

**Research Article****Fabrication and characterization of pantoprazole sodium Ora-Solv tablets using different superdisintegrants**

Sai Charitha CH.\*, Swathi N., Chandi Rani P., Nikitha M., Meghana N., Rama Rao N.

Department of Pharmaceutics,

Chalapathi Institute of Pharmaceutical Sciences, Lam, Guntur- 522043, Andhra Pradesh, India

Received: 21 June 2018

Revised: 13 July 2018

Accepted: 22 July 2018

**Abstract**

**Objective:** In the present investigation, an attempt has been made to formulate Ora – Solv tablets of pantoprazole sodium using two different superdisintegrants like crosspovidone and primogel by direct compression method. **Materials and methods:** ORA-SOLV tablets of pantoprazole were prepared by direct compression method. In the present investigation, each superdisintegrant was used in three concentrations (2.5, 5 and 10%). Weighed quantities of Pantoprazole sodium along with appropriate concentrations of superdisintegrants i.e crosspovidone and primogel, mannitol, microcrystalline cellulose, saccharin sodium were weighed and mixed in geometric progression in a dry and clean mortar. Superdisintegrants act by decreasing the disintegration time which leads to enhanced dissolution rate. Evaluation of formulations showed that all the preparations were within the standard limits and the disintegration time for formulations ranges from 12.10 sec to 27 sec. **Results and conclusion:** It was observed that with the increase in the concentration of superdisintegrant the disintegration time decreases and among all formulation, tablets containing crosspovidone shows less disintegration time due to more hydrophilicity. From the obtained results, formulation F3 containing 10% w/w concentration of crosspovidone was considered to be the optimized formulation which releases up to 99.78% of the drug in 15 minutes. The OST's have potential advantages over conventional marketed tablets with their better patient compliance, both in geriatrics and pediatrics, ease of administration and bio-availability.

**Keywords:** Ora – Solv tablets, Pantoprazole, Crosspovidone, Primogel, direct compression

**Introduction**

Ora-Solv tablets are also known as Fast dissolving tablets, Mouth dissolving tablets, Fast disintegrating tablets, Orally disintegrating tablets, Rapid disintegrating tablets, Oro dispersible tablets and Quick dissolving tablets (Rishi, 2004). Ora-Solv tablets are those which when placed in the tongue, instantaneously disintegrates and releases the drug that dissolves or disperses rapidly in the saliva without the need of drinking water or chewing. OST's usually dissolve in the oral cavity within 15 seconds to 3 minutes. The faster the drug into solution, quicker the absorption and onset of clinical effect (Panigrahi et al., 2005). Oral drug delivery system is the most convenient and widely accepted route of administration for

various therapeutic agents. Among many oral drug delivery systems, ora-solv tablets have gained importance over past 3 decades. Ora-solv tablets are suitable for patients who have dysphasia, paediatric, geriatric and psychiatric. It is also suitable for patients with nausea, vomiting and motion sickness (Sarada et al., 2014). When formulated as OST, some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach which in turn increases the bioavailability of the drug. This is known as pre gastric absorption. Thus in OST, the amount of drug that is subjected to first pass metabolism is reduced as compared to conventional tablets. OST offers a giant leap forward in drug administration by providing a new and easy way of taking medication (Srinivas et al., 2005). Pantoprazole is a potent and selective proton pump inhibitor. It is an effective agent in the treatment of Peptic ulcers, Gastro-oesophageal reflux disease (GERD), Oesophagitis, Zollinger-Ellison syndrome and other GI hypersecretory disorders. It has poor bioavailability (~50%) and aqueous solubility, thus it is absorption and dissolution rate limited,

**\*Address for Corresponding Author:**

Sai Charitha CH.

