Research Article
Available online at www.ijpras.com
ISSN 2277-3657
Volume 2, issue 3 (2013),38-49
International Journal of Pharmaceutical Research & Allied Sciences

Formulation and Optimization of Oro dispersible Tablet of Pentoprazole Sodium as Proton Pump Inhibitor

Jaimin Modi*, R.K. Kamble, Dr. Chetan Singh Chauhan
Department of Industrial Pharmacy, Bhupal Noble's College of Pharmacy, Udaipur, India
Email: jaiminjmodi@gmail.com

Subject: Pharmaceutics

Abstract

In the present study, the aim was to formulate and optimize an orodispersible formulation of pantoprazole sodium using a combination of superdisintegrants.cThe tablets were made by direct compression technique with superdisintegrants i.e. crosspovidone and sodium starch glycolate incorporated in it. Differential Scanning Calorimetry (DSC) studies exhibited physiochemical compatibility between pantoprazole sodium and various excipients used in the tablet formulation. In an attempt to construct a statistical model for the prediction of disintegration time and percentage friability, a 32 randomized full and reduced factorial design was used to optimize the influence of theamounts of superdisintegrants. Amount of crosspovidone and sodium starch glycolate were taken as independent variables and disintegration time and fribility as dependent responses. Concerning the optimization study, the multiple regression analysis revealed that an optimum concentration of crosspovidone and a higher percentage of sodium starch glycolate are required for obtaining rapidly disintegrating tablets with adequate friability and mechanical strength. A checkpoint batch was also prepared to prove the validity of the evolved mathematical modelStability studies carried out as per ICH Q1 A guidelines suggested the stable formulations for the tested time period of 3 months accelerated study.In conclusion, this investigation demonstrated the potential of experimental design in understanding the effect of the formulation variables on the quality of mouth dissolve tablets.

Keywords: *Orodispersible, Pantoprazole sodium, Crosspovidone, Sodium starch glycolate*

Introduction

The demand for development of orally disintegrating tablets (ODTs) has enormously increased as it has significant impact on the patient compliance. Orally disintegrating tablets offer an advantage for populations who have difficulty in swallowing. It has been reported that Dysphagia (difficulty in swallowing) is common among all age groups and more specific with pediatric, geriatric population along with institutionalized patients and patients with nausea, vomiting, and motion sickness complications. ODTs with good taste and flavor increase the acceptability of bitter drugs by various groups of population. [1,2]

Orally disintegrating tablets are also called as

- Oro dispersible tablets
- Quick disintegrating tablets
- Mouth dissolving tablets
- Fast disintegrating tablets
- Fast dissolving tablets
- Rapid dissolving tablets
- Porous tablets
- Rapimelts.

However, of all the above terms, United States pharmacopoeia (USP) approved these dosage forms as ODTs.

Definition:

- European Pharmacopoeia has used the term oro dispersible tablet for tablets that disperses readily and within 3 min in mouth before swallowing.[1]
- United States Food and Drug Administration (FDA) defined ODT as "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue." The disintegration time for ODTs generally ranges from several seconds to about a minute.[1,3]
- The Center for Drug Evaluation and Research defines ODT as solid dosage

forms containing medical substances which disintegrate rapidly, usually within a matter of second, when placed upon the tongue.[1]

Drug description

Class: Proton Pump Inhibitor

The proton pump inhibitors are a group of drugs that reduce the secretion of gastric (stomach) acid. They act by binding with the enzyme H+, K (+)-ATPase, hydrogen/potassium adenosine triphosphatase, which is sometimes referred to as the proton pump. This enzyme causes parietal cells of the stomach lining to produce acid. Although they perform much the same functions as the histamine H-2 receptor blockers, the proton pump inhibitors reduce stomach acid more and over a longer period.

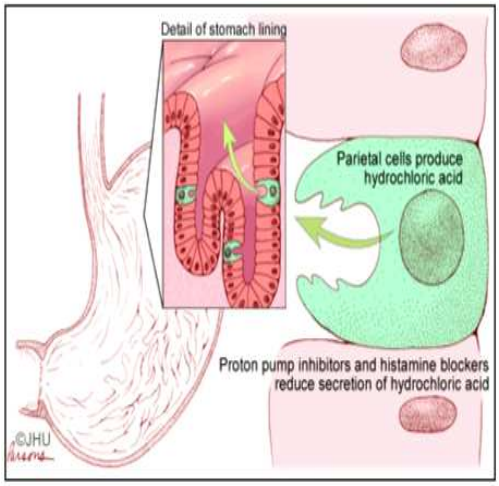
Purpose Proton pump inhibitors are used to treat ulcers; gastro esophageal reflux disease (GERD), a condition in which backward flow of acid from the stomach causes heartburn and injury of the food pipe(esophagus); and conditions in which the stomach produces too much acid, such as Zollinger-Ellison syndrome. Proton pump inhibitors may be used to protect against the ulcerogenic effects of non-steroidal antiinflammatory drugs and to help heal ulcers caused by these drugs.

