ECRONICON OPEN ACCESS

EC PHARMACEUTICAL SCIENCE
Research Article

Preparation and Evaluation of Zolmitriptan Rapimelt Tablet For Migraine

Aakanchha Jain[1]*, Sourabh Jain[1], Poorva Jain[2], Sourabh Bhargava[3] and Vijay Verma[4]

[1]*Associate Professor, Bhagyoday Tirth Pharmacy College, Sagar, Madhya Pradesh, India*

[2]*Assistant Professor, Bhagyoday Tirth Pharmacy College, Sagar, Madhya Pradesh, India*

[3]*United Institute of Pharmacy, Allahabad, India*

[4]*Bhagyoday Tirth Pharmacy College, Sagar, Madhya Pradesh, India*

***Corresponding Author**: Aakanchha Jain, Associate Professor, Bhagyoday Tirth Pharmacy College, Sagar, Madhya Pradesh, India.

Received: July 24, 2018

Abstract

The objective of the study was to develop mouth dispersible tablets for ZTN through direct compression method. The formulated tablets were optimized to obtain minimum disintegration time and friability to withstand friction and handling. The drug selected for the study was ZTN, which is basically used for migraine. Since migraine patients require fast relief, the dosage form prepared requires a rapid disintegration to help faster onset of action. For this an extensive literature review was done to form a basis of selection of super disintegrants, as it plays an important role in the rapid disintegration of tablets, due to swelling pressure exerted in the outer direction or radial direction of tablet or due to the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration. The envisaged work was planned under following headings: literature survey, preformulation studies, formulation of ZTN tablets along with different superdisintegrants e.g. crospovidone, sodium starch glycollate, low substituted hydroxyl propyl cellulose. The formulated tablet blends and tablets were evaluated for various micromeritic properties. The preformulation studies confirmed the characteristics of ZTN (API) including organoleptic properties, solubility, UV and spectral analysis. The FT-IR spectra shows characteristic API peaks at N-H, C=C, and C-N stretching. Drug excipients relationship evaluated by IR spectra shows that there was no interaction between pure drug and excipients. Angle of repose of all tablet composition was found to be between 35 - 38. Moisture content was 0.28%. Hardness of the tablets was within the range 25 - 36 Newton. Friability was found to be less than 1%. Wetting time was found 12 - 51 seconds. Cumulative percentage drug release from optimized tablet was found to be 98.15%. During stability studies the tablets showed no significant changes in drug content and dissolution profile. The evaluation results lead to the conclusion that formulations (tablets) with a combination of two superdisintegrants in 2.5%, shows mean disintegration time of 6 seconds. Overall it can be concluded that the use of superdisintegrants in suitable proportions resulted in a simpler and cost effective, rapid disintegrating mouth dispersible tablets of ZTN prepared by direct compression technique.

Keywords: *Dispersible; Migraine; Rapimelt; Superdisintegrants; Zolmitriptan*

Introduction

Drugs are more frequently taken by oral administration The ideal dosage regimen in drug therapy of any disease is that which immediately attains the desired therapeutic concentrations of drug in plasma or at the site of action and maintains it for the entire duration of treatment.

Although some drugs taken orally are intended to be dissolved within mouth, the vast majority of drugs taken orally are swallowed. Compared with alternate routes, the oral route of drug administration is popular and it has been successfully used for conventional delivery of drug. It is considered as most natural, convenient, uncomplicated, safe means of administering drugs [1]. Drugs are administered by oral route in a variety of pharmaceutical dosage forms. The most popular are tablets, capsules, suspensions, various pharmaceutical solutions. Among the drugs administered orally, solid dosage forms represent the preferred class of product. They are flexible in dosage

strength, versatile, relatively stability (chemical, mechanical, microbiological), packaging and convenient manufacturing. Moreover they present lesser problem in formulation, storage, handling and usage. Solid dosage form provides better protection to the drugs against temperature, humidity, light, oxygen and stress during transportation also. Among the solid oral dosage forms tablet formulation are widely used. This is exactly not possible with a conventional dosage form unless it is administered with a defined dosage regimen and by an appropriate route of administration.

In simple terms tablet can be said as a small usually round piece of medicine. Tablets can pharmaceutically be defined as solid dosage forms that generally contain medicament(s) with or without suitable excipients, equipped either by compression or by moulding. It is a small disk or cylinder of a compressed solid substance, typically a measured amount of a medicine or drug.

Recent advances in tablet technology aim to increase safety and efficacy of drug molecule by formulation of a convenient dosage form for administration and to achieve better patient compliance. One such approach is -"Mouth Dissolving Tablet". Mouth dispersible tablets are also known as "fast dissolving tablets", "melt in mouth tablet", "rapimelt", "porous tablet", "orally disintegrating tablet", "mouth dissolving tablet", "orodispersible tablet", "rapidly disintegrating tablet" or "mouth dispersible tablet".

Due to rapid onset of action rapimelts can prove to be one of the most convenient dosage forms that helps patients with ailments that show markedly reduced functional ability and restlessness.

