience and improved patient compliance. These tablets are formulated to rapidly disintegrate or dissolve in the mouth without the need for water, making them particularly beneficial for patients who have difficulty swallowing conventional tablets such as paediatric, geriatric, or psychiatric patients. ODTs are manufactured using various techniques and excipients tailored to facilitate rapid disintegration. Common techniques include direct compression [3], lyophilization, and spray-drying, while super disintegrants, sweeteners, flavours, and lubricants are often incorporated into the formulation to enhance

disintegration and palatability [4]. The key advantages of ODTs include their convenience, rapid onset of action, improved patient compliance, and flexible dosing options. The purpose of this research is to prepare ODTs consisting of super disintegrants and PPIs by direct compression method and to evaluate their quick disintegration [5] and immediate release properties.

MATERIALS AND METHOD:

For this research work drug, Pantoprazole Sodium was used as a representative for the class of PPIs. The drug Pantoprazole Sodium was obtained from Vasudha Pharma Chem Ltd., Vizag. The polymer Crospovidone was obtained from K. P. Pharmaceuticals. All other excipients and reagents used were of analytical grade and were procured from authorized dealers.

Pre formulation studies [6]:

Angle of Repose (θ):

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane. A funnel was filled to the brim and the test sample was allowed to flow smoothly through the orifice under gravity. From the cone formed on a graph sheet was taken to measure the area of pile, thereby evaluating the flowability of the granules. Height of the pile was kept constant to 2 cm.

$\tan \theta = h / r$ ----------(1)

$\theta = \tan^{-1}(h/r)$ ----------(2)

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

***Bulk Density, Tapped Density, Carr's Index*:**

Both loose bulk density (LBD) and tapped bulk density (TBD) was determined by tap density tester. A quantity of accurately weighed powder from each formula, previously shaken to break any agglomerates formed was introduced into a measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 s intervals. The taping was continued until no further change in volume was noted. LBD and TBD were calculated using following formula;

LBD = Wp/Vp ……(3)

TBD = Wp/Vp ……(4)

Where Wp and Vp are weight of powder and volume of packing.

The compressibility index of the granules was determined by Carr's compressibility index.

(%) CI can be calculated by using the following formula;

CI (%) = [(TBD-LBD)/TBD]×100 …..(5)

Post formulation Studies [7]:

Preparation of Oro dispersible tablets using combination of different super disintegrants method. In this approach pantoprazole Sodium ODTs were prepared by direct compression using a combination of two different super disintegrants in the ratio of 1:1. All the ingredients were passed through 60# mesh sieve separately and collected. The drug was weighed along with the other excipients and was mixed in geometrical order. This mixture was shaken for a few minutes to ensure proper mixing of all the ingredients. The tablets were compressed (Table 1) using a flat face 16.4 × 8 mm flat oval punch to get tablets (1300 mg weight) using ten stations Rimek tablet compression machine (Karnavati Engineering Ltd. Ahmedabad, India).

Table 1. Formulations of Orodispersible tablets using combination of superdisintigrants.

Chemical Used	Quantity used in mg			
	F1	F2	F3	F4
Pantoprazole	20	20	20	20
CP	-	32.5	32.5	32.5
SSG	32.5	32.5	-	-
CCS	32.5	-	32.5	-
L-HPC	-	-	-	32.5
Aspartame	52	52	52	52
Mannitol DC	12.5	12.5	12.5	12.5
Talc	26	26	26	26
SSF	13	13	13	13
Sodium bicarbonate	585	585	585	585
Potassium bicarbonate	520	520	520	520
Flavour	6.5	6.5	6.5	6.5

Evaluation of Tablets [8-12]:

***Uniformity of thickness*:**

The crown thickness of an individual tablet may be measured with a vernier caliper, which permits accurate measurements and provides information on the variation between tablets. Other techniques employed in production control involve 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 a vernier caliper.