Pantoprazole as PPIS[4]

- Like other PPIs, pantoprazole exerts its pharmacodynamic actions by binding to the proton pump (H+,K+-adenosine triphosphatase) in the parietal cells, but, compared with other PPIs, its binding may be more specific for the proton pump.
- Pantoprazole is well absorbed when administered as an enteric-coated, delayed-release tablet, with an oral bioavailability of ~77%. It is hepatically metabolized via cytochrome P2C19 to hydroxy-pantoprazole, an inactive metabolite that subsequently undergoes sulfate conjugation. The elimination half-life ranges from 0.9 to 1.9 hours and is independent of dose.
- Pantoprazole has similar efficacy to other PPIs in the healing of gastric and duodenal ulcers, as well as erosive esophagitis, and as part of triple-drug regimens for the eradication of Helicobacter pylori from the gastric mucosa.
- It is well tolerated, with the most common adverse effects being headache, diarrhea, flatulence, and abdominal pain. In clinical studies, it has been shown to have no interactions with various other agents, including carbamazepine, cisapride, cyclosporine, digoxin, phenytoin, theophylline, and warfarin.

Mechanism of action

Pantoprazole is a proton pump inhibitor (PPI) that suppresses the final step in gastric acid production by forming a covalent bond to two sites of the (H+, K+)-ATPase enzyme system at the secretory surface of the gastric parietal cell. This effect is dose-related and leads to inhibition of both basal and stimulated gastric acid secretion irrespective of the stimulus. The binding to the (H+, K+)-ATPase results in a duration of antisecretory effect that persists longer than 24 hours. (From FDA Label)



Materials and Methods:

Table A: Materials and its applications

Ingradient	Application
Pantoprazole Sodium	Anti-Ulcer Drug
Magnesium Oxide	Antioxidant
Ethyl Cellulose	Binder
Dichloro Methane	Solvent
Mannitol	Diluent, sweetening agent
Microcrystalline cellulose	Disintegrant
Crosspovidone	Superdisintegrant
Sodium Starch Glycolate	Superdisintegrant
Aspartame	Superdisintegrant
Lactose	Diluent
Talc	Lubricant
Magnesium Stearate	Lubricant
Vanillin	Flavoring Agent

Table B: Equipment and model

Name of equipment	Manufacturer/Supplier
Weighing balance	Mettler Toledo (PG 403-S)
U.V.Vis spectrophotometer Double beam	UV-1800 Shimadzu
FT-IR	Shimadzu 1800 S
DSC	DSC-60 (Shimadzu) calorimeter.
Bulk Density and Tapped Density apparatus	Electro lab (ETD -1020)
Rotary Compression machine(16 Station)	Cad mach
Dehumidifier	Retch
Hardness tester	Vankel (VK 200)
Disintegration test apparatus	ED-2L Electro lab, Mumbai, Ind
Friability testing machine	Electro lab (EF-1W)
Dissolution test apparatus	Electrolab,USPXXIII,(TDT-08L)plus
Stability chamber	Thermolab

Methods:

- **Development of uv spectrophotometric method for estimation of pantoprazole sodium**

UV Spectrum of Pantoprazole Sodium At the outset, method for the estimation for the drug was developed. Standard Stock Solution was prepared and scanned by UV Spectrophotometer and the □max was found to be 289 nm against distilled water as blank. The spectra obtained are shown in figure.

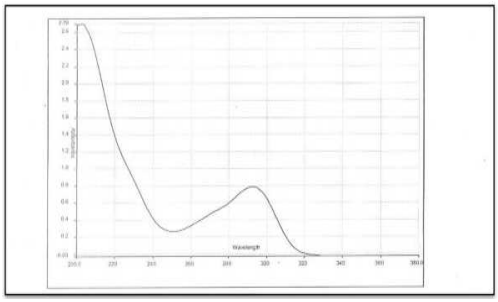


Fig. A: Pentaprazole UV Spectrum

Table C: Standard calibration curve of pantoprazole sodium in 6.8 phosphate buffer

	Absorbance			
Concentration (mcg/ml)	I	I I	III	Average
1	0.1352	0.1366	0.132	0.1346±0.001
2	0.2745	0.2721	0.2764	0.2743±0.012
3	0.4226	0.421	0.4236	0.4224±0.009
4	0.5509	0.5489	0.5523	0.5507±0.003
5	0.6551	0.6574	0.6525	0.655±0.002
6	0.7654	0.7641	0.7669	0.7654±0.010
7	0.858	0.8566	0.8549	0.8565±0.001
8	0.9773	0.9757	0.978	0.977±0.012
9	1.1126	1.1103	1.1139	1.1122±0.009
10	1.2173	1.2168	1.2178	1.2173±0.001

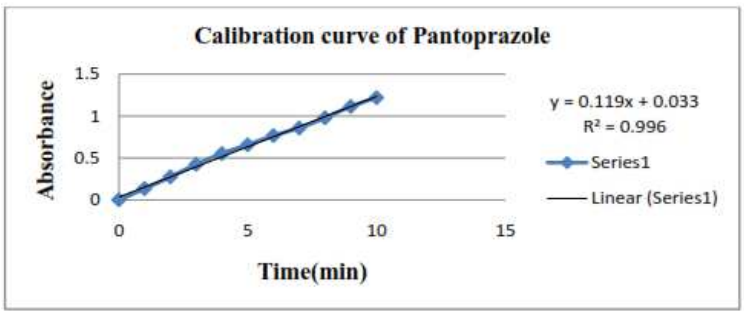


Fig.B: Standard Calibration curve of Pantoprazole sodium:

The Calibration Curve and the data were obtained and the linear plot between concentrations versusabsorbance showed that, Beer-Lambert's law was obeyed in concentration range of 1-10 µg/ml which one subjected to regression analysis. The r^2 value (regression co-efficient) was found to be 0.997which showed linear relationship between concentration and absorbance.

