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FORMULATION AND EVALUATION OF ZOLMITRIPTAN FAST DISSOLVING TABLET USING SYNTHETIC SUPERDISINTEGRANTS

Ch. Saidulu*, M. Jhansirani, R. Aruna, A.M.S. Sudhakar babu

Department of Pharmaceutics, A.M.Reddy Memorial College of Pharmacy, Narsaraopet, Guntur district, A.P, India

***Corresponding author e-mail:** saidull.ch@gmail.com

ABSTRACT

In recent decades, a variety of pharmaceutical research has been conducted to develop new dosage forms. Among them, the fast disintegrating tablet (FDTs) is one of the most widely employed commercial products to facilitate ease of medication. Upon introduction into the mouth, these tablets dissolve or disperse in the mouth in the absence of additional water and the active pharmaceutical ingredients are readily released from the dosage form. In present study Zolmitriptan tablets were formulated by using synthetic superdisintegrant namely Amberlite, Sodium starch glycolate and Indion in different ratio then compared with marketed Zolmitriptan tablets were prepared namely F_1 to F_{10} formulation and these are characterized by hardness, thickness, weight variation, friability, wettability time and dissolution studies. Fast dissolving tablets can be prepared by direct compression method using synthetic superdisintegrant. The values obtained from the evaluation studies indicate that all the parameters within the standard limits. *In vitro* disintegration studies showed that fast dissolving tablets from F_9 (Indion 1:3 ratio) showed the best disintegration time with in 32sec. *In vitro* dissolution studies showed that the formulation F_9 gave the maximum percentage drug release (100%) with in 7min.

Keywords: Zolmitriptan, Superdisintegrants and Fast disinintegrating tablet

INTRODUCTION

Fast dissolving tablets are continuously gaining great success in the pharmaceutical market. The most popular solid dosage forms are tablets and capsules but the major drawback of these dosage forms for some patients is the difficulty to swallow it [1]. FDTs are not only preferable for people who have swallowing difficulties, but also are ideal for active people. Suitable drug candidates for such systems include neuroleptics, cardiovascular agents, analgesics, antiallergics and drugs for erectile dysfunction [2]. Such a tablet disintegrates instantaneously when placed on tongue, releases the drug that dissolves or disperses in the saliva. As the oral mucosa is highly vascularized, drugs that are absorbed through the oral mucosa can directly enter into the systemic circulation, bypassing the gastrointestinal tract (GIT) and therefore first-pass metabolism in the liver. This result to a rapid onset of action, and greater bioavailability of the drug than those observed from conventional tablet dosage form [3,4]. There are several salient features of fast dissolving drug delivery system. These are ease of administration to the patient who cannot swallow, such as the pediatric, geriatric & psychiatric patients, elderly, stroke victims, bedridden patients, patient affected by renal failures. There is no need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling. It also undergoes rapid dissolution and absorption of the drug produces quick onset of action. These also provide good mouth feel property that helps to change the perception of medication as bitter pill particularly in pediatric patient. Pregastric absorption can result in improved bioavailability and as a result of reduced dosage; improve clinical performance through a reduction of unwanted effects [5].

Migraine is a chronic neurological disorder characterized by recurrent moderate to severe headaches often in association with a number of autonomic nervous system symptoms. A migraine is a severe, painful headache that is often preceded or accompanied by sensory warning signs such as flashes of light, blind spots, tingling in the arms and legs, nausea, vomiting, and increased sensitivity to light and sound. The excruciating pain that migraines bring can last for hours or even days[6]. Literature reveals the alternative formulations of Zolmitriptan as nasal spray and sublingual tablets prepared by direct compression with different polymers [7, 8].

MATERIALS AND METHODS

Materials: Zolmitriptan was gift sample from Tejkamal pharmaceuticals Ltd., Bangalore, Amberlite, Indion and Sodium starch glycolate were obtained from Signet chemical corporation Pvt. Ltd., Mumbai. Lactose and Aerosil were supplied by NR CHEM, Mumbai. All chemicals used in the study were of analytical grade.

Preformulation studies: Preformulation testing is the first step in the rationale development of dosage forms of a drug substance. It can be defined as an investigation of physical and chemical properties of a drug substance alone and when combined with excipients.