***Hardness test*:**

Tablets require a certain amount of strength, or hardness and resistance to friability, to withstand mechanical shocks of handling in manufacturing, packaging

and shipping. The hardness of the tablets was determined using Monsanto Hardness tester. It is expressed in Kg/cm^2.Three tablets were randomly pick ed from each formulation and the mean and standard deviation values were calculated.

***Friability test*:**

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

$F = [(Wi – Wf)/Wi] \times 100$ -----(6)

***Weight variation test*:**

The tablets were selected randomly from each formulati on and weighed individually to check for weight variatio n. The U.S Pharmacopoeia allows a little variation in the weight of a tablet. In all the formulations, the tablet weight was above 324 mg and, hence 5 % maximum difference was allowed.

***Drug Content Uniformity*:**

The content uniformity test was used to ensure that every tablet contained the amount of drug substance intended with little variation among tablets within a batch. For the content uniformity test, representative samples of 30 tablets were selected, and 10 tablets were assayed individually. At least 9 had to assay within ± 15 % of the declared potency, and none could exceed ±25 %. Twenty tablets were weighed and powdered. The blend equivalent to 20 mg of pantoprazole sodium was weighed and dissolved in a sufficient quantity of 0.1N HCl. The solution was filtered through Whatman filter paper (No.41), suitably diluted with 0.1N HCl, and assayed at 281.5 nm, using a UV-Visible double-beam spectrophotometer (UV- 1800 Shimadzu).

***In vitro disintegration time*:**

The disintegration time of the water dispersible tablets w as determined in accordance with the official European Pharmacopoeia monograph Dispersible tablets, stating a maximum disintegration time of 3 mins for dispersible tablets (European Pharmacopoeia, 2001). The disintegration apparatus (Pharma Test, Hain burg, Germany) had to be modified, since the standard glass tube is 21.5 mm in internal diameter and the tested tablets have, however, a mean diameter of 25 mm. The disintegration was carried out in a beaker consisting of a 200 ml medium. The medium consisted of water of temperature ranging between 15 and 25°C. Only one tablet at a time was tested and considered disintegrated when completely dispersed fragments were obtained.

***In vitro dissolution studies*:**

In vitro release studies were carried out using a modifi ed USP XXIII dissolutiontest apparatus. The normal USP XXIII dissolution apparatus was chosen in which a beaker was placed. The beaker was an elongated one generally used for TLC and other purposes. Another modification was that the basket was used in place of paddles because of the narrow mouth opening of the beaker. Outside this beaker water was poured at a level till the dissolution fluid in the beaker reached the temperature which was validated and kept at 40.1°C and the rotation of the basket was kept at 75 RPM. Only 190 ml dissolution fluid was used.

***Stability studies*:**

In the present study, the ODTs were packed in suitable packaging material and stored under the following conditions for a period of 90 days at 40 ±1^{0}C and RH 75 ± 5%. The tablets were withdrawn after a period of 15, 45 and 90 days respectively and analyzed for physical characterization (Visual defects, hardness, friability, disintegration, dissolution etc.) and drug content.

RESULTS AND DISCUSSION [13-22]:

FTIR Studies:

FTIR is one of the most widely used methods for checki ng the compatibility between substances and for the identification of the drug. Pantoprazole sodium, excipie nts and the selected formulations were analyzed using i nfrared spectrophotometer (Shimadzu FTIR 8-400, S model). The selected formulation shows the characteristic peak similar to that obtained in the pure pantoprazole sodium indicating that there is no incompatibility between the drug and the excipients used (Shown in Fig 1 to 3).

Shape of the tablets:

All the tablets have common flat oval shape.

Colour of the tablets:

The colour of the tablet was white and formulation prepared by addition of treatednatural gums shows

specific brown to black coloration depending on the colour of the dried treated gunpowder.