Approximately one-third of the population, primarily the geriatric and pediatric populations, has swallowing difficulties, resulting in poor compliance with oral tablet drug therapy which leads to reduced overall therapy effectiveness. A new tablet dosage format, the fast dissolving tablet has been developed which offers the combined advantages of ease of dosing even in the absence of water or fluid. These tablets are designed to dissolve or disintegrate rapidly in the saliva generally within a fast-dissolving/disintegrating dosage form, leads to increased revenue, while also targeting underserved and under-treated patient populations [2]. It is also beneficial in cases such as motion sickness, episodes of asthma or coughing, where a rapid onset of action is required. Bioavailability of mouth dispersible tablet get increased in cases of insoluble or hydrophobic drugs due to rapid disintegration and dissolution of these tablets in mouth [3]. These are stable for a longer duration of time as the medicament is in the solid matrix till it is consumed. So, these are better in terms of both stability and bioavailability and a combined beneficial effect of both solid and liquid oral dosage form is achieved [5].

ZTN (ZTN) was selected as model drug. The objective of the work undertaken was to study the various orally disintegrating platform technologies and develop a novel and non-infringing rapimelt tablet, by studying the effect of superdisintegrants, with rapid release and fast disintegration [5].

Material and Method

Zolmitriptan was supplied as a gift sample from Glenmark Pharma, Nasik, India.. Mannitol, colloidal silicon dioxide, magnesium stearate, aspartame, sodium starch glycolate, crospovidone, L-HPC, microcrystalline cellulose (Avicel102) was procured from Loba Chemi Pvt. Ltd. All other reagents and solvents were of analytical grade and purchased from local suppliers unless stated otherwise.

Fourier transform infrared spectroscopy/drug excipient compatibility study

IR absorption spectra of the pure drug, with different excipients were taken in the range of 4000 - 450 cm-1 using KBr disc method. 2 mg of the substance to be examined was triturated with 200 mg KBr to form a disc of 10-15mm diameter and pellet of suitable intensity by a hydraulic press. The Infrared spectrum of mixtures were recorded by using FT-IR spectroscopy (1600 series, Perkin-Elmer Inc, Norwalk, CT) and observed for characteristic peaks of drug.

Preparation and evaluation of rapimelt tablet

Pre-compression parameter of powder and powder blend

The drug (ZTN) and powder blend (Table 3) were evaluated for micromeritic properties (Bulk density and Tapped density), flow properties (Angle of repose, Compressibility index, Hausner's ratio) and moisture content of ZTN. The results obtained for drug are given in table 1 and 2. The observations for pre-compressed powder blend are summarized in table 4.

Sr. No.	Bulk Density (gm/ml)*	Tap Density (gm/ml)*	Compressibility Index* (Vo -V/Vo)×100	Angle of repose*	Hausner 's Ratio* (T_d/B_d)	Percentage loss on drying (moisture content)*
1	0.469 ± 0.010	0.622 ± 0.010	24.44 ± 0.04	37.03 ± 0.02	1.325 ± 0.001	0.28 ± 0.02

Table 1: *Physical characteristics of Zolmitriptan.*

Formula / Ingredients	S1	S2	S3	C1	C2	C3	H1	H2	H3	S1C1	S2C2
Zolmitriptan	5	5	5	5	5	5	5	5	5	5	5
Mannitol	40	40	40	40	40	40	40	40	40	40	40
Colloidal Silicon Dioxide	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Magnesium Stearate	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Aspartame	1	1	1	1	1	1	1	1	1	1	1
Flavour	1	1	1	1	1	1	1	1	1	1	1
Sodium starch glycollate	2.5	5	7.5	-	-	-	-	-	-	2.5	5
Crospovidone	-	-	-	2.5	5	7.5	-	-	-	2.5	5
L-HPC	-	-	-	-	-	-	2.5	5	7.5	-	-
MCC (Avicel102)	49.5	47	44.5	49.5	47	44.5	49.5	47	44.5	47	42

Table 2: *Prototype Formula Taken For Tablets (Weight in mg).*

Trials	Bulk density (gm/ ml)	Tapped density (gm/ml)	Compressibility index (%)	Angle of repose (^{0}C)	Hausner's ratio
S_1	0.429 ± 0.009	0.517 ± 0.008	17.02	27.58 ± 0.15	1.20
S_2	0.413 ± 0.006	0.501 ± 0.006	17.56	28.42 ± 0.25	1.21
S_3	0.466 ± 0.005	0.571 ± 0.006	18.38	25.88 ± 0.16	1.23
C_1	0.44 ± 0.005	0.537 ± 0.008	18.06	24.65 ± 0.15	1.22
C_2	0.432 ± 0.006	0.528 ± 0.005	18.18	25.53 ± 0.18	1.22
C_3	0.434 ± 0.008	0.531 ± 0.007	18.26	26.68 ± 0.20	1.21
H_1	0.450 ± 0.006	0.563 ± 0.005	20.07	26.03 ± 0.15	1.25
H_2	0.431 ± 0.005	0.546 ± 0.006	21.05	24.17 ± 0.20	1.26
H_3	0.447 ± 0.008	0.579 ± 0.008	22.79	24.89 ± 0.10	1.29
S_1C_1	0.436 ± 0.009	0.534 ± 0.009	18.35	23.87 ± 0.15	1.22
S_2C_2	0.463 ± 0.006	0.574 ± 0.005	19.33	28.12 ± 0.16	1.24

