IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
August 2021 Vol.:22, Issue:1

Effect of Combination of Superdisintegrants in Enhancing The Dissolution Rate of Pantoprazole in Its Oral Disintegrating Tablets

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Abbas Ali[1], Navyath Pandranki[1], Gowtham Reddy Cheruku[1], Akhil Naidu Adapala[1], Rohith Vanapalli[1], Ashok Thulluru[1*]

[1]Dept. of Pharmaceutical Quality Assurance, Shri Vishnu College of Pharmacy (Autonomous), Vishnupur, Bhimavaram-534 202, W.G. Dist., A.P., India

Submitted: 23 July 2021
Accepted: 29 July 2021
Published: 30 August 2021

Keywords: Pantoprazole, a proton-pump inhibitor, oral disintegrating tablets, super disintegrants, and dissolution rate

ABSTRACT

The objective of the study was to formulate and optimize Oral Disintegrating Tablets (ODTs) of pantoprazole (PZ), a proton-pump inhibitor for the treatment of heartburn, acid reflux, and gastro-oesophageal reflux disease (GORD). The dissolution rate of PZ was improved by the combination of super disintegrants in the ODTs. FTIR studies confirmed the absence of drug-super disintegrants interactions. Croscarmellose sodium (CCS), sodium starch glycolate (SSG), and crospovidone (CPV) and their combinations in a 1:1 ratio were used as super disintegrants. Seven formulations (F0-F6) of ODTs were prepared by the direct compression method. The directly compressible blends have good flow characteristics. The formulated tablets were evaluated for hardness, thickness, weight variation, friability, wetting time; *in-vitro* dispersion time, water absorption ratio, drug content, disintegration time and the results were within USP limits. Formulation F4 (with a combination of SSG: CCS) showed a shorter wetting time 22.15+0.03 sec; disintegration time of 73+0.12 sec and highest swelling index of 50.26+0.16 and dissolution efficiency at 10 min (DE_{10}) of 66.26+0.17 %, hence it was selected as an optimized formulation. The drug release from the optimized PZODTs (F4) follows first-order kinetics, it passes the test for stability as per ICH guidelines. Hence the combination of super disintegrants is superior to individual ones and the combination SSG: CCS in 1:1 ratio aids in enhancing the dissolution rate of PZ in its ODTs.

INTRODUCTION:

The oral route is the most preferred route of administration of dosage forms, due to its potential advantages like ease of administration, convenient dosing, self-medication, no pain, and patient compliance. Hence tablets and capsules are the most popular dosage forms[1], but the important drawback of these dosage forms is dysplasia[2] which can be solved by developing a novel drug delivery system (NDDS), Oral Disintegrating Tablets (ODTs) [3]. The sublingual route usually produces a faster onset of action than orally ingested tablets and the portion absorbed through the sublingual blood vessels bypasses the hepatic first-pass metabolic processes. An ODT can be defined as a dosage form for oral administration, which, when placed in the mouth, is rapidly dispersed or dissolved and can be swallowed in the form of liquid. For these formulations, the small volume of saliva is usually enough to disintegrate in the oral cavity. The drug can then be absorbed partially or entirely into the systemic circulation from blood vessels in the sublingual mucosa, or it can be swallowed as a solution to be absorbed from the gastrointestinal tract[4-5]. Pantoprazole (PZ), a proton-pump inhibitor for the treatment of heartburn, acid reflux, and gastro-oesophageal reflux disease (GORD) [6]. It is an off-white crystalline powder with a molecular weight of 383.4 g/Mol. It is freely soluble in water. Its absolute bioavailability is 77% when administered as an enteric-coated tablet. Its stability in aqueous solution is pH-dependent, unstable in acidic pH, and stable in alkaline pH, hence it is selected as a suitable candidate to formulate as ODTs. The purpose of this investigation was to formulate PZODTs by direct compression method and to study the effect of a combination of super disintegrants in enhancing the dissolution rate of PZ in its ODTs.

MATERIALS AND METHODS:

MATERIALS:

Pantoprazole was obtained from Hetero Drugs Pvt. Ltd., Hyderabad, India as a gift sample, powder vanilla flavor was a gift sample from Firmenich, Chennai. Sodium starch glycolate (Primogel®), croscarmellose sodium (Ac-Di-Sol®), Crospovidone (Crospovidone M®), microcrystalline cellulose (Avicel PH102), mannitol (Pearlitol® 200 SD), aspartame are purchased from S.D. Fine Chem. Pvt. Ltd., Mumbai. Magnesium stearate, talc, aspartame, potassium dihydrogen phosphate, and sodium hydroxide were purchased from Sigma

Chemical Industries, Hyderabad. All the excipients used in the study were of pharmaceutical grade.