Physical Characterization of Blend: Physical Characterization of Blend was done for Particle size distribution, Bulk Density, Tapped density and compressibility index.

Determination of Bulk Density, Tapped density and compressibility index: Firstly, the graduated cylinder was tare to zero, certain quantity of powder (W) was carefully poured into the graduated cylinder and the same was weighed. Also, the volume (V_0) was noted. The graduated cylinder was then closed with lid and set into the density determination apparatus (Bulk density apparatus, Campbell electronics). The density apparatus was set for 350 taps and after that the volume (V_f) was determined. The Bulk Density, Tapped density was calculated using the following formulas:

Bulk Density = W/V_0

Tapped density = M/ TV

Where M = Weight of sample in gm, Vt = Final volume of blend incm^3

Compressibility Index: The compressibility index and the Hausner's ratio are determined by measuring both the bulk volume and tapped volume of a powder.

Compressibility index = 100 * Tapped density / Bulk density

Hausner's ratio = Tapped density / Bulk density

Formulation of tablets by direct compression method: Zolmitriptan fast disintegrating tablets were prepared by direct compression method. Different concentration of excipients was used to prepare different formulations of fast disintegrating tablets. Compositions of various formulations are shown in Table 1. All the ingredients of the fast disintegrating tablets of Zolmitriptan were weighed and mixed in mortar with the help of pestle, then finally 1mg Magnesium Stearate and 1mg Aerosil was added material was slightly compressed on the 6mm flat-faced punch using a Rimek tablet press machine.

Evaluation of tablets:

Thickness: The thickness of the tablets was determined by using Vernier callipers.

Five tablets from each formulation were used and average values were calculated.

Hardness test: Hardness (diametral crushing strength) is a force required to break a tablet across the diameter. The hardness of a tablet is an indication of its strength.Thetablet should be stable to mechanical stress during handling and transportation. The permissible limit for hardness is 3 – 5 kg/cm3. The hardness was tested using Monsanto tester. "Hardness factor", the average of the five determinations was determined and reported.

Friability test: Roche friabilator was used to measure the friability of the tablets. It was rotated at a rate of 25 rpm. Five tablets were weighed collectively and placed in achamber of the friabilator. In the friabilator, the tablets were exposed to rolling,resulting from free fall of tablets within the chamber of the friabilator. After 100 rotations (4 minutes), the tablets were taken out from the friabilator and intact tablets were again weighed collectively. Permitted friability limit is 1.0%. The percent friability was determined using the following formula.

(W1 – W2)/W1 * 100

Where, W1 = weight of the tablets before test, W2 = weight of the tablets after test.

Uniformity of weight (Weight variation test): 20 tablets were weighed individually. Average weight was calculated from the total weight of the tablets. The individual weights were compared with the average weight. The percentage difference in the

weight variation should be within the permissible limits (7.5%). percent deviation was calculated using the following formula.

% weight variation = Individual weight – Average weight/ Average weight * 100.

Drug content: 10 tablets are accurately weighed and powdered. Tablets powder equivalent to 20 mg of medicament was taken in the test tube and extracted with methanol. The methanolic extract collected into 50ml volumetric flask and volume made upto 50ml with purified buffer. The solution was subsequently diluted and assayed for drug content.

Disintegration time (min): Tablets were placed in six tubes of the basket. Then the assembly was suspended in water maintained at a temperature of $37^0C \pm 0.5\ ^0C$, and then the apparatus was switched on.

Simultaneously, start the stopwatch results were noted. Stopwatch was stopped when the last tablet gets disintegrated. The tablets pass the test, if all tablets have disintegrated in the specified time (NMT 20 min), if 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets. Not less than 16 of the total of 18 tablets tested should be disintegrated completely.

Diisolution studies: In Vitro dissolution studies for all the prepared tablets was carried out using USP paddle method at 50 rpm in 900 ml of 0.1N Hcl as dissolution media, maintained at 37°C ± 5°C. 5 ml of sample was withdrawn from the dissolution medium at the specified regular intervals, filtered through Whatmann filter paper and assayed spectrophotometrically at 227 nm. An equal volume of pre warmed (37°C) fresh medium was replaced into the dissolution medium after each sampling, to maintain the constant volume throughout the test. Then the cumulative percentage of drug release was calculated and represented graphically.