Formation of granules of pantoprazole sodium[5]

Pantoprazole sodium is highly light sensitive drug. It rapidly gets degraded in atmospheric conditions. In concern with stability while handling the formulation there is need to add antioxidant to provide stability.

Granulation process Antioxidant-Magnesium Oxide (1:1) Binder- Ethyl cellulose (2 mg) Solvent-Dichloro Methane (q.s)

1. The amount of pantoprazole sodium and excipients required for granulation were weighed using electronic weighing balance.
2. Drug and all other excipient are individually passed through # 40 meshes to break agglomerates if any present in the raw materials for uniform distribution.
3. Drug and magnesium oxide is mixed thoroughly in 1:1 ratio. Mixture was than granulated using ethyl cellulose as binder and granules were made.
4. Granules were dried at room temperature for about 15 min and again passed through #60 sieves.
5. These prepared granules are subjected to check for physical parameters like bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose.

Formulation development of oro dispersible tablet

Pantoprazole oro dispersible tablet was prepared by direct compression Method. Direct compression: The most common and simplest method available for tablet compression is direct compression in which the drug with other excipients is mixed thoroughly with the help of various mixers followed by the compression of the resulting Powder. Using capsule shape punch in modified rotary compression machine (16 stations) by Cad mach CMD 3-16.

Unit operations for tablet preparation by direct compression method

1. **Weighing**: The amount of pantoprazole sodium and excipients required for batch of tablet formulation were weighed using electronic weighing balance.
2. **Screening**: After weighing, pantoprazole sodium and excipients was passing through # 40 meshes to break agglomerates if any present in the raw materials for uniform distribution.
3. **Mixing**: All the ingredients were mixed manually in polyethylene bag.
4. **Blend Lubrication**: The prepared blend was lubricated using magnesium stearate and talc in polyethylene bag for 15 minutes.
5. **Compression:** The prepared blend was compressed using 16.35mm X 60mm, capsule shape punch.

Development of preliminary trial batches

Development of preliminary trial batches for the selection superdisintegrants. Different Superdisintegrants are added to formulation to check its effect on tablet properties. Cross povidone, cross carmellose sodium and sodium starch glycolate is evaluated at 2%, 4%and 6% concentration. The best one is selected for optimization.

Table D: Preliminary trial batches

Ingradients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Drug	23	23	23	23	23	23	23	23	23
MgO	23	23	23	23	23	23	23	23	23
Ethyl Cellulose	2	2	2	2	2	2	2	2	2
Cross Povidone	3.6	7.2	10.8	-	-	-	-	-	-
CCS	-	-	-	3.6	7.2	10.8	-	-	-
SSG	-	-	-	-	-	-	3.6	7.2	10.8
MCC	27	27	27	27	27	27	27	27	27
Mannitol	32.5	32.5	32.5	32.5	32.5	32.5	32.5	32.5	32.5
Lactose	55.4	51.8	48.2	55.4	51.8	48.2	55.4	51.8	48.2
Aspartame	9	9	9	9	9	9	9	9	9
Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Mg stearate	3	3	3	3	3	3	3	3	3
Flavor	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
Total weight (mg)	180	180	180	180	180	180	180	180	180

- **Optimization using 3^2 full factorial design**[6,7]
  By using 3^2 full factorial design the optimization of independent factors (amount of superdisintegrant 1-cross Povidone and amount of superdisintegrant 2 - sodium starch glycolate) were done. Disintegration time and friability factors were represented as dependent factors. X_1 code for amount of superdisintegrant 1(cross Povidone) and X_2 code for amount of superdisintegrant 2 (sodium starch glycolate)

Table E: 3^2Full factorial design layout

Batch Code	Factor 1 X_1	Factor 2 X_2
A_1	-1	-1
A_2	-1	0
A_3	-1	1
A_4	0	-1
A_5	0	0
A_6	0	1
A_7	1	-1
A_8	1	0
A_9	1	1

Table F: Coded values for X_1 and X_2

Coded Value	Amount of superdisintegrant 1 (cross Povidone) in mg X_1	Amount of Superdisintegrant 2 (sodium starch glycolate) in mg X_2
-1	3.6	7.2
0	5.4	9
1	7.2	10.8