Department of Pharmaceutics,

Chalapathi Institute of Pharmaceutical Sciences, Lam, Guntur- 522043, Andhra Pradesh, India

Email: charithapharmacy1992@gmail.com

DOI: <https://doi.org/10.31024/ajpp.2018.4.5.8>2455-2674/Copyright © 2018, N.S. Memorial Scientific Research and Education Society. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

delaying its onset of action. Pantoprazole is available as conventional tablet in the market and many patients find it difficult to swallow these, especially paediatric and geriatric subjects which results in high incidence of non-compliance and ineffective therapy (Jawahar et al., 2012). In this present study, an attempt has been made to formulate ora-solv tablets of Pantoprazole using two different superdisintegrants viz. Crosspovidone and Primogel by direct compression method. The objective of this study was to enhance the safety and efficacy of the drug molecule, achieve better patient compliance, solve problem of difficulty in swallowing, enhance onset of action and provide a stable dosage form (Patel et al., 2006).

## Materials and methods

### Materials

Pantoprazole sodium was a kind gift from Vasudha Pharma Ltd. (Andhra Pradesh, India), Crosspovidone and Primogel obtained as gift sample from CDH Ltd, Mumbai. Aerosil and Mannitol were purchased from Loba Chemie, Mumbai. Microcrystalline cellulose, Saccharin sodium was purchased from S.D. Fine Chemicals, Mumbai. All other chemicals and reagents were of analytical grade.

**Preformulation studies** (Mohapatra et al., 2008)

### Compatibility studies

Fourier transform infrared (FT-IR) spectra were obtained. The spectra were recorded in a thermo-IR 200 FTIR spectrophotometer. Potassium bromide pellet method was employed and background spectrum was collected under identical conditions.

### Angle of repose

Angle of repose is determined by using funnel method. The accurately weighed blend is taken in a funnel. The height of the funnel is adjusted in such a way that the tip of the funnel just touches the apex of the heap of blend. The drug-excipient blend is allowed to flow through the funnel freely on to the surface. The diameter of the powder cone is measured and angle of repose is calculated using the equation.

$$\tan \Theta = h/r$$

Where h= height of cone and r = radius cone base respectively.

Angle of Repose less than 30° shows the free flowing of the material.

**Bulk density, Tapped density and Carr's index** (Banker et al., 1987)

Weighed quantity of powder blend was taken in a graduated cylinder and the bulk volume (V<sub>b</sub>) was measured, and weight of the blend (M) was determined. The measuring cylinder containing known mass of powder blend was tapped for a fixed time and the tapped volume (V<sub>t</sub>) occupied in the cylinder and the weight of the blend (M) was measured. From that bulk density, tapped density and Carr's index were calculated.

$$\text{Bulk density (e}_b\text{)} = \frac{M}{V_b}$$

$$\text{Tapped density (e}_t\text{)} = \frac{M}{V_t}$$

$$\text{Carr's index (I)} = \frac{e_b - e_t}{e_t} \times 100$$

### Preparation of ORA-SOLV tablets

ORA-SOLV tablets of pantoprazole were prepared by direct compression method. In the present investigation, each superdisintegrant was used in three concentrations (2.5, 5 and 10%). Weighed quantities of Pantoprazole sodium along with appropriate concentrations of superdisintegrants i.e crosspovidone and primogel, mannitol, microcrystalline cellulose, saccharin sodium were weighed and mixed in geometric progression in a dry and clean mortar. Then the blend was passed through sieve no. 60. Then magnesium stearate was added and mixed well. The dry blend was compressed into tablets using 8 mm convex faced punches in a 10 Station Rotary Tablet Machine (Cadmach, India). The composition of OST of Pantoprazole sodium is shown in table 1.

**Table 1.** Formulation of Pantoprazole Ora - Solv tablets

Formulation Code	Drug (mg)	Crosspovidone (mg)	Primogel (mg)	MCC (mg)	Mannitol (mg)	Aerosil (mg)	Saccharin Sodium (mg)	Magnesium Stearate (mg)
F1	20	6.25	-	201.75	15	3	2	2
F2	20	12.5	-	195.50	15	3	2	2
F3	20	25	-	183	15	3	2	2
F4	20	-	6.25	201.75	15	3	2	2
F5	20	-	12.5	195.50	15	3	2	2
F6	20	-	25	183	15	3	2	2

## Evaluation of Ora-Solv tablets

### Weight variation

The weight variation test is carried out in order to ensure uniformity in the weight of tablets in a batch. First the total weight of 10 tablets from each formulation is determined and the average is calculated. The individual weight of the each tablet is also determined to find out the weight variation (Silverstein et al., 1991).