Table 3: *Physical Evaluation of pre-compressed powder blend.*

Flow properties of powder

Bulk Density

Apparent Bulk density of the ZTN/powder blend was determined by pouring (pre-sieved 40 mesh) gently 25 gm of sample through a glass funnel into a 100 ml of graduated glass cylinder. Then powder bed was made uniform without disturbing and after that the volume

Trial	Drug Content (%)	Average Diameter (In mm)	Average Thickness (In mm)	Weight Variation (mg) limits of ± 10%	Hardness Range (Newton)	Friability (%)
S_1	98.52 ± 1.10	8.1 ± 0.15	2.5 ± 0.15	99.2 - 102.3	25 - 31	0.602 ± 0.008
S_2	99.28 ± 0.82	8.1 ± 0.12	2.7 ± 0.15	98.4 - 101.2	26 - 32	0.815 ± 0.006
S_3	99.21 ± 0.62	8.1 ± 0.20	2.8 ± 0.12	99.4 - 103.6	25 - 31	0.756 ± 0.005
C_1	98.71 ± 1.62	8.1 ± 0.20	2.7 ± 0.10	97.5 - 101.4	28 - 35	0.525 ± 0.006
C_2	99.88 ± 0.50	7.9 ± 0.25	2.5 ± 0.12	98.1 - 102.5	29 - 36	0.538 ± 0.008
C_3	98.36 ± 1.50	8.1 ± 0.16	2.6 ± 0.11	97.8 - 103.4	28 - 36	0.562 ± 0.005
H_1	98.71 ± 1.12	8.1 ± 0.25	2.8 ± 0.10	98.2 - 103.7	27 - 34	0.542 ± 0.006
H_2	99.27 ± 0.22	8.1 ± 0.10	2.8 ± 0.10	98.6 - 102.8	28 - 35	0.568 ± 0.006
H_3	98.78 ± 1.12	8.1 ± 0.12	2.7 ± 0.12	99.3 - 103.7	28 - 34	0.408 ± 0.008
S_1C_1	98.82 ± 1.12	8.1 ± 0.12	2.5 ± 0.12	98.3 - 102.4	28 - 33	0.522 ± 0.005
S_2C_2	98.81 ± 1.12	8.1 ± 0.16	2.5 ± 0.14	97.8 - 101.3	27 - 32	0.527 ± 0.006

***Table 4**: Physical characteristics of ZTN rapimelt tablets prepared from different blend.*

was measured directly from the graduation markings on the cylinder as ml [6]. The volume was measure and was called as the bulk volume. Bulk density was calculated as:

Bulk density = Weight of powder/Bulk volume

Tapped Density

Tapped density of ZTN and powder blend was determined by pouring gently 25 gm of drug sample by a glass funnel into a 100 ml graduated cylinder. The cylinder was tapped from height of 2 inches until a constant volume was obtained. In USP TAP DENSITY TESTER, Tap density is measured in 500 taps, 750 taps and 1250 taps with drop/time-299-302. Volume occupied by the sample after tapping were recorded and tapped density was calculated [7,8].

Tapped density = Weight of powder/Tapped volume

Carr's Compressibility Index

Compressibility is the ability of any powder to decrease in its volume under applied pressure. It is a measure that is calculated from density determinations. It is a simple method to determine powders flow property as follows:

Carr's index = Tapped density- Bulk density/Tapped density X 100

Hausner's Ratio

It provides a measure of the degree of densification which can result to form vibrations of the feeding hopper. A lower value of indicates better flow and vice versa [9].

Hausner's Ratio = Tapped density/Bulk density

Angle of Repose

The frictional forces in a loose powder are measured by the determination of angle of repose. Angle of Repose or □ (Theta) is the angle between the surface of a pile of powder and horizontal plane. It is determined by "Fixed Funnel Method "and is a measure of the flowability of powder or granules.

Using a glass funnel with 10 mm inner diameter of its stem was fixed at a height of 2 cm. above a fixed platform. About 10 gm of ZTN/powder blend was passed through the funnel till the tip of the pile formed and touched the stem of the funnel and a rough circle was drawn using a pencil around the formed pile base and radius of the powder cone was measured using following formula [10]:

$\theta = \tan^{-1}(h/r) = \tan^{-1}$ (Height of pile/Average radius of the powder cone)

Moisture content

Moisture content of the drug (ZTN) was analysed using METTLER TOLEDO HR73 Halogen Moisture Analyzer.

Compression: The rapimelt tablet was prepared following the protocol given by Gupta., *et al.* [11] and Shadeedi., *et al* [12]. This method includes direct compression of tablet by mixing drug and excipients as given in figure 1 (step 1 to step 8). The study was focused on developing the tablets using minimum concentration of superdisintegrant and evaluated for same parameters as given in evaluation of powder ZTN.