METHODS:

The standard calibration curve of PZ in pH 6.8 phosphate buffer solution (PBS):

Preparation of pH 6.8 PBS: Place 50 mL of 0.2 M potassium hydrogen phosphate in a 200 mL volumetric flask, add the 22.4 mL of 0.2 M sodium hydroxide and add water to the volume.

Preparation of stock solution-I (1000 µg /mL): Was prepared by dissolving 50 mg of PZ in a few mL of pH 6.8 PBS in a 50 mL volumetric flask and the volume was made up to mark with pH 6.8 PBS.

Preparation of stock solution-II (10 µg/mL):1 mL of stock solution-I was transferred to a 100 mL volumetric flask and the volume was made up to the mark with pH 6.8 phosphate buffer.

Preparation of working dilutions: Aliquots of 0.2, 0.4, 0.6, 0.8, and 1 mL of stock solution-II (10 µg/mL) were transferred to a series of 10 mL volumetric flasks and diluted with pH 6.8 PBS up to the mark to obtain the conc. of 2, 4, 6, 8, and 10 µg/mL PZ solutions respectively. The obtained dilutions were analyzed at the λ_{max} 279 nm using a UV-Visible spectrophotometer (UV-1700, Shimadzu, Mumbai, India) and their absorbance was noted. The standard calibration curve was plotted by taking the concentration of drug solution (µg/mL) on X-axis and absorbance on Y-axis[7].

Drug-excipient compatibility (FTIR) studies: FTIR absorption spectra of pure PZ and 1:1 ratio physical mixtures of PZ and all three super disintegrants used in the formulation were recorded, in the frequency range of 400-4000 cm^{-1} with a resolution of 2 cm^{-1}, by the direct sampling method with isopropyl alcohol as a solvent, using FTIR Cary 630 spectrophotometer. taken to confirm the identity of the PZ and to detect the interaction of the PZ with the super disintegrants used in the formulation[8].

Preparation of PZ ODT: All the formulations were prepared by direct compression method, by keeping the amount of PZ constant at 20 mg. The composition of other excipients is varied as mentioned in the formulation table (**Table 1**). In these formulations, CPV, CCS, and SSG

are used as super disintegrants. Microcrystalline cellulose (MCC), mannitol, and lactose as a directly compressible diluent. aspartame as an artificial sweetener, powder vanilla flavor as a flavoring agent, magnesium stearate as a lubricant and talc as a glidant. PZ and all the other excipients excluding magnesium stearate and talc were co-sifted through Sieve No. # 40 (ASTM), blended uniformly in a polybag for 5 min, and lubricated with Sieve No. # 60 (ASTM) passed magnesium stearate and talc by mixing in the same polybag for an additional 2 min. Tablets were compressed on a tablet compression machine (10 stations, Yogesh Pharma Machinery Pvt. Ltd., India) fitted with 8 mm standard round punches with an Avg. wt. of 200 mg and 3-4 kg/cm^2 of hardness[8].

Table No. 1: Formulation table of PZODTs

INGREDIENT (mg)	**Control**	**10% SSG**	**10% CCS**	**10% CPV**	**5%SSG + 5%CCS**	**5% SSG + 5%CPV**	**5%CCS + 5%CPV**
	F0	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Pantoprazole	20	20	20	20	20	20	20
SSG		10			5	5	
CCS			10		5		5
CPV				10		5	5
MCC	158	148	148	148	148	148	148
Mannitol	14	14	14	14	14	14	14
Lactose	2	2	2	2	2	2	2
Powder Vanilla Flavor	2	2	2	2	2	2	2
Aspartame	2	2	2	2	2	2	2
Magnesium stearate	2	2	2	2	2	2	2
Talc	1	1	1	1	1	1	1
Total	**200**	**200**	**200**	**200**	**200**	**200**	**200**

Pre-compression studies: The directly compressible PZ ODT blends were evaluated for their flow and compression properties[9].

The angle of Repose (AR): This was determined by the funneling method, the blend was poured through the walls of a funnel, which was fixed at a position such that its lower tip was

at a height of exactly 2 cm above the hard surface. The blend was poured till the time when the upper tip of the pile surface touched the lower tip of the funnel. The AR (θ) is calculated by the equation.

$$\theta = \tan^{-1} h/r \qquad \text{Eq. No. (1)}$$

Where θ = angle of repose, h = height of the heap, and r = radius of the base of the heap circle.