### Hardness

The hardness of tablet is an indication of its strength. Measuring the force required to break the tablet across tests it. The force is measured in kg and the hardness of about 3-5 kg/cm<sup>2</sup> is considered to be satisfactory for uncoated tablets. Hardness of 10 tablets from each formulation is determined by Monsanto hardness tester, Pfizer hardness tester etc (Silverstein et al., 1991).

### Friability test (Banker et al., 1987)

Friability is the loss of weight of tablet in the container due to removal of fine particles from the surface. Friability test is carried out to access the ability of the tablet to withstand abrasion in packaging, handling and transport. Roche friabilator is employed for finding the friability of the tablets. Weigh the 20 tablets from each batch and place in Roche friabilator that will rotate at 25 rpm for 4 minutes. Dedust the all tablets and weigh again. The percentage of friability can be calculated using the formula (Silverstein et al., 1991).

$$\% \text{ Friability} = [(W1-W2)100]/W1$$

Where, W1= Weight of tablet before test, W2 = Weight of tablet after test

### Thickness and diameter (Wade et al., 1994)

The thickness and diameter of the tablets were carried out using vernier calipers (Mitutoyo corps, Japan). Five tablets were used for the above tests from each batch and results were expressed in millimeters.

### Wetting Time

Wetting time is closely related to the inner structure of tablets and to the hydrophilicity of the excipients. A linear relationship exists between wetting time and disintegration time. Thus wetting time is an important step for disintegration process to take place. A piece of tissue paper folded twice was placed in a small petridish (internal diameter = 6.5cm) containing 6ml of water. A tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. Three trials for each batch were performed and standard deviation was also determined.

### Water Absorption ratio (Moen et al., 2006)

A piece of tissue paper folded twice was placed in a small

petridish (internal diameter = 6.5cm) containing 6ml of water. A tablet was placed 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:

$$R = 100 \times \frac{W_a - W_b}{W_b}$$

W<sub>a</sub> = Weight of tablet after water absorption

W<sub>b</sub> = weight of tablet before water absorption

### In-vitro dispersion time

In-vitro dispersion time was measured by dropping a tablet in a measuring cylinder containing 6ml of pH 6.8 (simulated saliva fluid). The time for the tablet to completely disintegrate into fine particles was noted. Three tablets from each batch were randomly selected and in-vitro dispersion time was performed.

### In-vitro disintegration time

The disintegration time of the tablets was determined as per Indian Pharmacopoeial monograph. The test was carried out using Tablet disintegration apparatus. Six tablets from each batch were placed and one litre of distilled water was used as the disintegration medium. The time required to obtain complete disintegration of all the six tablets was noted.

### In-vitro dissolution studies

Dissolution apparatus II USPXX1 model [Paddle type] was used to study in-vitro drug release for Ora-Solv tablets of Pantoprazole Sodium. 900ml of Phosphate buffer solution [pH 6.8] was used as the dissolution medium. The tablet was placed in the dissolution medium and rotated at a speed of 0.50 50 rpm maintained at a temperature of 37°C. 5ml of sample was withdrawn at periodic intervals 0, 5th, 10th, and 15th minute. 5ml of fresh dissolution medium (maintained at the same temperature) was replaced after each time of withdrawal of samples. The samples were analyzed spectrophotometrically at 287.4 nm for the drug content against the respective buffer blank. The mean percentage of pantoprazole sodium released at various time intervals was calculated from standard graph and plotted against time.