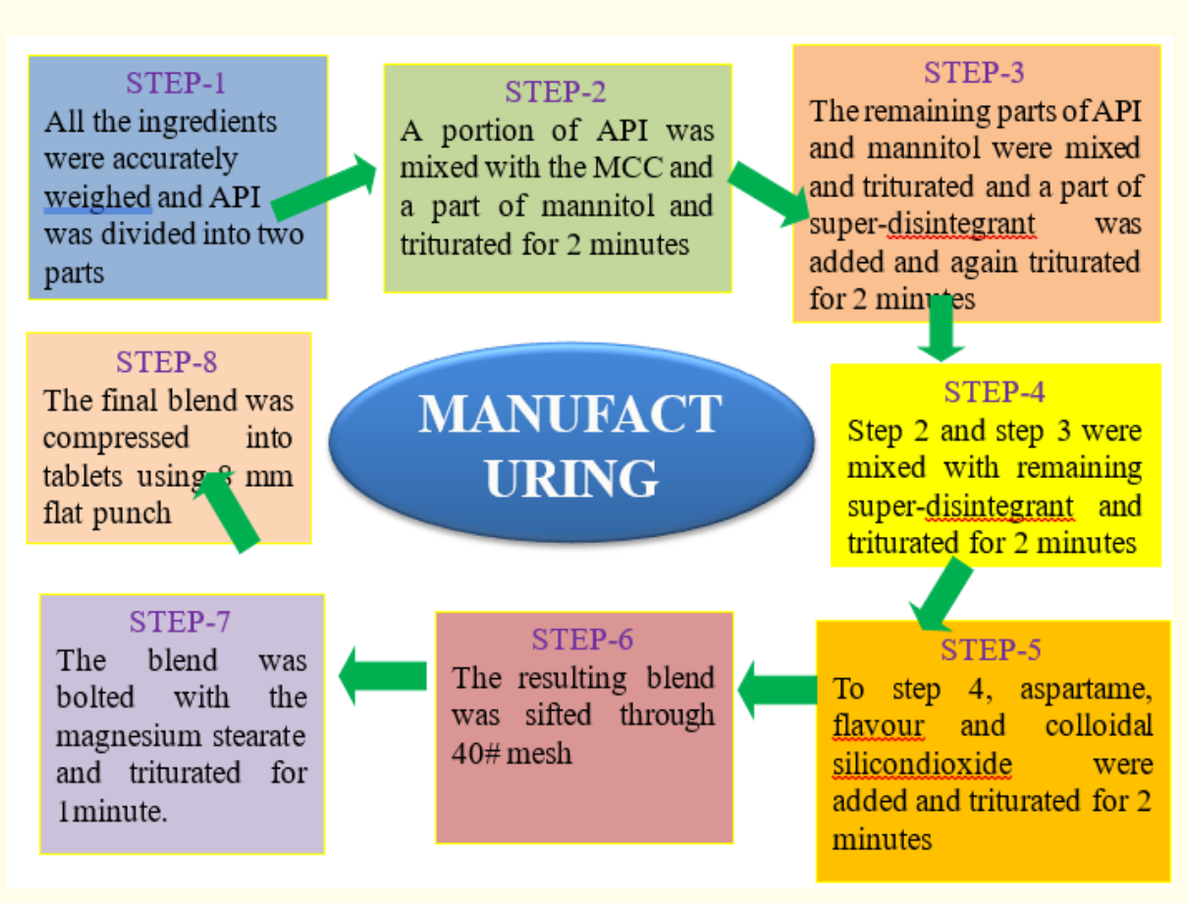

Figure 1: *Manufacturing steps of tablets.*

Post compression evaluation of tablets (Kar., *et al.* 2009)

The tablets were evaluated for content uniformity, average diameter, average thickness, hardness, weight variation, Friability (%F), disintegration, wetting time and dissolution.

Content uniformity test

Five tablets were selected randomly and powdered. 10 mg of ZTN was dissolved in 50 ml of 0.1N HCl, stirred for 60 min and filtered. 1 ml of the filtrate was diluted to 50 ml with 0.1 N HCl. Absorbance of this solution was measured at 225 nm and content of ZTN was estimated using UV Spectrophotometer (Thermo Scientific Evolution, 201).

Tablet thickness

Variation in the tablet thickness may cause problems in counting and packaging in addition to weight variation beyond the permissible limits. Tablet thickness was controlled within ± 5% of a standard value. Tablet thickness was measured by Vernier calliper. Determination was made in triplicate [13].

Hardness

It was an important parameter which shows resistance of the tablet to chipping, breakage and abrasion under the conditions of handling, transportation and storage [14]. Five tablets from each batch were selected and hardness was measured using Electrolab Digital hardness tester to find the average tablet hardness or crushing strength in Newton [15].

Weight variation

Weight variation was calculated as per method descried in USP. 20 tablets were weighed individually and the average weight is calculated. The requirements are met if the weights of not more than 2 of tablets differ by more than the percentage listed in table 4 and no tablets differ in weight by more than double that percentage. Determination was made in triplicate [15].

Friability (%F)

20 tablets from each batch were sampled randomly and weight was taken. These tablets were then placed to friability testing using Roche Friabilator for 100 revolutions. The tablets were subjected to the combined effect of abrasion and shock in a plastic chamber which revolved at 25 rpm and dropped a tablet at height of 6 inches in each revolution. After that tablets were removed and de-dusted and weighed again [16-18]. Determination was made in triplicate. The formula used to calculate friability is as follows:

Percentage friability = 1 - (loss in weight/ initial weight) X 100

Disintegration time (DT)

Many reports suggest that conventional DT apparatus may not give correct values of DT for rapimelt. The amount of saliva available in the oral cavity is very limited (usually less than 6 ml) whereas the conventional DT apparatus uses a large amount of water with very rapid up and down movements. Rapimelt is required to disintegrate in such small amount of saliva within a minute without chewing the tablet. In a simplest method to overcome this problem, 6 ml of phosphate buffer of pH 6.8 was taken in a 25 ml measuring cylinder. Temperature was maintained at 37 ± 2°C. Tablets were put into it and time required for complete disintegration of the tablet was noted [18,19].