Bulk density (BD): A quantity of 2 gm of SLT blend from each formulation, previously lightly shaken to break any agglomerates formed, was introduced into a 10 ml measuring cylinder, and the volume is noted as bulk volume. The BD was calculated by the equation.

$$BD = \text{wt. of blend} / \text{Bulk volume} \qquad \text{Eq. No. (2)}$$

Tapped density (TD): After the determination of BD, the measuring cylinder was fitted to a tapped density apparatus. The tapped volume was measured by tapping the powder for 500 times. Later the tapping was done for another 750 times and the tapped volume was noted (the difference between these two volumes should be less than 2%). If it is more than 2%, tapping is continued for another 1250 times and the constant tapped volume was noted. The TD was calculated by the equation.

$$TD = \text{Wt. of blend} / \text{Tapped volume} \qquad \text{Eq. No. (3)}$$

Carr's Index (CI): The percentage of CI is calculated by the equation.

$$CI = (TD-BD) \times 100/TD \qquad \text{Eq. No. (4)}$$

Hausner's Ratio (HR): This is a number that correlates to the flowability of a powder. It is calculated by the equation.

$$HR = TD/BD \qquad \text{Eq. No. (5)}$$

Post compression studies[9]:

Avg. wt. of tablets: An electronic balance (Mettler Toledo, 3- MS-S / MS-L, Japan) was used to accurately weigh the individual wt. of twenty tablets (n=20) which were randomly selected from each formulation and checked for the acceptability of wt. variation.

Friability test: The friability of the 20 tablets from each batch (n=1) was tested by a friabilator (SINGLA, TAR 120, Germany) at a speed of 25rpm for 4min. The tablets were then dedusted, reweighed, and percentage weight loss was calculated by the equation,

$$\% \text{ Friability} = (\text{initial wt.} - \text{wt. after friability}) \times 100 / \text{initial wt.} \qquad \text{Eq. No. (6)}$$

Hardness test: To evaluate the diametrical crushing strength, 3 tablets from each formulation were tested using a hardness tester (Monsanto type hardness tester, MHT-20, Campbell Electronics, India).

Thickness: The thickness of 3 tablets from each formulation was determined using a Vernier caliper (Mitutoyo Corporation, Japan).

***In-vitro* disintegration time & fineness of dispersion:** It is specified in the European Pharmacopeia (EP), the disintegration time determination procedure for fast disintegrating tablets is the same as that of conventional uncoated tablets and the tablets should be dispersed within less than 3 min. The obtained tablet's dispersion was passed through a sieve screen with a nominal mesh aperture of 710 mm to confirm the fineness of dispersion[10].

Wetting time and Swelling Index: A piece of tissue paper folded twice was placed in a petri dish having an internal diameter of 5.5 cm, containing 6 mL of water. A tablet was placed on the paper and the time required for complete wetting was measured as wetting time (WT), using a stopwatch. The wetted tablet was then reweighed and the swelling index (SI) was determined using the following equation 11.

$$SI = [(W_a - W_b) / W_b] \times 100 \qquad \text{Eq. No. (7)}$$

Where W_b and W_a were the weights of the tablet before and after swelling.

Assay: To evaluate the drug assay, 3 tablets (n=3) from each formulation were powdered in mortar and pestle. Blend equivalent to 1 mg of NFD was accurately weighed and transferred into a 100 mL volumetric flask containing 10 mL of methanol, and the volume was made up to 100 mL with pH 6.8 phosphate buffer and ultrasonicated for 2 min to extract the NFD from the tablet blend and filtered through 0.45 µm poly tetra flour ethylene (PTFE) filter disc. The filtrate was suitably diluted if necessary and its absorbance was measured by UV- Visible spectrophotometer at 279 nm[8].

***In-vitro* dissolution studies:** Were performed on all F0 to F6 formulations on 6 tablets from each batch (n=6) using the dissolution apparatus (Lab India Disso2000, Lab India Analytical Instruments Pvt. Ltd., India) with USP-II / Paddle**.** Each dissolution flask contains 900 mL of pH 6.8 PBS; the speed of the paddle was maintained at 50 rpm; the temperature was kept stable at 37 °C± 0.5 °C. At required time intervals, 5 mL of dissolution media was withdrawn with a pipette containing 0.45 µ (PTFE) filter disc, suitably diluted if necessary and its absorbance was measured by UV-Visible spectrophotometer at 279 nm. Furthermore, 5 mL of fresh pH 6.8 PBS was replaced with the dissolution flask to keep the volume of dissolution medium constant[8].

***In-vitro* dissolution kinetics:** The *in vitro* drug release data was fitted into zero-order plots/ dissolution profiles (%CDD*Vs* time) and first-order plots (Log % CDUD*Vs* time) as per the following equations[11].

$$\textit{Zero-order equation: } Q_t = Q_0 + K_0 t \qquad \textit{Eq. No. (8)}$$

$$\textit{First-order equation: } \text{Log } Q_t = \text{Log } Q_0 - K_1 t/2.303. \qquad \textit{Eq. No. (9)}$$

Where Q_t is the amount of the drug dissolved in time t, Q_0 is the initial amount of drug in the solution; K_0 & K_1 refers to the rate constants of zero & first order respectively.

Dissolution Efficiency at 30 min (DE_{30}) by Trapezoid Rule; and time for 50 % drug release (t_{50}) were calculated from dissolution profiles.