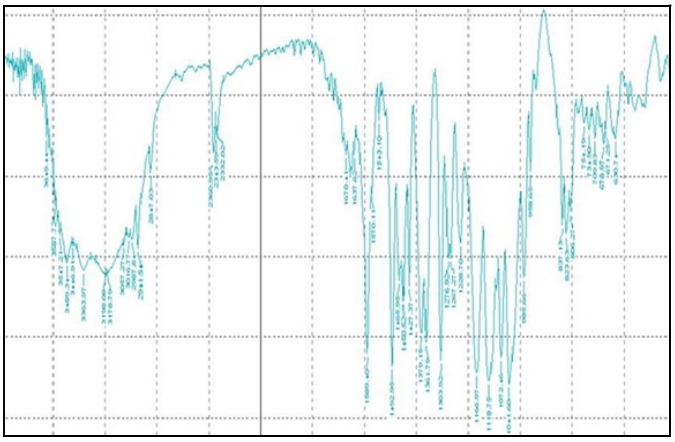

Fig 1: FTIR scan of Pantoprazole sodium.

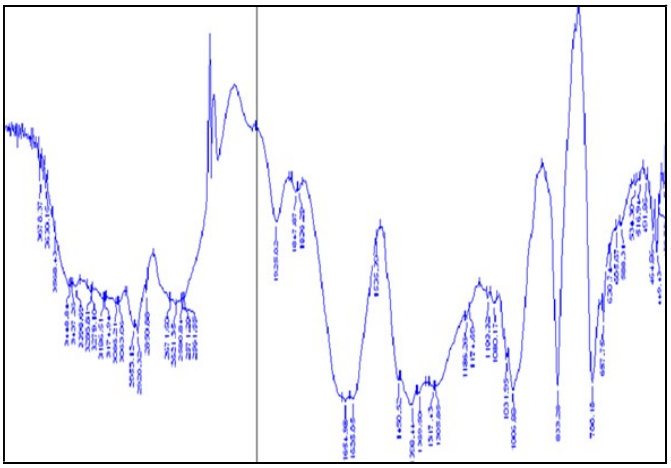

Fig 2. FTIR scan of formulation code F4.

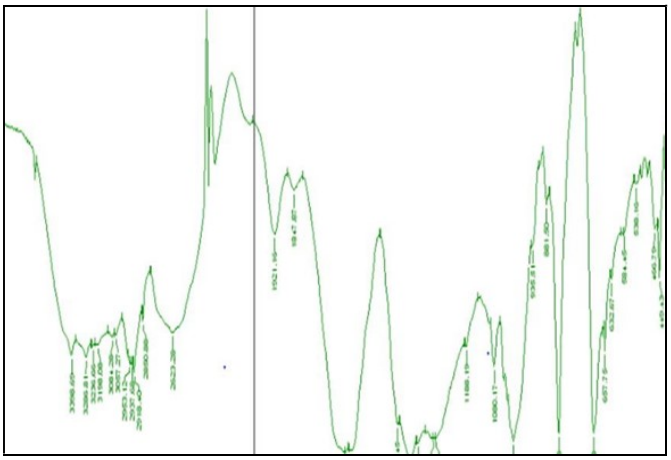

Fig 3. FTIR scan of formulation code F3.

Thickness:

Thickness of all the tablets were found to be between 6.86 to 7.05 mm.

Tablet Hardness:

The crushing strength of the tablets of each batch ranged between 3.13 to 4.23 kg/cm^2. This ensures good handling characteristics of all batches.

Friability Test:

The values of the friability test were in the range from 0.21 to 0.64 %. The percent friability of all the formulations was less than 1% ensuring that th e tablets were mechanically stable.

Table 2: Evaluation of different powder blend prepared by combination of different super disintegrants.

FC	Angle of repose	LBD (g/cm^3)	TBD (g/cm^3)	CI (%)	HR
F 1	25.11	0.69	0.80	14.28	1.17
F 2	28.18	0.690	0.79	12.48	1.14
F 3	26.19	0.70	0.81	12.72	1.14
F 4	23.50	0.67	0.78	14.54	1.17

Weight Variation Test:

The percentage weight variations for all formulations were done. All the formulated tablets passed weight variation test as the percent weight variation was within the pharmacopoeia limits as the formulation blend of all the formulations had a good flow thus the percent weight deviation was in between ±5 % of the average weight. The weights of all the tablets were found to be uniform with low standard deviation values (Shown in Table 3).