Wetting time

It represents the time taken for the tablet to disintegrate when kept motion less on the tongue. In this test, the tablet placed on a piece of tissue paper folded double in a petri plate (internal diameter is 6.5 cm) containing 6 ml of water. Then the tablet's complete wetting time was noted. The test is carried out at 37oC in triplicate [8,20,21].

In vitro drug release/dissolution studies

The tablet samples were subjected to *in-vitro* dissolution studies using USP Type II dissolution apparatus at 37 ± 2°C and 50 rpm speed. As per the official recommendation of USFDA, 500 ml of pH 6.8 was used as dissolution medium. Aliquot equal to 5 ml was withdrawn at specific time intervals and. The dissolution media volume was complimented with fresh and equal volume of blank media (pH 6.8). The aliquots were filtered and scanned with appropriate dilution and amount of ZTN released from the tablet samples was determined spectrophotometrically at a wavelength of 225 nm by comparing with the standard calibration curve [22].

Stability study

Tablets of formulation S1C1 were put on short term stability by packing in HDPE containers as per ICH guidelines $25^0C \pm 2^0C/60\%$ RH ± 5% RH and $40^0C \pm 2^0C/75\%$ RH ± 5% RH for the period of six months. After which, the tablets were withdrawn and analysed for physical characterization and dissolution study [7].

Trial	Disintegration Time (in Sec)	Wetting Time (in Sec)
S_1	15 ± 0.60	40 ± 1.05
S_2	15 ± 1.09	45 ± 1.20
S_3	17 ± 1.25	51 ± 1.15
C_1	10 ± 0.20	19 ± 1.22
C_2	7 ± 0.50	16 ± 1.50
C_3	6 ± 0.10	14 ± 1.25
H_1	12 ± 0.62	23 ± 0.25
H_2	15 ± 1.02	25 ± 1.50
H_3	13 ± 1.0	35 ± 0.25
S_1C_1	6 ± 0.80	16 ± 1.10
S_2C_2	8 ± 0.25	18 ± 1.20

Table 5: *Disintegration time and wetting time of ZTN Rapimelt tablets prepared from different blend.*

Storage condition		**25^{0}C ± 2^{0}C/60% RH ± 5% RH**	**40^{0}C ± 2^{0}C/75% RH ± 5% RH**
Period→	**Initial**	**6 Months**	**6 Months**
Parameters↓	**Observations**		
Physical Appearance	White	White	White
Hardness (Newton)	28-33	28-36	27-38
Disintegration time (sec)	6.0	6.5	7.0
Wetting time (sec)	16	16	17
Assay (%)	98.05	98.15	98.81
Dissolution Study			
Time	% Dissolution		
(2 min)	87	86	87
(4 min)	92	90	91
(6 min)	96	97	98
(8 min)	97	98	99
(10 min)	97	98	100
(12 min)	98	99	99

Table 6: *Stability data of the optimized formulation.*

This article does not contain any studies with human and animal subjects performed by any of the authors.

Result and Discussion

The interaction between the drug and the excipients may lead to identifiable changes in the FT-IR profile of the drug. So ZTN and the excipients in 1:1 ratio were subjected to FT-IR analysis. The characteristic absorption peaks of ZTN were obtained at 3350 cm^{-1} due to NH Stretching, 1735 cm^{-1} due to C=O stretching, 1259 cm^{-1} due to C-O Stretching, 1479 cm^{-1} due to C=C Aromatic. FTIR techniques have been used here to study the physical and chemical interaction between drug and excipients used. In the present study, it has been observed that there is no chemical interaction between ZTN and the excipients used. From the IR spectrum figure 2a-2f, it was observed that there were no changes in these main peaks, which shows that there were no physical interactions because of some bond formation between drug and polymers. This indicates that the drug was compatible with the formulation components.