Equations for calculating DE_{30}:

$$[AUC]_{t1}^{t2} = \Sigma\left[\frac{1}{2}(c_1+c_2)\,(t_2-t_1)\right] \qquad \textit{Eq. No (10)}$$

$$DE_{30} = \frac{[AUC]_{t1}^{t2}}{\textit{Total area under 30 min}} \qquad \textit{Eq. No. (11)}$$

Where,

$[AUC]_{t1}^{t2}$ = Area under curve between time points t_1 to t_2

Total area under 30 min = 30 x 100 = 3000 cm^2

Accelerated stability studies of the optimized PZODTs (F4): Were carried according to an international conference on harmonization (ICH) guidelines. 20 tablets were packed in each 10 CC HDPE bottle and sealed thermally and were placed in a humidity chamber (NSW-175, Narang Scientific work, India) maintained at 45 °C ± 2 °C and 75 % ± 5 % RH. Up to 3 months, at the end of every month the respective samples were withdrawn and evaluated [13].

RESULT AND DISCUSSION:

The standard calibration curve of PZ in pH 6.8 PBS: Based on the measurement of absorbance at ʎ max of 279 nm in pH 6.8 PBS in the conc. range of 2-10 µg/mL, a straight line with an equation, y = 0.0036x - 0.004, and a regression coefficient (r^2) of 0.999 was obtained, which indicates it follows the Beers-Lambert law in the concentration range of 2-10 µg/mL.

Drug-excipient compatibility (FT-IR) studies: The FT-IR spectrum of PZ is characterized by sharp characteristic peaks at 3482.81 cm^{-1}: (N-H) band, 1590.99 cm^{-1}: C-O bond, 1036.55 cm^{-1}: C-F stretching vibration, 1168.65 cm^{-1}: C=S stretching vibration, and 1036.55 cm^{-1}: Sp^2 C-O aromatic ether stretch. All the above characteristic peaks appear in the (1:1 ratio) physical mixtures of PZ with super disintegrants at the same wavenumbers indicating no modification or interaction in the drug with the combination of super disintegrants used in the study[14] (**Fig .1**).

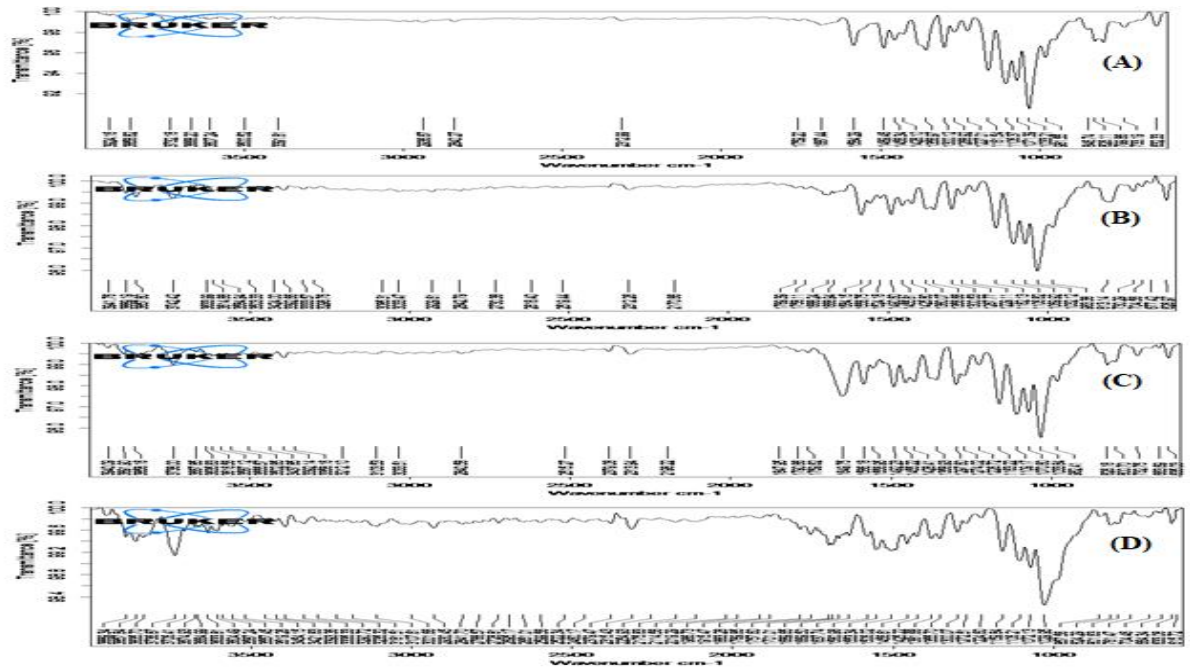

Figure No.1: FTIR spectra of A) PZ, B) PZ + CCS, C) PZ+ CPV & D) PZ + SSG

Pre-compression studies: The directly compressible blends of PZ ODTs, reveals that the AR was found between 22˚.51' ± 2.01 to 26˚.28'± 0.73, HR between 1.30 to 1.40 and CI between 21.82 to 28.92 %. The micrometric studies indicate good flow and compression characteristics of all the blends. In these formulations, directly compressible mannitol and MCC are used as diluents, which impart good flow and compressibility to the blends. Mannitol also exhibits sweetness and cooling effect due to negative heat of solution and imparts a pleasant mouth feel[15]. Pre-compression studies of PZODTs consolidated results were tabulated in (Table 2).