Table G: Formulation using 3^2 full factorial design

Ingradients	A1 (mg)	A2 (mg)	A3 (mg)	A4 (mg)	A5 (mg)	A6 (mg)	A7 (mg)	A8 (mg)	A9 (mg)
Drug	23	23	23	23	23	23	23	23	23
MgO	23	23	23	23	23	23	23	23	23
Ethyl Cellulose	2	2	2	2	2	2	2	2	2
Cross Povidone	3.6	5.4	7.2	3.6	5.4	7.2	3.6	5.4	7.2
SSG	7.2	7.2	7.2	9	9	9	10.8	10.8	10.8
MCC	27	27	27	27	27	27	27	27	27
Mannitol	32.5	32.5	32.5	32.5	32.5	32.5	32.5	32.5	32.5
Lactose	48.2	46.4	44.6	46.4	44.6	42.8	44.6	42.8	41
Aspartame	9	9	9	9	9	9	9	9	9
Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Mg stearate	3	3	3	3	3	3	3	3	3
Flavor	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
Total weight (mg)	180	180	180	180	180	180	180	180	180

- **Evaluation of oro dispersible tablets**
  The mixture of powder was evaluated for bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose. The tablets were evaluated for thickness, hardness, friability, weight variation test, drug content and In-Vitro release rate studies

- **Pre compression parameters evalution**[8,9]
  The mixture of drug and excipient (i.e. blend) prepared for tablet compression is evaluated for following parameters.

  - **Bulk Density (BD):** Weigh accurately 25 g of drug (M), which was previously passed through 20 # and transferred in 100 ml graduated cylinder. Carefully level the powder without compacting, and read the unsettled apparent volume (V_0). Calculate the apparent bulk density in gm/cc by the following formula

  - **Tapped bulk density (TD)**: Weigh accurately 25 g of drug, which was previously passed

through 20 # and transfer in 100 ml graduated cylinder. Then mechanically tap the cylinder containing the sample by raising the cylinder and allowing it to drop under its own weight using mechanically tapped density tester that provides a fixed drop of 14± 2 mm at a nominal rate of 300 drops per minute. Calculate the tapped bulk density in gm/ml by the following formula.

- **Carr's Index:** It is one of the most important parameter to characteristic the nature of powders and granules. The Compressibility Index of the powder blend was determined by Carr's compressibility index. It is a simple test to evaluate the BD and TD of a powder and the rate at which it packed down. It can be calculated from the following formula:

Carr's Index= [(TD-BD)×100]/ TD

- **Hausner's Ratio:** The Hausner's ratio is a number that is correlated to the flow ability of a powder or granular material.

Hausner's Ratio = TD / BD

- **Angle of repose:** The angle of repose of API powder was determined by the funnel method. The accurately weight powder blend were taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

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

Where, 'Θ' is the angle of repose ,
'h' is height of pile,
'r' is radius of the base of pile

- **Post compression parameters evaluation**

All prepared tablets were evaluated for the following official and unofficial parameters.

- **Hardness:** Tablets require a certain amount of strength, or hardness, to withstand the mechanical shocks of handling in manufacturing, packaging as well as in shipping. The hardness of the tablets here was measured using a simple Monsanto hardness tester. In this, a tablet was placed between the plungers, and was tightened from one end, and pressure required to break the tablet was measured. It was expressed in kg/cm2

- **Friability:** The friability of the tablets was determined using Roche friabilator. It is expressed in percentage (%). Ten tablets were initially weighed and transferred into the friabilator. The friabilator was operated at 25rpm for 4min. After 4min the tablets were weighed again. The friability was then calculated using the formula,

Friability (%) = Initial weight-final weight x100/Initial weight

- **Dimensions:** A compressed tablet's shape and dimensions were determined by the tooling during the compression process. Thickness was the only dimensional variable related to the process. The dimensions of tablets were measured using the vernier callipers scale. Tablet thickness should be controlled within a ±5% variation of the mean value.

- **Weight variation test:** Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 20 tablets were calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weights deviate from the average weight by more than the percentage shown in Table 6.10 and none deviate by more than twice the percentage shown.

Table H: Weight variation specs.

Avg. Wt. of Tablets (mg)	Max. % diff. allowed
130 or less	10
130-324	7.5
more than 324	5

- **Assay:** 20 tablets from each batch were weighed and powdered. 20 mg of pantoprazole sodium equivalent to pantoprazole was weighed and dissolved in ethanol; the solution was filtered and made the volume up to 50 ml with distilled water into volumetric flask. Absorbance was measured at 289 nm using shimadzu UV spectrophotometer and percent purity was determined.

***Invitro* drug release:**

Medium: 900 ml; 7.2 phosphate buffer
Apparatus : USP-II (paddle)
RPM : 50
Temperature : 37 °C ± 0.5 °C
Time : 30 minutes

Preparation of dissolution medium (6.8 Phosphate Buffer): Dissolve 6.8 gm. of Potassium phosphate (monobasic) in 1000 ml of distilled water. To this solution add 1N NaOH solution until solution has a pH of about 6.8. Standard solution: Transfer an accurately weighed quantity of about 20 mg of Pantoprazole sodium working standard to a 100-ml volumetric flask. Add about 50 ml of dissolution medium and sonicate to dissolve. Make volume up to the mark with dissolution medium and mix. Dilute 5.0 ml of this solution to 50.0 ml with dissolution medium and mix. Test solution: Set the dissolution parameters of the instrument as mentioned above. Place one tablet each in six different baskets and operate the apparatus exactly for specified time. At the end of specified time, withdraw about 10 ml of solution from a zone midway between the surface of the dissolution medium and top of the basket, not less than 1 cm from the bowl wall. Filter the solution through 0.45 µm Millipore HVLP filter; collect the filtrate by discarding first few ml of the filtrate.