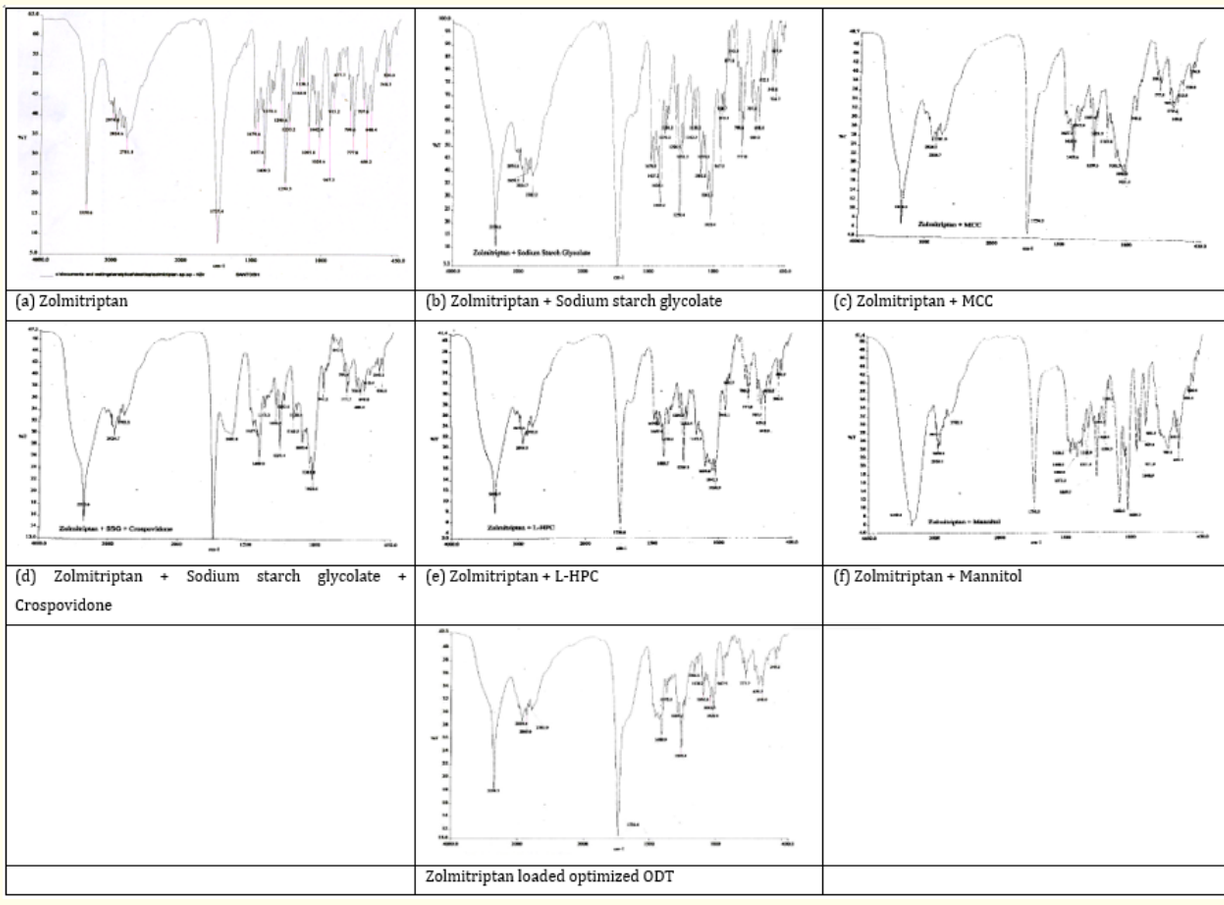

Figure 2: *FTIR studies of drug and drug excipient mixture.*

The micromeritic properties and flow properties of ZTN and pre-compressed powder blend were studied. Drug was found to have compressibility index of 24.44 ± 0.04, Hausner's ration of 1.325 ± 0.001 and angle of repose of 37.03 ± 0.02 (Table 1). Values of all the 3 parameters are in passable range i.e. suitable for compression.

Values of compressibility index of powder blend were in the range of 17 to 22.79, Hausner's ratio was found to be between 1.2 to 1.29 and angle of repose was found to be lesser than 30° for every batch prepared, it was found to be minimum for S1C1 i.e. 23.87 and all others are greater than this (Table 3). The compressibility index has been proposed as an indirect measure of bulk density, size and shape, surface area, moisture content and cohesiveness of materials because all of these can influence the observed compressibility index. The outcomes of these parameters indicated good flow properties and that the blends were suitable for direct compression. The flow property of the pure drug was enhanced by addition of glidant colloidal silicon dioxide, further the major excipients in the blend were filler. Microcrystalline cellulose is granular and has good flow. Also mannitol is highly moldable. Moisture content was found to be 0.28%.

The prepared rapimelts were subjected to various quality control tests and the data observed from the various tests are given in table 4. Hardness of the tablets was within the range 25 - 36 Newton, highest being for C1 and C2. This indicates adequate mechanical strength. Diameter of the rapimelts of all batches was close to 8 mm. Thickness varied from 2.5 - 2.8 mm. The percentage friability was less than 1% in all the formulations ensuring that the prepared tablets were mechanically stable. All the formulated tablets passed weight variation test as the percentage weight variation was within the limits of ± 10% of the weight. Thus, the prepared formulation complies with the weight

variation test. The maximum percentage drug content among all the formulations was found to be 99.88% and minimum percentage drug content from the all formulations was found to be 97.8% which was within the acceptable limits as per USP XXVII.