Table No. 2: Results of pre-compression studies on PZODTs*

F. Code	AR (°)	BD (gm/cm^3)	TD (gm/cm^3)	CI (%)	HR ( )
F0 (control)	25.19±2.11	0.44±0.02	0.58±0.03	23.80	1.40
F1	26.27±0.62	0.32±0.02	0.46±0.05	27.92	1.38
F2	23.64±2.15	0.46±0.01	0.62±0.02	22.81	1.32
F3	25.19±2.27	0.44±0.01	0.58±0.09	23.80	1.40
F4	26.37±2.31	0.40±0.01	0.54±0.02	26.41	1.36
F5	26.28±0.73	0.33±0.04	0.47±0.06	28.92	1.39
F6	22.51±2.01	0.45±0.02	0.53±0.03	21.82	1.30

*All the tests except for CI & HR were performed in triplicate (n=3) and the values are expressed as (Mean ± SD). CI & HR were calculated from the mean values of BD & TD.

Post-compression studies:

Reveals that the Avg. wt. of tablets was found to be 198±0.02 to 202±0.04 mg. The Avg. thickness of tablets was found to be 3.1±0.02 to 3.3±0.01 mm. The Avg. hardness of the tablets ranges between 4.2±0.12 to 4.5±0.14 Kg/cm^2, indicating satisfactory mechanical strength. The % wt. loss in the friability test ranges from 0.334 to 0.447 % w/w, which was NMT 1 % w/w as per pharmacopeia limits indicating a good mechanical resistance of tablets. Assay of all the prepared batches is within 99.7±0.13 to 101.2±0.11 % of the labeled content, indicating the content uniformity of all the formulations. The DT of F4 (5% SSG + 5% CCS; 1:1 ratio**)** achieved the fastest (73±0.12 sec) of all, as it produces the highest tablet braking force at a given compression force. The wetting time of all the formulations was obtained in the range of 15±0.03 to 82±0.01 sec. Wetting is related to the inner structure of the tablets, the hydrophilicity of the components, and the swelling mechanism of super disintegrant. The swelling index is also related to the hydrophilicity of the matrix. The ODTs with CPV were fully hydrated and soft throughout because CPV quickly wicks water into the tablet by imparting porosity[16]. Water wicking is the ability to draw water into the tablet matrix. Both the extent and the rate of water uptake are critically important. Exposure to water can cause ingredients to swell and exert pressure against surrounding tablet ingredients, causing existing bonds between particles to break[17]. Water wicking and swelling are the two most important mechanisms of disintegrant action for CCS[18]. SSG is a commonly used super disintegrant employed to promote rapid disintegration by swelling mechanism[19]. The water-insoluble super disintegrants show better disintegration properties than the slightly water-soluble ones since they do not tend to swell. Superdisintegrants that tend to swell show slight retardation of the disintegration property due to the formation of viscous barrier[20]. Hence, among the used single super disintegrants, CPV alone is superior[21]. The order of single and combined super disintegrants efficiency was observed as SSG+CCS > SSG+CPV > CCS+CPV > CPV > CCS > SSG > Control, indicates combined super disintegrants are superior to single ones[22]. The formulation F4 (5% SSG + 5% CCS; 1:1 ratio) shows a min wetting time of 15±0.03 sec and disintegration time of 73±0.12 sec and the highest SI of 50.26±0.16 % is selected as an optimized formulation. The consolidated results of post-

compression studies as, (mean ± SD) were tabulated in (**Table 3**). Pictures while measuring the DT of optimized PZODTs (F4) were shown in **(Fig.2).**

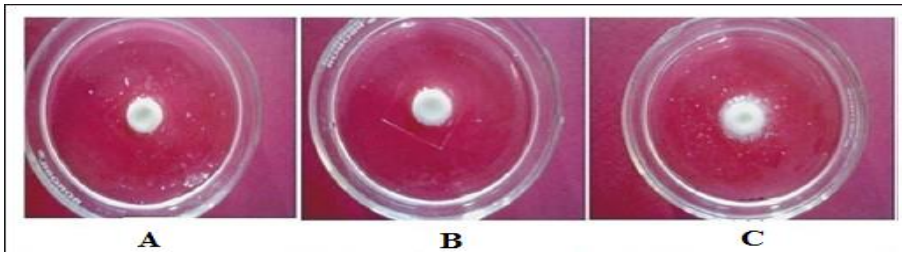

Figure No. 2: Pictures while measuring the DT of optimized PZODT; F6 A) Initial stage, B) at 20 sec and C) at 52.12 sec