RESULTS AND DISCUSSOIN

The compositions of different formulations are presented in (Table 1). The preformulation studies and evaluation parameters like weight variation, friability, hardness, thickness, disintegration time, wetting time, dissolution rate and assay for drug content were found to be satisfactory and the results were presented in (Table 2 & 3). When Amberlite, Sodium Starch Glycolate, Indion was used alone in the formulations using different ratios, disintegration time was noticed not more than 2 min. The formulation (F9) containing Indion (1:3) shows significant decrease in a disintegration time was achieved (i.e. 23 sec.) among all the formulation. In vitro dissolution rate study shows that after 10 min formulation F1, F2, F4, and F5, F6 % drug release 96%, 98%, 95%, 97% and 100% respectively. The other formulation F3, F7, F8 % drug release 100% at the end of 9^{th} min. Among all formulations F7 was shown (Fig 1-4) best drug release (after 7min % drug release 100%) and Drug content studies were done on selected batches and results are presented in (Table3) which shows that the drug content is within limit.

CONCLUSION

From the present study it may be concluded that fast dissolving tablet of zolmitriptan can be formulated by direct compression method by using suitable superdisintigrant (amberlite , sodium starch glycolate and indion). Fast dissolving tablets formulated employing indion-414 gave 100% release with in 7 min. There is slight difference with profiles of other (sodium starch glycolate,amberlite) synthetic superdisintegrants, so indion is an effective superdisintegrant.the proposed fast disintegrating formulations possess ideal and reproducible characteristics of disintegration time and enhanced dissolution and thus give better patient compliance.

Table-1: DEVELOPMENT OF FORMULATION:

MATERIALS	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)	F10 (plain tablet)
Zolmitriptan	5mg	5mg	5mg	5mg	5mg	5mg	5mg	5mg	5mg	5mg
Amberlite	5mg	10mg	15mg	-	-	-	-	-	-	-
Sodium starch glycolate	-	-	-	5mg	10mg	15mg	-	-	-	-
Indion	-	-	-	-	-	-	5mg	10mg	15mg	-

Lactose	78mg	73mg	68mg	78mg	73mg	68mg	78mg	73mg	68mg	83mg
MCC	10mg	10mg	10mg	10mg	10mg	10mg	10mg	10mg	10mg	10mg
Aerosil	1mg	1mg	1mg	1mg	1mg	1mg	1mg	1mg	1mg	1mg
Magnesium Stearate	1mg	1mg	1mg	1mg	1mg	1mg	1mg	1mg	1mg	1mg
Peppermint	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Table.2. Pre-compression parameter

S.NO	FORMULATION CODE	BULK DENSITY(g/ml)		COMPRESSIBILITY INDEX (%)	HAUSNER'S RATIO	ANGLE OF REPOSE (DEGREES)
		Untapped	Tapped			
1	F_1	0.462	0.539	14.46	1.16	24.0
2	F_2	0.469	0.561	16.39	1.19	23.6
3	F_3	0.478	0.586	18.43	1.22	25.0
4	F_4	0.480	0.637	24.6	1.32	23.6
5	F_5	0.446	0.560	20.35	1.25	24.5
6	F_6	0.462	0.591	21.8	1.27	22.6
7	F_7	0.451	0.565	20.17	1.25	23.1
8	F_8	0.480	0.560	14.28	1.16	24.1
9	F_9	0.475	0.565	16.03	1.19	24.6
10	F_{10}	0.442	0.572	21.3	1.25	22.1

Table.3. Post compression parameter

Tests	F_1	F_2	F_3	F_4	F_5	F6	F_7	F_8	F_9	F_{10}
Hardness (kg/cm2)	3.8	3.7	3.9	3.8	3.9	3.7	3.8	3.7	3.8	3.6
Friability (%)	0.35	0.34	0.39	0.37	0.38	0.37	0.19	0.38	0.37	0.39
Thicknes(mm)	2.8	2.7	2.8	2.7	2.9	2.6	2.8	2.7	2.5	2.8
Drug content(mg/tablet)	97.8	98.9	97.8	96.8	96.7	98.6	99.5	97.9	99.8	96.5
Disintegration Time(Sec)	65	58	51	71	60	55	58	42	23	89

