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*Research Article*

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**EFFECT OF SUPERDISINTEGRANTS ON ORAL DISINTEGRATING  
TABLETS OF ZOLMITRIPTAN**

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**Abstract**

Orally disintegrating tablets (ODTs) are getting popularity over conventional tablets due to their convenience in administration and suitability for patients having dysphasia (difficulty in swallowing). Zolmitriptan is a selective serotonin receptor agonist. The absolute bioavailability is only approximately 40% due to extensive hepatic first pass metabolism (CYP1A2-mediated). Hence the main objective of the study was to formulate oral disintegrating tablets of Zolmitriptan to achieve a better dissolution rate and further improving the bioavailability of the drug. Orally disintegrating tablets prepared by direct compression method by using, Cross povidone, Cross carmellose sodium, Sodium starch glycolate, were prepared and evaluated for the precompression parameters such as bulk density, tapped density, compressibility index, angle of repose etc. The prepared batches of tablets were evaluated for hardness, weight variation, friability, disintegration time and in-vitro dissolution profile found to be satisfactory. Among these F1-F6 formulations, F6 showed maximum dissolution rate with drug release (94.4%) within 10 minutes and it containing Crosspovidone as a superdisintegrant showed minimum disintegration time within 15 seconds and the formulation (F6) shows the maximum drug content 95.9%. In all the f1-f6 formulation are subjected to the kinetic studies, the results shows, best fit in first order drug release and followed by the 'n' value shows between (0.002-0.089), follows Fickian's release mechanism.

**Keywords:** Zolmitriptan, ODT, Cross Povidone, Effect of Super disintegrants.

**Introduction**

Oral disintegration tablets are the novel technology for administration of the drug through the oral route. The tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness and ease in manufacturing. However, many patients especially children and elderly have difficulty in swallowing

tablets and capsules and consequently unable to take medicine as prescribed. Almost 50% of the population is affected by such problem, resulting in the high incidence of non compliance and infective therapy. To overcome such problems, fast disintegrating tablets or orally disintegrating tablets have emerged as an alternative dosage forms.

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Oral disintegrating tablets are solid unit dosage forms, which disintegrate or dissolve rapidly in the mouth without chewing and water. A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue. Orally disintegrating tablets have been found to be the choice for Psychiatric as well as patient suffering from stroke, thyroid disorder, Parkinson's diseases and multiple sclerosis, patients with nausea, vomiting and motion sickness. These systems are also called melt-in-mouth tablets, Rapid melts, porous tablets, Oro dispersible, quick dissolving or rapidly disintegrating tablets.

In today's era many people are suffering from migraine. Migraine is a one sided throbbing headache followed by neurological and visual disturbances. Attack may prolong for long period. Patients routinely report the pain of an attack as being the most severe they have ever experienced, or Migraine is often disabling neurovascular disorder. Changes in the metabolism and the central processing of serotonin, as well as abnormalities in the modulation of the central and peripheral trigeminal nociceptive pathways, have been shown to play significant roles in migraine pathophysiology. Recent evidence suggests that a low serotonin state facilitates activation of the trigeminal nociceptive pathways. In addition, several pharmacological agents that modulate serotonin are used in the treatment of migraine. Specifically there are seven FDA approved, 5-hydroxytryptamine (5-HT) 1B/1D receptor agonists, used for the acute abortive therapy of migraine. Zolmitriptan is one such triptan.

Zolmitriptan is a second-generation triptan prescribed for patients with migraine attacks, with and without an aura, and cluster headaches. It has a selective action on serotonin receptors and is very effective in reducing migraine symptoms, including pain, nausea and photo or photophobia. It is currently available as a conventional tablet, an oral disintegrating tablet and a nasal spray (2.5 mg and 5 mg) per dose. The absolute bioavailability of zolmitriptan is up to (40%- 50%) for both oral and nasal dosage forms. The faster clearance of the drug from the nasal cavity could explain the low bioavailability. The half-life of the Zolmitriptan is 2.5 to 3 hrs and it undergoes hepatic metabolism. In

the present study we intend to prepare oral disintegrating tablet of Zolmitriptan (2.5 mg) in order to improve the bioavailability and efficacy by using Crosscarmellose sodium, Sodium starch glycolate, Crosspovidone as super disintegrates.