## Results and discussion

### Compatibility Studies

The compatibility between the drug and the excipients was evaluated using FT-IR spectroscopy (Figure 1-3). There was no appearance or disappearance of peaks in the drug – excipient mixture, which confirmed the absence of any chemical interaction between the drug and the polymers.

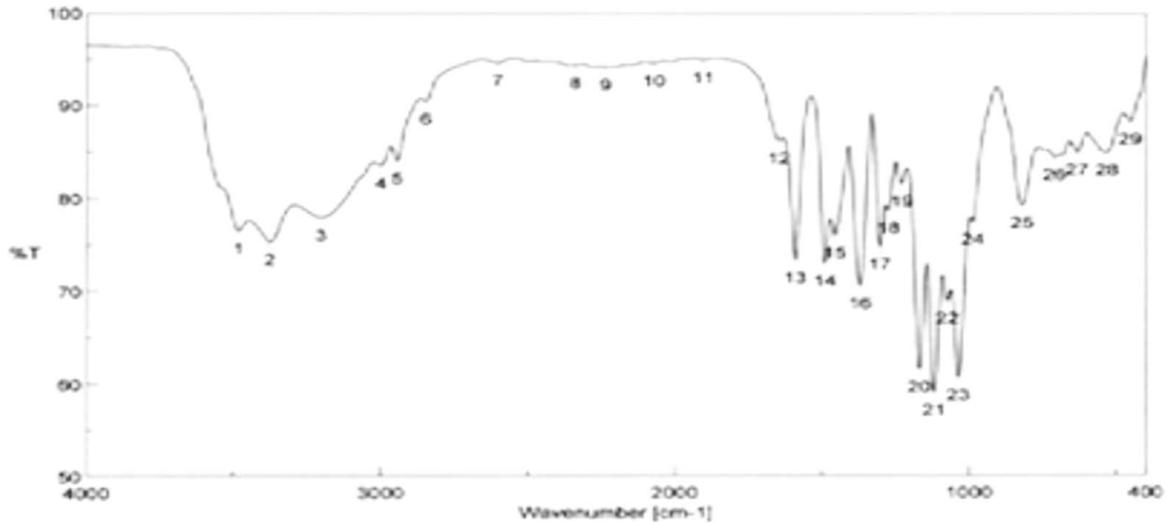


Figure 1. FT-IR spectra of pantoprazole sodium

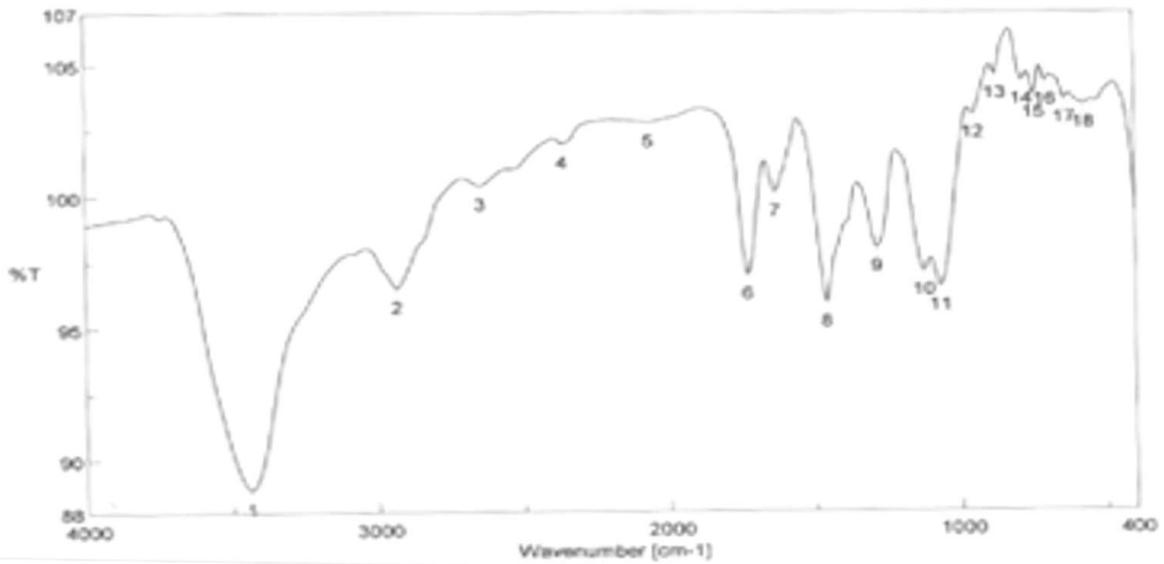


Figure 2. FT-IR spectra of pantoprazole sodium and crosspovidone

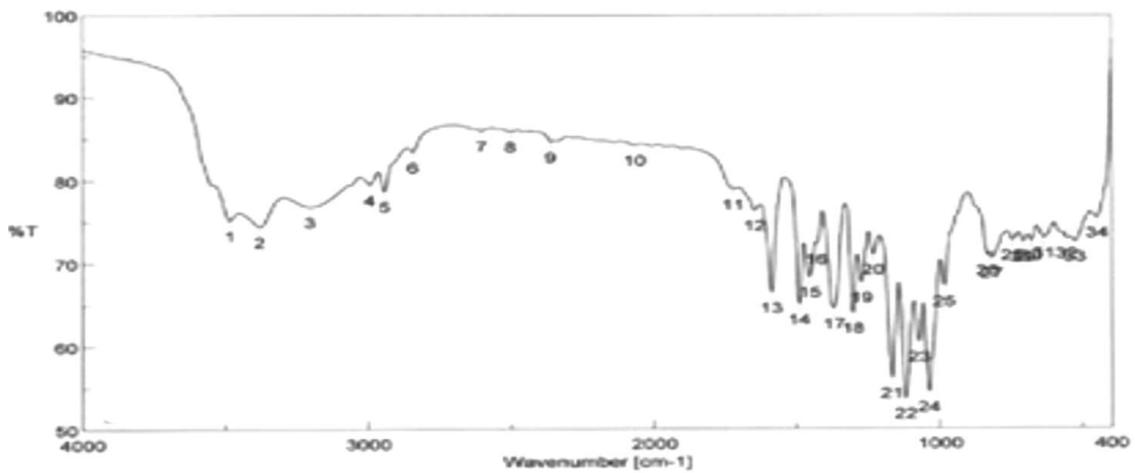


Figure 3. FT-IR spectra of pantoprazole sodium and primogel

**Flow properties**

The angle of repose for all the formulations exhibits good flow properties. Further, Bulk Density, Tapped Density and Carr's

Index were studied. From the obtained values of Bulk density and Tap density values Carr's index was calculated. Since the Carr's index was below 15% for all batches of

powder blends, the flow property was good. The results for Angle of repose, Bulk Density, Tapped Density and Carr's Index were tabulated in table 2.

**Table 2.** Flow properties of powder blend

Parameters	F1	F2	F3	F4	F5	F6
Bulk Density (g/ml)	0.489	0.464	0.446	0.510	0.509	0.499
Tapped Density (g/ml)	0.512	0.509	0.470	0.410	0.390	0.380
Carr's Index (%)	9	9.002	9.109	6	6.10	6.71
Angle of Repose ( $\Theta$ )	26	25	24	20	22	24

### Thickness, Diameter and Hardness

The thickness and diameter of the tablets were found to be in the range of  $4.16 \pm 0.21$  mm to  $4.33 \pm 0.21$  mm and  $8.00 \pm 0.08$  mm to  $8.16 \pm 0.23$  mm respectively. The hardness of the different formulations ranged from 3.76 to 4.10 Kg/cm<sup>2</sup>.

### Friability and Weight Variation Test

The weight of tablets was fixed based on the ingredients present in the formulations. In each formulation, weight variation was within the I.P. Limit. Mostly the variation was within 1%. All the formulations exhibited less than 1%. Friability and weight variation data were within the I.P. Limit and the results are given in table 3.