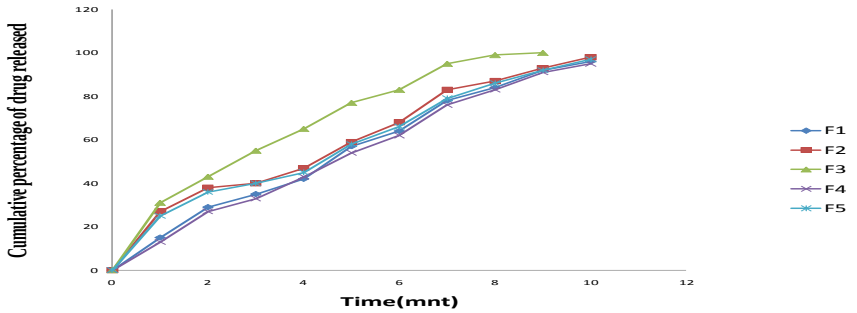

Fig.1. dissolution profile of zolmitriptan fdts with different types of super disintegrents

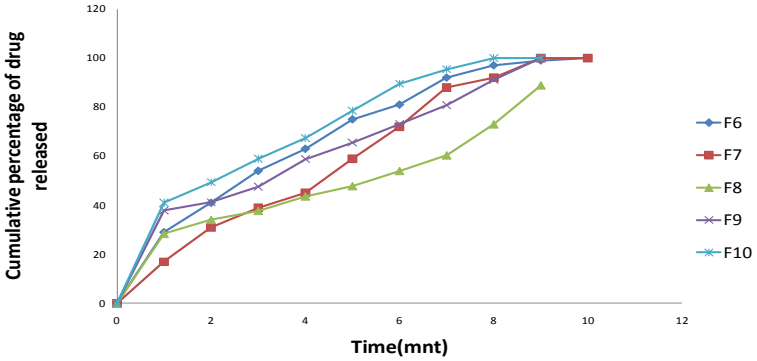

Fig.2. dissolution profile of zolmitriptan fdts with different types of super disintegrents

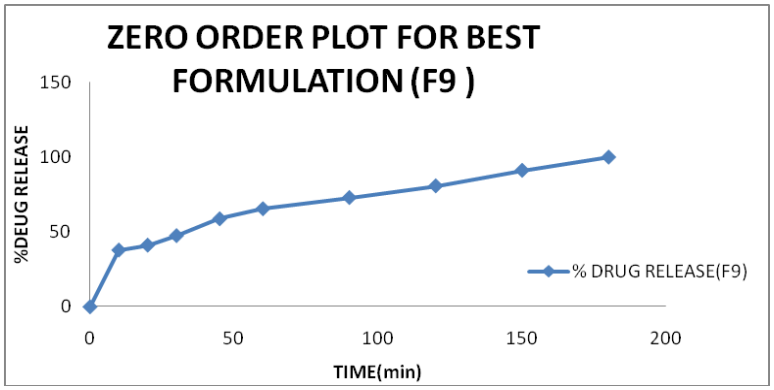

Fig.3 Zero Order Plot for Best Formulation F_9

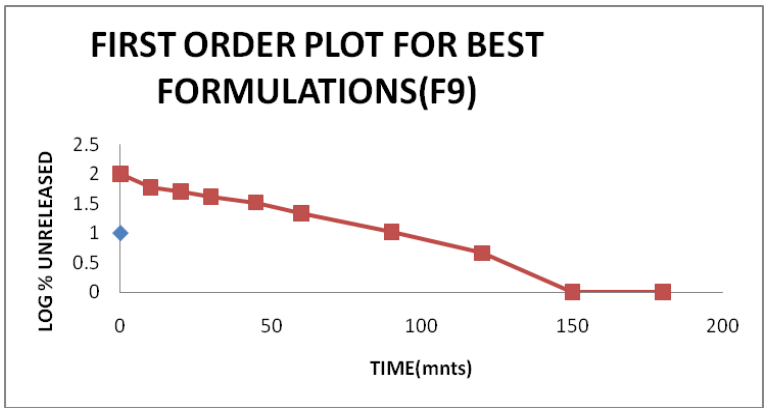

Fig.4 First Order Plot for Best Formulation F_9

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