### Materials and methods

Zolmitriptan was a gift sample from Aurobindo, Aerosil was provided by Cabiril and Mannitol by Spi Polyous ine and Croscarmellose sodium, Sodium Starch glycolate was provided by DMV International, and Crosspovidone was purchased by BASF, and Peppermint Flavour by LUX Flavour, Sucralose from TJTE and LYCE, Magnesium stearate by Sunshine Organics, and finally talc from luzinac.

### Preformulation studies

Preformulation testing is an investigation of physical and chemical properties of drug substance alone and combined with pharmaceutical excipients

### Procedure

Potassium Bromide pellet method was used in the study. Test samples were prepared by physical mixing of Zolmitriptan and excipients in ratios of 1:1 initially 100mg of potassium bromide power was mixed with 1 mg of each sample, thoroughly triturated in mortar and pestle. A portion of mixture was compressed using IR pelletizing press. Then the KBR pellet was placed in sample holder of Bruker FT-IR spectrophotometer. The spectra were recorded in the wave number region of 4000-500cm<sup>-1</sup>. In each case the spectra was compared with the pure zolmitriptan spectrum to detect the interactions between drug and excipients.

### Precompression studies

#### Result and discussion

##### Angle of Repose

The angle of repose for the formulated blend was carried out by the funnel method. It concludes all the formulations blend was found to be in the range 26°.08'±0.36-29°.73±0.09

##### Bulk density

Bulk density is used as a measure to describe the packing materials or granules. It is the ratio of given mass of powder and its bulk volume. It concludes all the formulations blend was found to be in the range 0.43±0.01-0.53±0.04 (g/ml)± SD

**Tapped density**

Tapped density of all the formulations was carried out by tapped density apparatus. The entire formulations blend was found to be in the range of  $0.52 \pm 0.02 - 0.90 \pm 0.03$  (g/m)  $\pm$ SD

**Compressibility index**

Based on the apparent bulk density and tapped density the percentage compressibility of the blend was determined; it is in the range of 15.69-47.63

**Formulation procedure**

1. Sieve Zolmitriptan, Mannitol through 40mm mesh by geometrical mixing and sieve, Crosscarmellose Sodium, Sucralose, Citric acid, Aerosil, talc, and Peppermint flavor through 40 mesh and add above blend for 5 mints.
2. And finally Magnesium Stearate was pass through the 40mm mesh and add to the above blend for 2mints.
3. Finally the blend should be compressed in to tablets in CLIT Single Rotatory 16 Stationary.

**Evaluation of oral disintegration tablets****Thickness**

Thickness was determined for 20 pre-weighed tablets of each batch using a digital Vernier scale. The average thickness of the tablet was found to be  $1.8 \pm 0.02$  to  $2.97 \pm 0.01$  mm.

**Weight variation**

20 tablets were selected randomly from a batch and were individually weighed and then the average weight was calculated was found to be  $0.097 \pm 3$  to  $0.765 \pm 4$  gm.

**Hardness**

The hardness of tablet is an indication of its strength. Measuring the force required to break the tablet .the hardness of the tablet was found to be 2.3 to 4 Kg/Cm<sup>2</sup>.

**Friability**

It is the measurement of mechanical strength of tablets. Roche friabilator was used to determine the friability of the tablet and it was found to be 0.4 to 2.8.

**Disintegration time**

Disintegration time is the time taken by the tablet to break up into smaller particles. The disintegration

test is carried out in an apparatus containing a basket rack assembly with six glass tubes of 7.75 cm in length and 2.15 mm in diameter, the bottom of which consists of a #10 mesh sieve. The basket is raised and lowered 28-32 times per minute in a medium of 900 mL which is maintained at  $37 \pm 5^\circ\text{C}$ . Six tablets were placed in each of the tubes and the time required for complete passage of tablet fragments through the mesh (#10) was considered as the disintegration time of the tablet. The disintegration time that patients can experience for oral disintegrating tablets ranges from 5 to 30 seconds.