Procedure: Measure the absorbance of standard preparation and sample preparation in 1 cm cell on suitable spectrophotometer at 289nm, using dissolution medium as blank. Calculate the quantity as percentage of Drug dissolved by using formula.

- **Statistical analysis of response**

Statistical analysis is performed by multiple regression analysis using software Design Expert 8.0.7.1. Nine batches were prepared and polynominal equation was derived for desired response. Contour plots were prepared for dependent variable. Derived equation is validated by preparing a check point batch.

- **Factorial equation for response 1 : disintegration time**

$$R_1 = +26.62 - 5.67 * A - 9.33 * B - 2.00 * A * B + 1.83 * A + 10.83 * B$$

Where, R_1= Disintegration time

A=Amount of Crosspovidone

B=Amount of Cross carmellose sodium

Result obtained from factorial design is explained below

Table I : Regression Output of R_1 for 3^2 full factorial Design

PARAMETER	VALUE	PARAMETER	VALUE
Sum of Squares	1255.8	**Mean ±SD**	34.31±4.91
Degree of Freedom	5	**C.V%**	10.39
Mean Square	251.15	**R Square**	0.9363
Model F Value	10.4	**P Value**	0.0039

The Model F-value of 10.40 implies the model is significant. There is only a 0.39% chance that a"Model F-Value" this large could occur due to noise.

Values of P value less than 0.0500 indicate model terms are significant. Values greater than 0.1000 indicate the model terms are not significant.

P values for A, B, A^2, and B^2 was found to be 0.0019, 0.0288, 0.0392, 0.0031 which is less than 0.05, thus significant effect on dependent variable R_1, P value for term AB was found to be 0.3428 which is greater than 0.05, thus non significant effect on R_1.

The R^2 0.9363) was high indicating the adequate fitting of quadratic model.

The polynominal equation can also be used to draw the conclusion considering the magnitude of coefficient and the mathematical sign it carries, I,e, +ve or –ve. -ve sign of variable indicates that as the concentration of superdisintegrants increase disintegration time decreases.

- **Factorial equation for response 2 :**

$$\text{Friability } R_2 = +0.78 + 0.022 * A + 0.037 * B$$

Where, R_2= Friability

A=Amount of Crosspovidone

B=Amount of Cross carmellose sodium Result obtained from factorial design is explained below

Table J: Results

PARAMETER	VALUE	PARAMETER	VALUE
Sum of Squares	0.011	**Mean ±SD**	0.78± 0.033
Degree of Freedom	2	**C.V%**	4.2
Mean Square	5.44E-03	**R Square**	0.5039
Model F Value	5.08	**P Value**	0.0301

The Model F-value of 5.08 implies the model is significant. There is only a 3.01% chance that a "Model F-Value" this large could occur due to noise. P value less than 0.0500 indicate model terms are significant. In this case B are significant modelterms. Values greater than 0.1000 indicate the model terms are not significant. P values for B was found to be0.0207, which is less than 0.05, thus significant effect on dependent variable R_2. P value for term A was found to be 0.1360 which is greater than 0.05, thus non-significant effect on R_1.The R_2 0.9363) was high indicating the adequate fitting of quadratic model. The polynominal equation can also be used to draw the conclusion considering the magnitude of co efficient and the mathematical sign it carries, I,e, +ve or –ve. +ve sign of variable indicates that as the concentration of superdisintegrants increase friability also increses.

Result and Discussion

A=Amount of Crosspovidone B=Amount of Cross carmellose sodium Even though pantoprazole sodium is well absorbed after oral dosing, it has first pass metabolism which leads to a reduced oral bioavailability of the drug.

The present investigation is concerned with the development of the Oro dispersible tablet which are soluble in saliva are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into stomach, thus enhance the bioavailability by avoiding first pass metabolism.

As the pantoprazole is highly light sensitive, its environmental stability is achieved by granulating it with antioxidant.

Suitable analytical method based on UV-Visible spectrophotometer was developed for Pantoprazole sodium. λmax of 289 nm was identified in phosphate buffer solution, pH 6.8.
In present study during selection of excipient (MCC, SSG, CP, Talc, Magnesium stearate) DSC study was performed to ensure that they not interact with each other and with drugs.

Various concentration(,2%,4%,6%) of superdisintegrants (SSG, CP) were added in formulation, all processing steps are carried out at temperature below 250c and relative humidity less than 35%. Procedure to manufacture orodispersible tablets by direct compression was established. Developed ODT gave satisfactory results for various physicochemical evaluations like hardness, friability, weight variation, drug content, in vitro disintegration time and in vitro dissolution profiles.

Disintegration time and % Friability of ODT depends on concentration of superdisintegrants. The disintegration time and % Friabilityof all the formulation varied from81±1.37 to 18±0.92 seconds And 0.87±1.95 to 0.70±1.43.