**Table 3.** Evaluation parameters for tablets

Formulation Code	Thickness (mm)	Hardness Kg/cm <sup>2</sup>	Friability (%)	Weight Variation (mg) $\pm$ SD	Wetting Time (Sec)	Water Absorption Ratio
F1	$4.16 \pm 0.21$	3.0	0.435	$241.5 \pm 0.12$	$7.10 \pm 0.06$	31.98
F2	$4.10 \pm 0.13$	3.4	0.410	$248.90 \pm 0.98$	$7.34 \pm 0.12$	32.14
F3	$4.19 \pm 0.05$	4	0.594	$251.34 \pm 0.43$	$6.89 \pm 0.14$	35.02
F4	$4.24 \pm 0.17$	4.2	0.390	$239.90 \pm 0.76$	$7.98 \pm 0.04$	33.89
F5	$4.30 \pm 0.45$	3.8	0.445	$247.14 \pm 0.89$	$8.10 \pm 0.01$	32.17
F6	$4.33 \pm 0.21$	3.9	0.463	$250.89 \pm 0.23$	$8.24 \pm 0.08$	30.92

**Table 4.** In vitro dispersion and disintegration time and drug content

Formulation Code	In vitro dispersion Time (Sec)	In vitro Disintegration Time (Sec)	Drug Content (%)
F1	14.93	17.10	88.12
F2	12.23	15.19	90.45
F3	8	12.10	97.21
F4	20	27	95.08
F5	18.14	25.97	96.38
F6	16.42	22.16	90.01

### Wetting Time and Water Absorption Ratio

The results of wetting time and water absorption ratio are presented in Table 4. The wetting time was found to be least in case of formulation F3 (7.89 sec) and maximum in case of formulation F5 (8.10 sec) and water absorption ratio ranges from 30.92 to 35.02. Wetting time is least for crosspovidone containing formulations and maximum for primogel containing formulations, which indicates that crosspovidone has higher hydrophilicity compared to primogel.

### Drug content

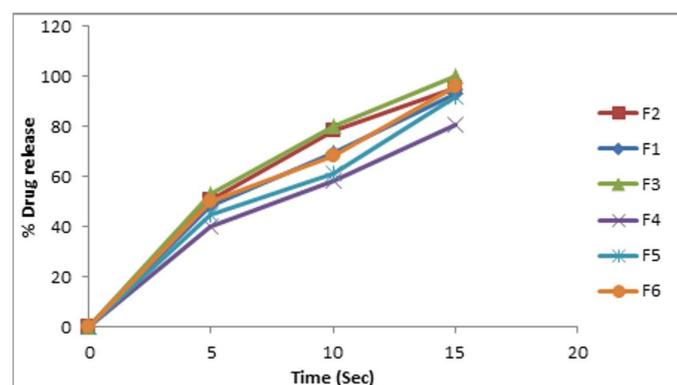
The developed formulations were subjected to test for content uniformity using HPLC and the obtained results prove that the drug is distributed uniformly throughout the tablets dosage form. The results were presented in table 5.

### In-vitro dispersion time

All the formulations were subjected to In-vitro dispersion time by dropping a tablet in a measuring cylinder containing 6ml of pH 6.8 (simulated saliva fluid). The time for the tablet to completely disintegrate into fine particles was noted. In vitro dispersion time ranges from 8 sec to 20 sec. The results show that formulation prepared by using primogel takes more time for dispersion than formulations containing crosspovidone.

**Table 5.** In vitro dissolution data

Time (min)	Cumulative Percentage Release (%)					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	48.17	50.71	52.82	40.17	44.91	50.21
10	69.42	78.10	80.17	58.19	61.03	68.17
15	92.79	95.41	99.78	80.32	91.73	95.70

**Figure 4.** Cumulative drug release profile**In-vitro disintegration time**

The disintegration time of the ora solv tablets was determined as per Indian Pharmacopoeia monograph and was carried out using Lab India Tablet disintegration apparatus. The disintegration time ranges from 12.10 sec to 27 sec. It was observed that with the increase in the concentration of superdisintegrant the disintegration time decreases. And among all formulation, tablets containing crosspovidone shows less disintegration time due to more hydrophilicity. The results were given in table 4.