Table No. 3: Results of post-compression studies on PZODTs*

F CODE	Avg. Wt. (mg)	Hardness (Kg/cm^2)	Thickness (mm)	Friability (%)	WT (sec)	SI (%)	DT (sec)	Assay (%)
F0 (control)	201±0.04	4.5±0.11	3.2±0.04	0.425	82±0.01	18.32±0.11	202±0.12	99.9±0.12
F1	198±0.03	4.2±0.12	3.2±0.02	0.347	64±0.02	24.04±0.12	142±0.13	100.7±0.14
F2	199±0.01	4.3±0.01	3.1±0.02	0.443	63±0.02	26.53±0.14	124±0.11	99.7±0.13
F3	201±0.02	4.5±0.14	3.3±0.01	0.447	50±0.01	30.12±0.13	120±0.13	101.2±0.11
F4	199±0.01	4.2±0.15	3.2±0.02	0.334	15±0.03	50.26±0.16	73±0.12	100.5±0.15
F5	202±0.04	4.3±0.11	3.2±0.01	0.433	25±0.03	49.48±0.11	113±0.13	99.8±0.12
F6	198±0.02	4.2±0.05	3.2±0.03	0.434	25±0.01	39.03±0.13	119±0.14	100.7±0.11

*Post compression studies of PZODTs, except for Avg. wt. (n=20) and friability test (n=1); all other tests are carried out in triplicate (n=3) and the results are represented as (Mean ± SD).

***In-vitro* dissolution studies:** The order of single and combined superdisintegrants in comparison with the control in enhancing the dissolution rate of PZ from its ODTs is SSG + CCS > SSG + CPV > CCS + CPV > CPV > CCS > SSG > Control. The dissolution profiles were represented graphically in (**Fig.3**).

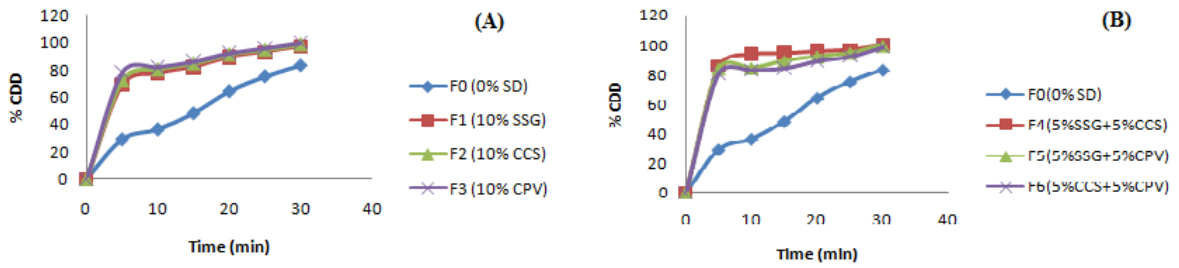

Figure No. 3: *In-vitro* dissolution profiles of PZODTs; A. F1 to F3 & B. F4-F6 in comparison with control (F0)

***In-vitro* dissolution kinetics:** Reveals formulation F4 (5% SSG + 5% CCS; 1:1 ratio) had the highest DE_{30} (66.22 %); K_1 (0.198 min^{-1}) with r^2 (0.987) and lowest t_{30} (below 5 min). Hence, it is considered as an optimized PZODT. First-order dissolution rate constant (K_1) and regression coefficient (r^2) of first-order profiles were calculated from first-order plots. The consolidated *in-vitro* dissolution kinetic parameters of PZODTs were tabulated in (**Table 4)**.

Table 4. Results of *in vitro* dissolution kinetic studies on PZODTs

F. Code	Dissolution plots		First-order plots	
	t_{30} (min)	DE_{30} (%)	K_1 (min^{-1})	r^2
F0 (control)	Below 20	23.63	0.055	0.974
F1	Below 5	53.91	0.104	0.957
F2	Below 5	56.12	0.117	0.941
F3	Below 5	59.65	0.193	0.954
F4	Below 5	66.22	0.198	0.987
F5	Below 5	63.10	0.134	0.827
F6	Below 5	61.11	0.101	0.845

Accelerated stability studies of the optimized PZ ODT (F4): There were no significant differences in post compression studies of initial and accelerated stability samples of optimized PZODTs; F4 (5% SSG + 5% CCS; 1:1 ratio) up to 3 months in a 20 cc HDPE pack, hence it passes the test for stability as per ICH guidelines. The consolidated results of post-compression studies on accelerated stability samples of optimized PZODTs (F4); were tabulated in **(Table 5)**. *In vitro* dissolution profiles of initial and accelerated stability samples of optimized PZODTs (F4) were represented graphically in **(Fig. 4)**. Comparative FTIR

spectra of PZ optimized PZODTs (F6)-Initial samples and 45°C/ 75% RH-3M sample are shown in **(Fig. 5)**.