**Dissolution studies**

Dissolution is a process by which the disintegrated solid solute enters the solution. The test determines the time required for a definite percentage of the drug in a tablet to dissolve under specified conditions. The dissolution test was carried out in USP Apparatus Type II (paddle) with 0.1 N Hydrochloric acid as the dissolution medium. The samples were drawn at 5, 10, 15, 20, 30 mints. Fresh volume of the medium was replaced with the withdrawn volume to maintain the sink conditions. Samples withdrawn were analyzed for the percentage of drug released.

**Drug content****Standard preparation**

Accurately weigh and transfer 50 mg of Zolmitriptan working standard into a 50 ml volumetric flask add about 25 ml of mobile phase and sonicate to dissolve it completely and make volume up to the mark with the same solvent. Further pipette 5 ml of the above prepared solution into a 50 ml volumetric flask and dilute up to the mark with diluents. Mix well and filter through 0.45  $\mu\text{m}$  filter.

**Sample Solution Preparation**

Accurately weigh and transfer 50 mg of Zolmitriptan sample powder into a 50 ml volumetric flask add about 25 ml of mobile phase and sonicate to dissolve it completely and make volume up to the mark with the same solvent. Further pipette 5 ml of the above prepared solution into a 50 ml volumetric flask and dilute up to the mark with diluents. Mix well and filter through 0.45 $\mu\text{m}$  filter.

**Kinetic release studies****Kinetic analysis of in vitro release studies**

In all the f1-f6 formulation are subjected to the release kinetics. In the kinetic results shows, best

fit in first order drug release and followed by the 'n' value shows between (0.002-0.089), follows Fickian's release mechanism.

**Table No. 01: Pre formulation evaluation parameters of all the formulations of zolmitriptan**

S.No	Formulation	Angle of repose( <sup>0</sup> ) ±SD	Bulk Density (g/ml)±SD	Tapped Density (g/m) ±SD	Carr's index ± SD
1	F1	27 <sup>0</sup> .54±0.04	0.49±0.03	0.56±0.03	15.69
2	F2	27 <sup>0</sup> .38 ±0.06	0.53±0.04	0.57±0.01	16.28
3	F3	29 <sup>0</sup> .73±0.09	0.45±0.01	0.54±0.03	16.28
4	F4	26 <sup>0</sup> .66±0.36	0.49±0.01	0.52±0.02	15.18
5	F5	26 <sup>0</sup> .85± 0.24	0.47±0.02	0.90±0.03	47.63
6	F6	26 <sup>0</sup> .08±0.36	0.43±0.01	0.76±0.02	43.42

**Table No. 02: Formulations of zolmitriptan oral disintegration tablets**

Ingredients (mg)	F-1	F-2	F-3	F-4	F-5	F-6
Zolmitriptan	2.5	2.5	2.5	2.5	2.5	2.5
Mannitol	68.5	58.5	72	69.5	55.5	68.5
Crosspovidone	-	-	-	-	30	20
Crosscarmellose sodium(CCNA)	-	-	10	15	-	-
Sodium starch glycolate(SSG)	20	25	-	-	-	-
Sucralose	2	4	5	4	3	2
Citric acid	1	2	2	1	2	1
Aerosil	2	2	2	3	1	2
Talc	1	1	1	2	2	1
Magnesium stearate	2	4	4	2	3	2
Peppermint flavor	1	1	1	1	1	1

**Table No. 03: HPLC assay of formulation (F6) zolmitriptan oral disintegrating tablets**

S.No	Standard	Test A1	Test A2
1	6192129	5932532	5907691
2	6202065	5941328	5915152
3	6217339	-	-
4	6198350	-	-
5	6197642	-	-
6	6265651	-	-
Average	6212196	5936930	5911422
S.D	27541.75	6219.71	5275.72
%RSD	0.44	0.10	0.09
%assay	-	95.92	95.99
Drug content(mg)	-	2.43	2.41