The disintegration time was found to be better when sodium starch glycolate was combined with crosslinked polyvinyl pyrrolidone. In case of sodium starch glycolate, disintegration occurs by rapid uptake of water followed by rapid and enormous swelling. Disparate other disintegrant, the disintegrating competence of sodium starch glycolate is unaugmented in the presence of hydrophobic excipients. Increasing the tablet compression pressure also appears to have no effect on disintegration time [23]. Crospovidone quickly wicks saliva into the tablet to generate the volume expansion and hydrostatic pressures necessary to provide rapid disintegration in the mouth. Unlike other superdisintegrants, which rely principally on swelling for disintegration, Crospovidone superdisintegrants use a combination of swelling and wicking. When examined under a scanning electron microscope, crospovidone particles appear granular and highly porous. Due to the unique granularity its particles facilitates wicking of liquid into the tablet promoting rapid disintegration. Due to its high cross-link density, crospovidone swells rapidly in water without gelling [24,25]. Other superdisintegrants usually form gels when fully hydrated. Disintegration time for various formulations was found to vary in the range 6 to 17 seconds, minimum i.e. 6 seconds for C2, S1C1 and maximum for S2. Wetting time for various formulations was found to vary in the range 12 - 51 seconds, minimum i.e. 14 seconds for C2, S1C1 and maximum 51 seconds for S2. Thus, though the disintegration time and wetting time of 5%, 7.5 % crospovidone were similar to that of mixture of both, formulation C1S1 was taken as the best one.

In vitro release studies were carried out using USP XXIII tablet dissolution test apparatus paddle method at 37 ± 0.5°C at pH 1.2. The *in vitro* dissolution profile (Figure 3) indicated faster and maximum drug release from formulation S1C1. Formulation S1C1 prepared by direct compression showed release 98.15% drug at the end of 15 min. The drug release profile was faster in the formulations containing combination of superdisintegrants. The lower levels of disintegrants providing faster release were identified by using the combination of superdisintegrants viz. sodium starch glycolate and crospovidone at different ratios and it was found that the release was better without compromising the disintegration time, when both were used at concentration of 2.5% each.

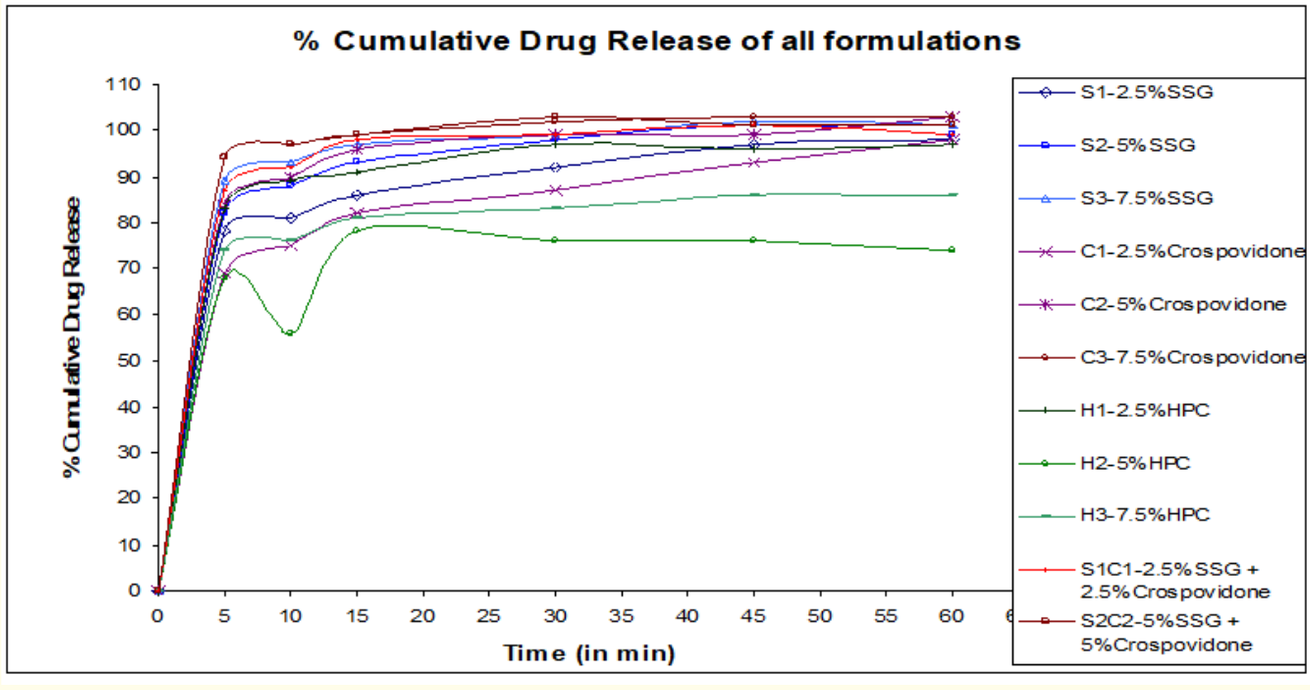

Figure 3: *Percentage Drug release from various formulations.*

The results showed that formulation containing this combination of superdisintegrants shows complete release within 30 minutes, wetting time of 16 seconds and disintegration time of around 6 seconds.

The stability studies were performed as per ICH guidelines on this formulation to ensure that they remain stable over their designated shelf-life. Stability study indicated that formulated tablets were more stable at 250C ± 20C / 60% RH ± 5% RH than at 400C ± 20C / 75% RH ± 5% RH.

Conclusion

On the basis of obtained results it can be concluded that the use of superdisintegrants in suitable proportions and combination resulted in a rapid disintegration of mouth dispersible tablets of ZTN prepared by direct compression technique. As compared to the tablets formulated with other methods like dry granulation or wet granulation technique, the method is simpler and cost effective. Also an improved formulation may be prepared by the using combination of superdisintegrants through direct compression method. In addition to complying with the physical testing parameters, the optimized formulation in conjunction with decreased disintegration time shows better drug release profile also. Thus, it can be concluded that the efficacy of dosage form has been increased and the prepared tablet could be a cost effective treatment for migraine.