Table No.5: Results of post-compression studies on accelerated stability samples of optimized PZODTs (F4)*

Parameter	Initial	45°C / 75% RH		
		1M	2M	3M
Avg. wt. (mg)	199±0.01	198±0.12	199±0.09	199±0.10
Hardness (kg/cm^2)	4.2±0.15	4.5±0.51	4.5±0.44	4.4±0.74
Thickness (mm)	3.2±0.02	3.5±0.09	3.5±0.04	5.4±0.02
*Friability (%)	0.334	0.345	0.354	0.432
Assay (%)	100.5±0.15	98.6 ±0.42	97.7 ±0.65	96.9 ±0.21
DT (Sec)	73±0.12	76±0.12	78±0.03	79±0.04
WT (Sec)	15±0.03	15 ±0.10	16 ±0.01	16±0.05
SI (%)	50.3±0.16	50.8±1.98	52.2±1.09	52.8±1.10

*Post compression studies of optimized PZODTs (F4) accelerated stability samples; except for Avg. wt. (n=20) and friability test (n=1); all other tests are carried out in triplicate (n=3) and the results are represented as (Mean ± SD).

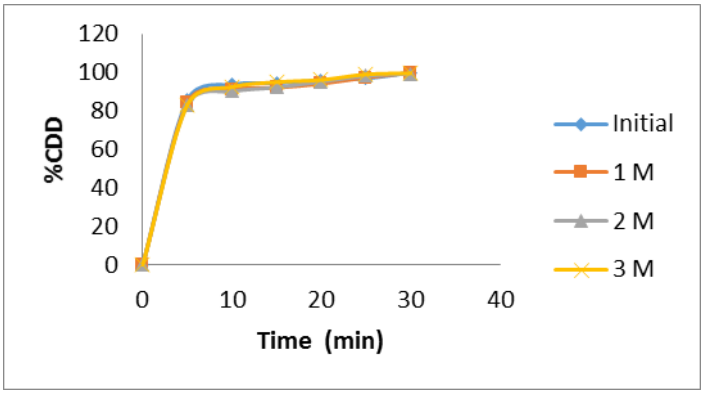

Figure No. 4: *In vitro* dissolution profiles of accelerated stability samples of optimized PZODTs (F4)

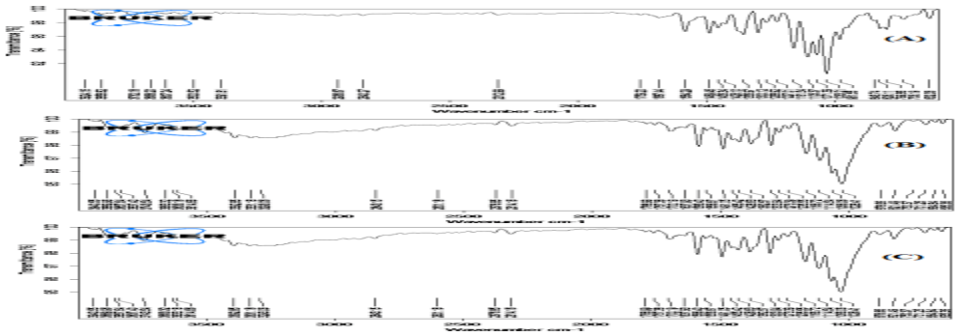

Figure No. 5: Comparative FTIR spectra of A. PZ, B. Optimized PZODTs (F4) - Initial and C. Optimized PZODTs (F4) - 45°C/ 75% RH-3M samples

CONCLUSION:

Because of the above findings, there is good compatibility between drugs and super disintegrants used in the study. All the formulations passed the pre- & post- compression evaluation parameters as per USP. The order of single and combined super disintegrants efficiency was observed as SSG + CCS > SSG + CPV > CCS + CPV > CPV > CCS > SSG > Control. The combination of super disintegrants SSG and CCS are superior among all at 1:1 ratio. The optimized PZODTs; F4 (5% SSG + 5% CCS; 1:1 ratio) passes the test for stability as per ICH guidelines. Hence a combination of super disintegrants, that too SSG and CCS at 1:1 ratio are more beneficial in the dissolution rate enhancement of drugs like PZ in their ODTs than used alone.

ACKNOWLEDGEMENT:

The authors are thankful to Sri. K.V. Vishnu Raju, Chairman-Sri Vishnu Educational Society (SVES) and Dr. B. V. Raju Foundation; Dr. Kumar V. S. Nemmani, Director and Dr. K.S. Nataraj, Principal Shri Vishnu College of Pharmacy (Autonomous), Vishnupur, Bhimavaram, Andhra Pradesh, India for providing the required resources and being constant support n bringing out this review work.