**Table No. 04: Evaluations of all the formulation of zolmitriptan**

S.No	Formulation code	Weight variation test(gm)	Thickness test (mm)	Hardness test (Kg/Cm <sup>2</sup> )	Friability test (%)	Disintegrating Time (sec)
1	F1	0.646±3	2.0±0.02	2.9	0.27	53±2
2	F2	0.701±2	1.8±0.02	2.5	0.4	45±3
3	F3	0.765±4	1.8±0.02	2.6	0.37	47±4
4	F4	0.684±2	1.9±0.01	2.3	0.46	43±2
5	F5	0.102±4	2.97±0.01	4	2.4	20±3
6	F6	0.097±3	2.95±0.01	3.5	2.8	15±4

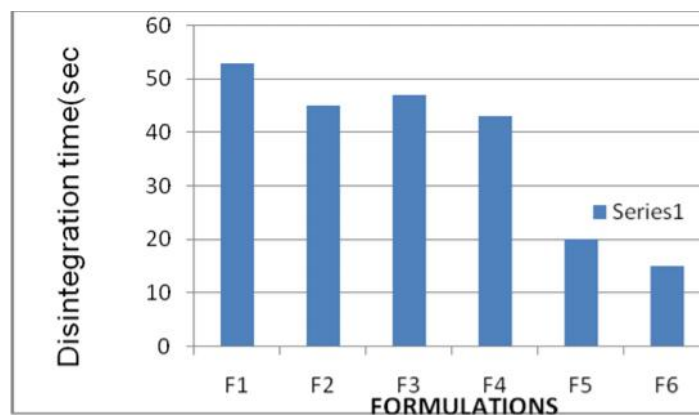


Fig. No. 01: The disintegration time of zolmitriptan formulations (F1-F6)

Table No. 05: Comparative study of invitro % drug release profile of zolmitriptan

Time	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	54.36	62.9	66.7	71.5	80.16	83.06
10	68.6	71.53	72.2	74.43	91.56	94.4
15	73.86	74.46	77.8	80.14	97.3	97.36
30	80.16	83	86.7	88.6	98.7	99.06

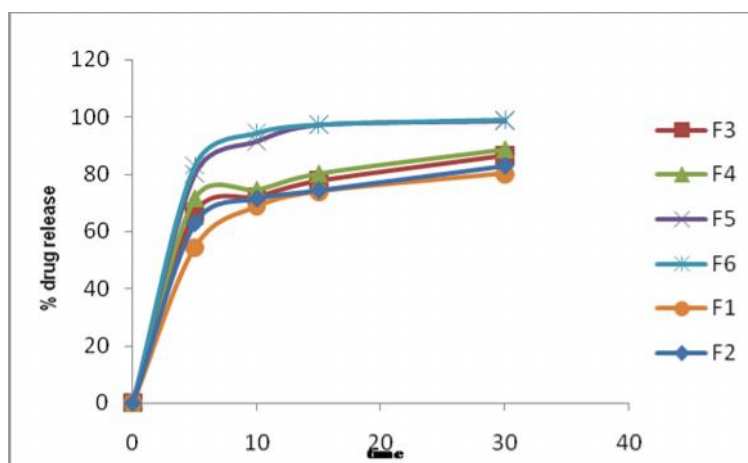


Fig. No. 02: Comparative study of invitro drug release (F1-F6)

Table No. 06: Kinetic values obtained from different plot of formulation (F1to F6)

Formulation Code	Zero order plot	First order plot	Higuchi's plot	Korsemeier peppas plot		Possible mechanism of drug release
	R <sup>2</sup>	R <sup>2</sup>	R <sup>2</sup>	R <sup>2</sup>	n	
F1	0.690	0.728	0.868	0.987	0.052	Fickian release
F2	0.629	0.896	0.976	0.972	0.002	Fickian release
F3	0.687	0.953	0.994	0.95	0.063	Fickian release
F4	0.846	0.969	0.979	0.945	0.065	Fickian release
F5	0.893	0.988	0.772	0.968	0.089	Fickian release
F6	0.614	0.998	0.733	0.998	0.051	Fickian release

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