Table 3: Evaluation of different powder blend prepared by combination of different super disintegrants.

FC	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Weight Variation (mg)
F 1	7.03±0.01	3.3±0.1	0.38±0.20	1307.5±65.38
F 2	7±0.01	3.5±0.1	0.39±0.20	1299.5±64.98
F 3	7.05±0.01	3.47±0.06	0.33±0.09	1303.5±65.18
F4	6.99±0.01	3.27±0.06	0.35±0.11	1306.5+65.38

Each data is expressed as Mean± Standard Deviation, n=3.

Drug Content Uniformity:

The percentage of drug content for all formulation was f ound to 91.98 to 100.94 % which lies in the IP limit for enteric coated formulation of 90 to 110 % which was taken into consideration as ODTs of pantoprazole sodium is not official in any pharmacopoeia.

***In vitro* Disintegration Test [20-22]:**

This is the most important test with respect to ODT form ulations. Five super disintegrants, three subliming agents and two treated gums were used for these studies. Among all CP was selected as the best super disintegrant as it gave the least *in vitro* disintegration time. It was noted that no super disintegrant was able to give the *in vitro* disintegration time within 180 s at a

concentration of 2 % except CP. As for concentration, CP was increased *in vitro* disintegration time reduced; least *in vitro* disintegration time was obtained at a concentration of 5 %.

In vitro Dissolution Studies [23-25]:

All the selected formulations, which passed the in vitro disintegration test, were subjected to *in vitro* release studies using modified USP dissolution apparatus II in 0.1N HCl pH 1.2. Depending on the *in vitro* disintegration test, *in vitro* dissolution test and the similarity factor formulation F3 and F4 were selected as optimized formulations. Formulation F3 released the maximum amount of drug. (98.86 ± 1.24) within 2 min and for the formulation F4 the maximum drug release (102.52 ± 0.23) was found within 1 min. These results are in tune with those obtained for the disintegration time for the respective formulations.

Accelerated Stability Study [26-29]:

The selected formulations were subjected to accelerated stability studies and the formulations were evaluated for appearance, hardness, friability, drug content, *in vitro* disintegration time and *in vitro* dissolution test. The formulations were stored at 40 ± 1°C and RH 75 ± 5 %. All the formulations were analyzed after every 15, 30, 45, and 90 days. All the formulations show no change in all the above parameters thus successfully passes the accelerated stability study, which was conducted for 90 days.

CONCLUSION:

The *in vitro* disintegration test revealed that the tablets prepared with CP, and mixture of super disintegrants with CP show faster disintegration as compared to tablets prepared with rest of super disintegrants, subliming agents and treated natural gums usedas super disintegrants. Even the dissolution studies confirmed that tablets prepared with CP, and its mixture show faster drug release as compared to table ts prepared with rest of super disintegrants, subliming agents and treated natural gums used as super disintegrants.

The flow properties of the formulation powder have good flow properties which is an important aspect for the ODT formulations. Direct compression method is the best method for the formulation of ODTs. This method is also very economical and time saving. C P was found to be the best super disintegrant among all with 5 % concentration yielding the best results. It was also concluded that 1.1 g of bicarbonate is required for the stability of the PPIs in acidicconditions. *In vitro* disintegration time and *in vitro* drug release shows that among all the super disintegrants used CP gives the least *in vitro* disintegration time and releases the maximum amount of drug within 1 to 3 min. The results show that an increase in CP level leads to a decrease in the *in vitro* disintegration time and thus decrease in the *in vitro* drug release time. Thus, formulations F4 and F3 were selected as best formulations among those examined. Stability studies revealed that the formulation F3 and F4 i.e. formulations with 3 and 5 % CP have good stability in accelerated stability testing.

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