Conflict of Interest

All the authors declare that they have no conflict of interest.

Acknowledgments

All the authors would like to thank Principal, Bhagyoday Tirth Pharmacy College, Sagar for providing necessary lab chemicals and equipments for the work. One of the authors Vijay Verma would like to thank Glenmark Pharma, Nasik, India for drug.

Bibliography

1. Asthana A., *et al*. "Oral Dispersible Tablets: Novel Technology and development". *International Journal of Pharmaceutical Sciences Review and Research* 20.1 (2013): 193-199.

2. Bhardwaj V., *et al*. "Formulation and Evaluation of Fast Dissolving Tablets of Amlodipine Besylate Using Different Super Disintegrants and Camphor as Sublimating Agent". *American-Eurasian Journal of Scientific Research* 5.4 (2010): 264-269.

3. Kannuri R., *et al*. "A review on taste masking and evaluation methods for orodispersible tablets". *International Journal of Pharmacy and Industrial Research* 1 (2011): 200-203.

4. Kalia A., *et al*. "Formulation and evaluation of Mouth dissolving tablets of Oxcarbazepine". *International Journal of Pharmacy and Pharmaceutical Sciences* 1.1 (2009): 12-23.

5. Bhargava HN., *et al*. "An evaluation of SMECTA as a tablet disintegrant and dissolution aid". *Drug Development and Industrial Pharmacy* 17.15 (1991): 2093-2102.

6. Pandey S., *et al*. "Recent trends with present and future prospects of Fast dissolving tablet: A new venture in Drug delivery". *International Journal of Pharma and Bio Sciences* 2 (2013): 379-404.

7. Chaurasia V., *et al*. "Orodispersible tablets: an overview of technology". *International Journal of Advanced Research and Review* 1.6 (2016): 156-172.

8. Kumar DL., *et al*. "Formulation and evaluation of Fast dissolving tablets of Ranitidine Hydrochloride by Hole Technology". *Asian Journal of Pharmaceutical and Clinical Research* 6.4 (2013): 143-147.

9. Singh SK., *et al*. "Formulation and evaluation of taste masked rapid release tablets of sumatriptan succinate". *International Journal of Pharmacy and Pharmaceutical Sciences* 4.2 (2012): 168-174.

10. Niranjan P., *et al*. "Formulation Design and in vitro Evaluation of Zolmitriptan Immediate Release Tablets using Primojel and AC-Di-Sol". *Journal of Pharmaceutical Sciences and Research* 7.8 (2015): 545-553.

11. Gupta AK., *et al*. "Fast dissolving tablet- a review". *Pharm Innovation* 1.1 (2012): 1-8.

12. Shadeedi MI., *et al*. "Formulation and evaluation of Carbimazole Orodispersible Tablet". *International Journal of Pharmacy and Pharmaceutical Sciences* 5.1 (2013): 232-239.

13. Samineni R., *et al*. "Formulation and evaluation of sumatriptan succinate mouth disintegrating tablets". *American Journal of Advanced Drug Delivery* 1 (2013): 759-769.

14. Bandari S., *et al*. "Orodispersible tablets: An overview". *Asian Journal of Pharmaceutics* 2.1 (2008): 2-11.

15. Rao KS., *et al*. "Design and evaluation of orodispersible tablets of sumatriptan succinate". *Journal of Pharmaceutical Sciences* 2 (2012): 41-413.

16. British pharmacopoeia. Published by the Stationary office on behalf of The Medicine And Health Care Products Regulatory Agency, Volume 5 (2011): A457.

17. United States Pharmacopeia- National formulary. Published by USP33-NF28, R76-R88 (2010).

18. Parashar B., *et al*. "Fast dissolving tablet". *International Journal of Applied Pharmaceutics* 4 (2012): 17-22.

19. Indian Pharmacopoeia, Ministry of Health and Family Welfare, Government of India (1996).

20. Kela S and Kesharwan D. "Formulation characterization and evaluation of taste masked rapid disintegrating tablet of ofloxacin by ion exchange resin technique". *International Journal of Pharmaceutical Sciences Review and Research* 21.2 (2013): 246-253.

21. Bhowmik D., *et al*. "Fast Dissolving Tablet: An overview". *Journal of Chemical and Pharmaceutical Research* 1.1 (2009): 163-177.

22. Farshid A., *et al*. "Formulation and evaluation of orodispersible tablets of zolmitriptan". *Asian Journal of Pharmaceutical and Clinical Research* 7.1 (2014): 127-134.

23. Mangal M., *et al*. "Superdisintegrants: An Updated Review". *International Journal of Pharmacy and Pharmaceutical Science Research* 2.2 (2012): 26-35.

24. Kiran RS., *et al*. "Influence of various super disintegrating agents on the aceclofenac fast dissolving tablets". *Research Journal of Pharmaceutical, Biological and Chemical Sciences* 2.2 (2011): 99-105.

25. Liberman HA., *et al*. "Pharmaceutical Dosage Forms: Tablets". Volume 2 (1989).

Volume 3 Issue 1 October 2018