Combination of superdisintegrants is used to derive satisfactory result.Concentration of superdisintegrants were optimized by using 3^2 full factorial design with the help of design expert 8.0.7.1 version software, in that two independent factors were concentration of crosspovidone(2%-4%)and concentration of crosscarmellose sodium (4%-6%). Three different levels were coded as (-1,0,+1) .From the polynominal equation and contour plots the best optimized batch found.

The optimized batch was evaluated for thickness, weight variation, hardness, friability, disintegration time dissolution and accelerated stability study for period of 3 months. The similarity factor was calculated for comparison of dissolution profile before and after stability studies. The f2 value was found more than 50 that indicate a good similarity between both the dissolution profiles. . Hence, the results of stability studies reveal that the developed formulation has good stability. This work needs to be proved more effective by its bioavailability, pre-clinical, and clinical studies Further studies are needed to investigate these formulations for its performance in vivo. The result of the study indicates that orodispersible tablet of Pantoprazole sodium that can be successfully prepared. Undoubtedly the availability of various technologies and the manifold advantages of ODT will surely enhance the patient compliance and its popularity in the near future.

Table 1: Organoleptic Properties OF Pantoprazole sodium

Parameters	Results
State	Solid
Color	White
Odour	None
Taste	Characteristic
Form	Amorphous

Table 2: Flow property characterization of Pantoprazole sodium

Sr. No.	Parameters	Results
1	Bulk Density	0.40±0.01 gm/ml
2	Tapped Density	0.58±0.03gm/ml
3	Carr's Index	31.03±0.09%
4	Hausner's ratio	1.45
5	Angle of Repose	47.36±0.078
6	Flow Property	Cohesive Powder/Poor flow

Table 3: Flow property characterization of Pantoprazole sodium Granules

Sr. No.	Parameters	Results
1	Bulk Density	0.55±0.03 gm/ml
2	Tapped Density	0.61±0.01 gm/ml
3	Carr's Index	10.52±0.07
4	Hausner's ratio	1.1
5	Angle of Repose	29.13±0.02
6	Flow Property	Excellent

Table 4: Evaluation of physical properties of Preliminary Trial Batch tablet blends

Batch Code	Bulk Density* (gm/cc)	Tapped Density* (gm/cc)	Carr's Index (%)	Hausner's ratio (%)	Angle of repose*
F1	0.51±0.02	0.58±0.05	1.13	12±0.01	32.11±0.01
F2	0.52±0.01	0.58±0.02	1.13	11.86±0.09	31.95±0.08
F3	0.50±0.04	0.57±0.07	1.14	12.28±0.04	33.75±0.05
F4	0.56±0.04	0.63±0.04	1.12	11.11±0.05	31.74±0.0
F5	0.50±0.05	0.57±0.08	1.13	11.68±0.01	32.74±0.0
F6	0.54±0.06	0.60±0.02	1.11	10±0.03	30.74±0.0
F7	0.51±0.02	0.57±0.03	1.11	10.52±0.01	30.74±0.0
F8	0.52±0.06	0.60±0.08	1.15	13.33±0.02	34.74±0.02
F9	0.50±0.04	0.57±0.03	1.14	12.28±0.07	33.92±0.02

***The values represent mean ± standard deviation, n = 5**

Table 5: Evaluation of physical properties of Optimization Batch tablet blends (n=5)

Batch Code	Bulk Density* (gm/cc)	Tapped Density* (gm/cc)	Carr's Index (%)	Hausner's ratio (%)	Angle of repose*
A1	0.52±0.42	0.59±0.05	1.13	11.86±0.21	32.19±0.01
A2	0.54±0.01	0.60±0.22	1.11	10±0.09	30.95±0.08
A3	0.51±0.75	0.58±0.78	1.13	12.06±0.04	32.74±0.09
A4	0.50±0.05	0.57±0.09	1.13	11.68±0.11	32.74±0.07
A5	0.53±0.34	0.59±0.41	1.11	10.17±0.05	30±0.02
A6	0.56±0.08	0.63±0.04	1.12	11.11±0.05	31.74±0.20
A7	0.55±0.53	0.61±0.01	1.1	10.52±0.07	29.13±0.02
A8	0.52±0.61	0.58±0.09	1.13	11.86±0.09	31.95±0.08
A9	0.50±0.04	0.57±0.45	1.14	12.28±0.07	33.92±0.02