**In-vitro dissolution studies**

Formulations prepared with different concentrations of crosspovidone showed release of 92.79% to 99.78% at the end of 15 minutes, whereas those prepared with primogel as superdisintegrant showed the release of 80.32% to 95.7% (Table 5). The percentage of drug release increased with increase in concentration of superdisintegrant from 2.5% to 10%. The higher dissolution rates observed with primogel may be due its strong swelling power which exerts sufficient hydrodynamic pressure which in turn facilitates complete and rapid disintegration. From the obtained results, formulation F3 containing 10% w/w concentration of crosspovidone was considered to be the optimized formulation which releases up to 99.78% of the drug in 15 minutes. The results were shown in table 5.

**Conclusion**

The Pantoprazole Sodium Ora-Solv Tablets (OST's) were

prepared by direct compression method using various super disintegrants such as crosspovidone and primogel. Among all formulations, F3 formulation containing 10% w/w concentration of crosspovidone with appropriate amount of other excipients was considered to be the optimized formulation with the desired drug release (99.78%). All the formulations have sufficient mechanical strength, quick disintegration in mouth and good dissolution. The Ora-Solv Tablet formulation of Pantoprazole sodium provides instant relief from Hyper-gastric disorders. The OST's have potential advantages over conventional marketed tablets with their improved patient compliance, both in geriatrics and pediatrics, ease of administration and bio-availability.

**Conflicts of interest:** Nil

**References**

- Banker GS, Anderson GR, Lachman, Liberman HA, Kanig JL. 1987. Theory and practice of Industrial pharmacy, 3rd edition, Varghese Publishing house, Mumbai, pp 293.
- Jawahar N, Jain K, Sood S, Barath M. 2012. Formulation and evaluation of ora-solv tablets of pantoprazole sodium. Journal of Pharmaceutical Science & Research, 4(6): 1839–1843.
- Moen MD, Keating GM. 2006. Sumatriptan fast-disintegrating /rapid release tablets. Drugs, 66(6):891-2.
- Mohapatra A, Parikh RK, Gohel MC. 2008. Formulation, development and evaluation of patient friendly dosage forms of metformin, Part-1: Orally disintegrating tablets. Asian Journal of Pharmacy, 2(3):167-71.
- Panigrahi P, Baghel S, Mishra B. 2005. Mouth dissolving tablets: An overview of preparation techniques, evaluation and patented technologies. Journal of Pharmaceutical Research, 4:33-8.
- Patel PB, Chaudhary A, Gupta GD. 2006. Fast dissolving drug delivery systems: An update. www.pharmainfo.net.
- Rishi RK. 2004. Fast dissolving tablet-A review. The Pharma Review, 34-36.
- Sarada K, Firoz S, Ramya sudha E, Himaja N, Padmini K. 2014. Formulation and evaluation of oral disintegrating tablets of pantoprazole. Journal of Global Trends in Pharmaceutical Sciences, 5(4):2191–2198.
- Silverstein RM, Basselot GC, Morrill TC. 1991. Spectrometric identification of organic compounds, 5th edition, John Wiley & Sons, New York, pp 100-31.
- Sreenivas SA, Dandaji PM, Gadad AP, Godbole AM,

- Hiremath SP, Mastiholimath VS, Bhagwati ST. 2005. Oro dispersible tablets: Newfangled drug delivery system- A review. *Indian Journal of Pharmaceutical Education and Research*, 39(4):177-81.
- Wade A, Weller P. 1994. *Handbook of Pharmaceutical Excipients*, 2nd edition. The Pharmaceutical Press, London, 84,141,143,280,294,392,418,424,462.