CONFLICT OF INTEREST:

The authors declare no conflict of interest.

REFERENCES:

1. Sharma S and G D Gupta. Formulation and characterization of fast dissolving tablet of Promethazine Theoclate. *Asian J. Pharm.* 2008; 2(1): 70-72.
2. Nehal Siddiqui M, G Garima, and P K Sharma. Fast dissolving tablets: preparation, characterization, and evaluation. *International Journal of Pharmaceutical Sciences Review and Research.* 2010; 4(2): 87-96.
3. P. A. Hannan, J. A. Khan, A. Khan and S. Safiullah. Oral Dispersible System: A New Approach in Drug Delivery System. Indian J Pharm Sci. 2016; 78(1): 2-7
4. K. Sarada, S. Firoz, E. Ramya sudha, N. Himaja and K.Padmini. Formulation and evaluation of oral disintegrating tablets of pantoprazole. *Journal of Global Trends in Pharmaceutical Sciences*. 2014; 5(4): 2191-98.
5. N. Jawahar, Sumeet Sood, Kunal Jain and M.Barath. Formulation and Evaluation of Ora-Solv Tablets of Pantoprazole Sodium. *Journal of Pharmaceutical Science and Research*. 2012; 4(6): 1839-43.
6. Wanjari B.E, Khalode K. D, Bhendarkar K. R., Bhongade Y. M., Rehpade V.T., Rangari M. N. and Sheikh N. V. Formulation and evaluation of mouth dissolving drug delivery system of pantoprazole sodium. *Open Access International Journal of Science and Engineering*. 2018; 3(4): 84-90.
7. Susanta Paul, **A**nannya Bose, Indrani Konar, Pradip Kumar Kara, Tathagata Roy and Payel Mukherjee**.** Comparative in-vitro characterization of different commercially available brands of pantoprazole sodium tablets. *World Journal of Pharmacy and Pharmaceutical Sciences*. 2017; 6(11): 778-83.
8. Jaimin Modi, R.K. Kamble, and Chetan Singh Chauhan. Formulation and Optimization of Orodispersible Tablet of Pantoprazole Sodium as Proton Pump Inhibitor. *International Journal of Pharmaceutical Research and Allied Sciences*. 2013; 2(3): 38-49.
9. Banker GS, Anderson NR, Lachman L, Liberman HA. The Theory and Practice of Industrial Pharmacy, 3rd ed. Mumbai: Varghese Publishing House; 1987, p: 293-94.
10. European Pharmacopeia 6th ed. Strasburg, France; 2007, p: 2435.
11. Gautam Singhvi, Mahaveer Singh. Review: *In vitro* Drug Release Characterization Models. *International Journal of Pharmaceutical Studies and Research.* 2011; 2(1): 77-84.
12. D.M. Brahmankar; Sunil. B. Jaiswal. Bio- pharmaceutics and Pharmacokinetics: A Treatise. 2nd ed. New Delhi: Vallabh Prakashan; 2009, p:254-55.
13. http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Organisation/SADC/Guideline_for_Stability_Studies.pdf
14. Jatinder Kaur, Geeta Aggarwal, Gurpreet Singh, A.C. Rana. Formulation and evaluation of Fast Dissolving Tablet Containing Nifedipine Solid Dispersion. *Int J Pharm Pharm Sci.* 2012; 4(1): 409- 16.
15. Duriez X, Joshi AA. Starches: A Versatile Source. *Pharma Form. Qual*. 2004; 6 (3): 48-50.
16. Rakesh Pahwa and Nisha Gupta. Superdisintegrants in the Development of Orally Disintegrating Tablets: A Review. *International Journal of Pharmaceutical Sciences and Research.* 2011; 2(11): 2767-80.
17. Parakh SR, Gothosakar AV. A Review of Mouth Dissolving Tablet Technologies. Pharm Technol. 2003; 27 (11): 92-100.
18. Weller PJ. Croscarmellose Sodium. Ainely Wade and Paul (London). 1994; 2: 141-42.
19. Banker GS. Sodium Starch Glycolate. 2nd Wade and Paul, London.1994.
20. Duriez X, Joshi AA. Starches A Versatile Source. Pharma Form. Qual. 2004; 6(3): 48–50.
21. Juanita Tanuwijaya and Karsono. The Effects of Crospovidone and Croscarmellose Sodium as Superdisintegrants on the Characteristics of Piroxicam Nanoparticles ODT (Orally Disintegrating Tablet). *International Journal of PharmTech Research*. 2013; 5(4): 1590-97.
22. Nani Parfati, Karina Citra Rani, Meilany. The Effect of Co-processed Superdisintegrants Ratio (Crospovidone-Sodium Starch Glycolate) to the Physicochemical Characteristics of Atenolol Orally Disintegrating Tablets. *Asian J Pharm Clin Res*. 2018; 11(2): 318-24.