***The values represent mean ± standard deviation, n = 5**

Table 6: Data for post compression parameters of preliminary trial batches

Batch Code	Thickness* (mm)	Avg Weight* (mg)	Hardness* (Kg/cm^2)	Friability* %	D.T.* (Sec)	% Drug Content*	% Drug Release*
F1	1.99±0.06	182.8 ±0.54	3.85± 0.19	0.81±1.58	71±0.58	99.76± 0.74	98.12 ± 3.72
F2	2.12±0.03	179.0 ±2.18	3.51±0.15	0.87±1.93	45±0.95	98.18 ± 0.3	91.88 ± 3.72
F3	2.02±0.12	179.6 ±0.70	3.88±0.11	0.79±1.06	68±1.86	96.12± 0.07	92.56 ± 9.45
F4	2.11±0.12	181.6 ±1.11	3.54±0.11	0.85±1.51	64±2.01	98.02± 1.20	97.54 ± 5.60
F5	1.96±0.12	180.4 ±0.91	3.58±0.17	0.82±0.94	69±0.88	97.11± 0.09	94.13 ± 2.81
F6	2.08±0.16	181.3±1.79	3.91±0.15	0.79±1.26	81±1.37	99.35± 1.25	97.88 ± 3.72
F7	2.12±0.16	181.8 ±0.17	3.63±0.14	0.76±1.72	63±1.66	97.99± 0.75	95.37 ± 5.84
F8	1.98±0.15	178.5 ±1.36	3.52±0.16	0.81±1.43	51±1.91	96.15± 1.25	93.00 ± 1.03
F9	1.97±0.08	180.5 ±2.59	3.59±0.12	0.78±1.59	57±0.86	98.18± 0.49	88.65 ± 8.62

***The values represent mean ± standard deviation, n = 5**

Table 7: Data for post compression parameters of optimization batches

Batch Code	Thickness* (mm)	Avg Weight* (mg)	Hardness* (Kg/cm2)	Friability* %	D.T.* (Sec)	% Drug Content*	% Drug Release*
A1	2.11±0.12	179.6 ±0.70	4.09±0.13	0.71±o.89	54±0.11	98.84±0.86	95.48 ± 9.45
A2	1.96±0.12	180.8 ±1.17	3.86±0.12	0.76±0.74	42±0.69	99.76±0.34	97.29 ± 3.72
A3	2.08±0.16	181.1 ±0.57	3.88±0.19	0.70±1.43	48±0.44	96.11± 0.3	92.13 ± 2.81
A4	1.99±0.02	179.6± 2.18	3.64±0.17	0.77±1.51	32±0.12	98.67±0.21	91.61 ± 3.72
A5	2.12±0.03	181.6 ±1.11	3.48±0.11	0.79±0.93	28±0.71	97.68±0.72	99.27 ± 3.73
A6	2.02±0.12	180.4 ±0.91	3.52±0.10	0.86±1.07	18±0.92	98.38±0.29	97.80 ± 3.72

A7	2.05±0.12	178.5 ±0.36	3.72±0.13	0.76±1.29	38±0.75	99.76±0.74	95.10 ± 2.81	
A8	2.08±0.16	180.5 ±2.59	3.64±0.16	0.82±0.81	26±0.14	96.41±0.11	97.51 ± 9.45	
A9	2.03±0.11	182.8 ±0.54	3.54±0.13	0.81±0.97	24±0.36	99.91±0.21	97.51 ± 9.45	

*The values represent mean ± standard deviation, n = 5

Table 8: Comparative dissolution data of formulation F1 to F9

% Drug Release in 900ml 6.8 PHOSPHATE BUFFER 50 RPM, 37°C ± 0.1°C, USP Type II (Paddle)									
Time	**Batch Code**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0	0	0	0	0	0	0	0	0
1	26.19	38.9	35.97	38.75	30.35	18.12	26.19	28.9	42.23
2	40.57	59.25	50.51	51.67	45.67	31.67	40.57	42.25	58.59
4	63.72	74.31	64.18	65.31	61.49	50.31	63.56	62.31	72.31
6	71.71	81.35	76.56	78.36	75.71	73.36	74.01	81.35	85.56
8	82.94	87.26	81.35	89.95	86.11	84.95	85.94	89.26	92.35
10	90.13	91.88	92.56	97.54	94.13	97.88	95.37	93	98.65

Table 9: Comparative dissolution data of formulation A1 to A9

% Drug Release in 900ml 6.8 PHOSPHATE BUFFER 50 RPM, 37°C ± 0.1°C, USP Type II (Paddle)									
Time	**Batch Code**								
	A1	**A2**	**A3**	**A4**	**A5**	**A6**	**A7**	**A8**	**A9**
0	0	0	0	0	0	0	0	0	0
1	18.12	28.34	23.12	30.85	35.26	46.19	18.9	26.23	39.23
2	31.67	40.8	36.67	43.92	52.75	59.57	42.25	48.59	54.49
4	50.31	53.49	56.31	56.34	69.08	73.92	62.31	65.82	69.96
6	68.36	68.36	74.36	70.05	82.23	84.71	74.35	75.56	78.56
8	79.95	82.95	88.95	83.27	91.15	93.94	83.26	84.95	86.54
10	91.48	93.29	92.13	94.61	99.27	97.8	95.1	97.51	95.51

Table 10: Response data for 3^2 Full factorial optimization design

Batch code	**Factor 1 X_1** **Amount of Crosspovidone(mg)**	**Factor 2 X_2** **Amount of SSG(mg)**	**Response 1** **Disintegration Time(sec)**	**Response 2** **% Friability**
A1	5.4	9	28	0.79
A2	7.2	10.8	24	0.81
A3	5.4	10.8	26	0.82
A4	7.2	9	18	0.86
A5	7.2	7.2	48	0.7
A6	3.6	9	32	0.77
A7	3.6	7.2	54	0.71
A8	3.6	10.8	38	0.76
A9	5.4	7.2	42	0.76

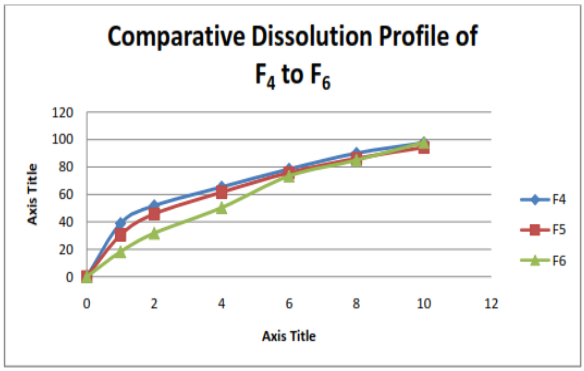


Figure 1: Comparative Dissolution Profile of F4 to F6

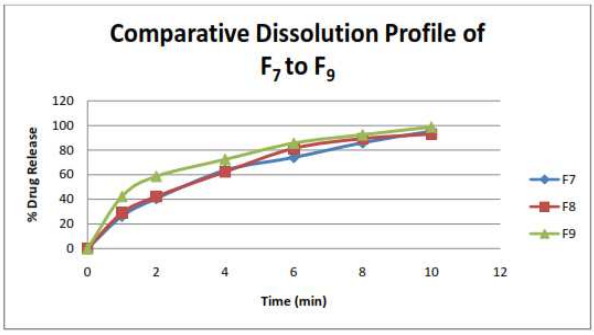


Figure 2: Comparative Dissolution Profile of F7 to F9

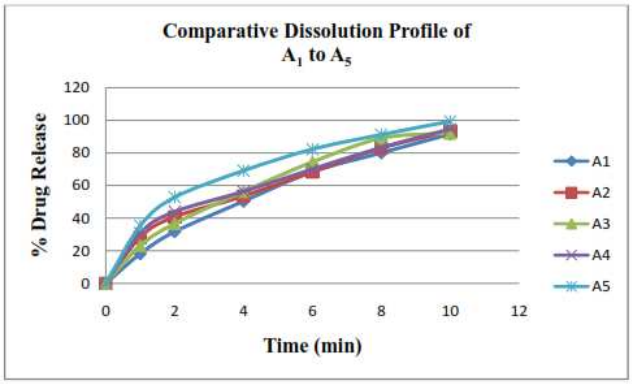


Figure 3: Comparative Dissolution Profile of A1 to A5

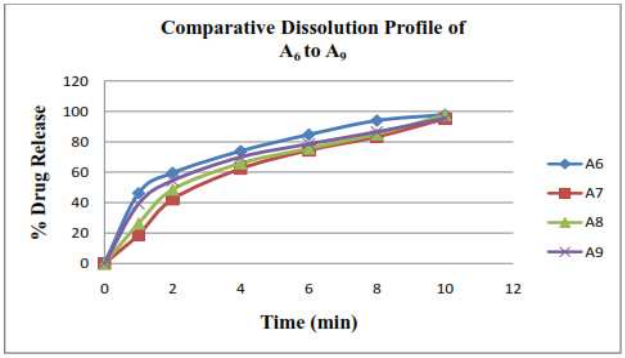


Figure 4: Comparative Dissolution Profile of A6 to A9

"Cite this article"

J. Modi, R.K. Kamble, C. S. Formulation and Optimization of Oro dispersible Tablet of Pentoprazole Sodium as Proton Pump Inhibitor" Int. J. of Pharm. Res. & All. Sci.2013; Volume 2, Issue 3,38-49

REFERENCES

1. Yamamoto Y, Fujii M, Watanabe K, Tsukamoto M, et al. Effect of powder characteristics on oral tablet disintegration. International Journal of Pharmaceutics 2009; 365:116-120.
2. C.Kumaresan. Orally Disintegrating Tablet-Rapid Disintegration, Sweet Taste, And Target Release Profile. 2008 Sep;6
3. Bandari S, Mittapalli RK, Gannu R, Rao YM. Orodispersible tablets: An overview. Asian Journal of Pharmaceutics 2008 Jan.
4. Paul W. Junnickel Pantoprazole : A New Proton Pump Inhibitor, Clinical Therapeutics, Vol 22, Issue11, Pg 1268-1293
5. Raviraj Pillai, Pradeep Karatgi Pharmaceutical Technology Europe Volume 21, Issue Orallydisintegrating tablets: the path to improved patient compliance and enhanced life cycle management
6. Schwartz JB, Connor RE. Optimization techniques in pharmaceutical formulation and processing. In Banker GS, Rhodes CT, editors. Modern Pharmaceutics, 3rd edition,MC Dekker, New York,1996,pp 727-752.
7. Doornbos CA, Haan PD,Optimization techniques in formulation and processing. In Swarbrick J, Boylan JC, editors. Encyclopedia of Pharmaceutical Technology, Marcel Dekker, 4th Edn., New York,1995,pp 77-160.
8. Particle size analysis by sieve analysis, October2012, http://www.astm.org/Standards/C136.htm.
9. Castell D. Review of immediate-release omeprazole for the treatment of gastric acid-related disorders, informa health care, Expert opinion on pharmacotherapy, November 2005; 6(14): 2501-2510 (doi:10.1517/14656566.6.14.2501