The Study of Guar Gum and Starch on Disintegration Time and Drug Release of Fast Dissolving Tablet in Rabbit Using Single Dose Randomized Parallel Design Method

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ABSTRACT

The aim of this study is to find the effect of starch and guar gum 4000 on disintegrating time and dissolution behavior of drug Zolmitriptan from fast dissolving tablet (FDT). The FDT was prepared by direct compression method. The precompression parameters were evaluated with subjected to angle of repose, bulk and tapped density, hausner's ratio and Carr's index and all were within limit. The prepared tablets were evaluated for thickness, uniformity of content, hardness, friability, wetting time and in vitro disintegration time and in vivo release of drug. The in vitro release and assay of drug was performance by UV spectrophotometer. The in vivo study reveals that when guar gum (5%) and starch (10%) were used in formulation, the plasma concentration of drug was increased because, it disintegrate tablet rapidly and drug was released rapidly from dosage form and reach quickly in to systemic circulation resultant bioavailability is increased.

Keywords: FDT, guar gum, Single Dose Randomized Parallel Design Method, Zolmitriptan.

INTRODUCTION

Oral drug delivery is the most preferred method of drug administrating therapeutic agents for their systemic effects. Nevertheless, it is probable that at least 90% of all drugs used to produce systemic effects are administered by oral route [1].

Tablet is the most popular among all dosage forms existing today because of its convenience of self administration, compactness and easy manufacturing, however, swallowing is common phenomenon which leads to poor patient compliance [2].To overcome these drawbacks, fast dissolving tablets (FDT), mouth dissolving tablets (MDT) or orally disintegrating tablets (ODT) has emerged as alternative oral dosage forms. These are novel types of tablets that disintegrate/dissolve/ disperse in saliva within few seconds [3, 4].

According to European Pharmacopoeia ODT should disperse /disintegrate in less than three minutes but according to United State Pharmacopoeia (USP) the disintegrating time of fast dissolving tablet approximately 30 seconds or less [5,6].

The basic approach used in development of FDT is the use of superdisintegrants like Cross linked carboxy melhyl cellulose, Sodium starch glycolate, Polyvinylpyrrolidone etc. which provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva.

Guar gum is a galactomannan, commonly used in cosmetics, food products, and pharmaceutical formulations. Guar gum is used in solid-dosage forms as a binder and disintegrant. It has also been investigated in the preparation of sustained-release matrix tablets in the place of cellulose derivatives such as methylcellulose. The aim of present research work is to study the effect of

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the guar gum (4000) and starch in fast dissolving tablet as a disintegrating agent [7].

Zolmitriptan is a selective agonist of serotonin (5-hydroxytryptamine; 5HT) type 1B and 1D receptors. Zolmitriptan is a drug for management of severe migraine headaches. Severe migraine headaches are believed to result from dilation of the blood vessels in the brain and intolerable. Zolmitriptan causes constriction of the blood vessels and thereby relieves the pain of a migraine headache and very effective in relieving migraine [8].

MATERIAL

The drug was procured from Emcure Pharmaceutical, Pune (Maharashtra) as a gift sample. Microcrystalline cellulose (grade PH 102) was purchased from Ases chemicals, Jodhpur. Mannitol, Talc, Mg-stearate, starch and guar gum (4000) were purchased from Loba chemicals (shyama scientific) Jodhpur. All other chemicals and reagents were of laboratory grade.

METHOD

Experimental

λ_{max} of zolmitriptan was determined by UV spectrophotometer (CECIL 7400). Accurately weighing 100 mg of drug and dissolved it in 100 ml 0.1 N HCl. The further dilutions were made of and scanned in the range of 200-400 nm. λ_{max}, was obtained at 224 nm (USP monograph 2011 draft 1). The graph is shown in **Fig 1.**

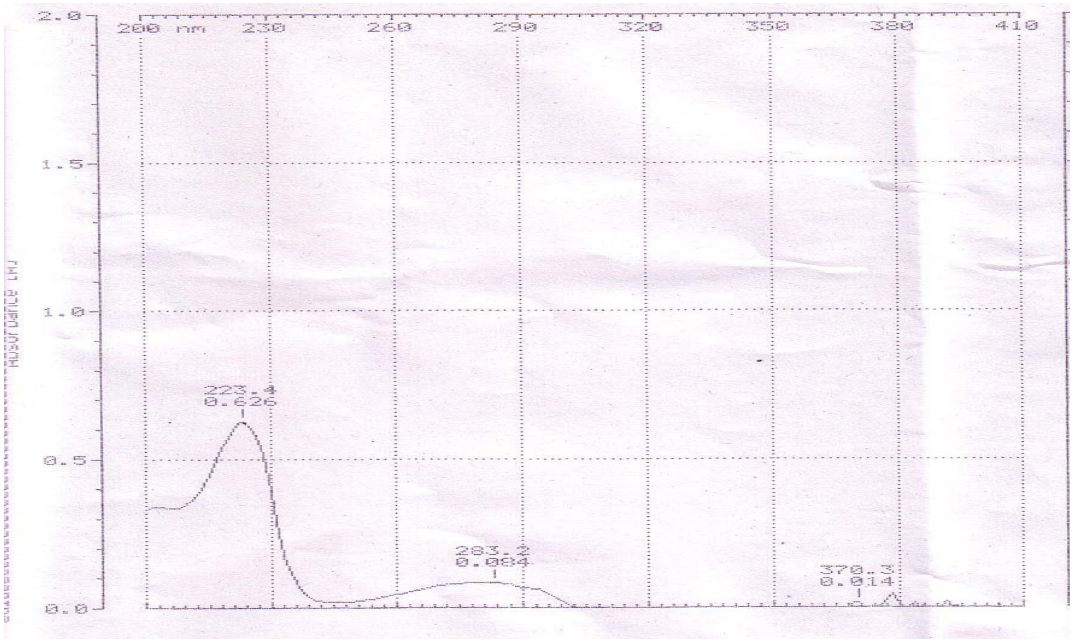

Figure 1. λ_{max} of zolmitriptan

The identification of drug was performed by FTIR that shown in fig. No. 2. It was found that the drug was shown all essential peaks in spectra.

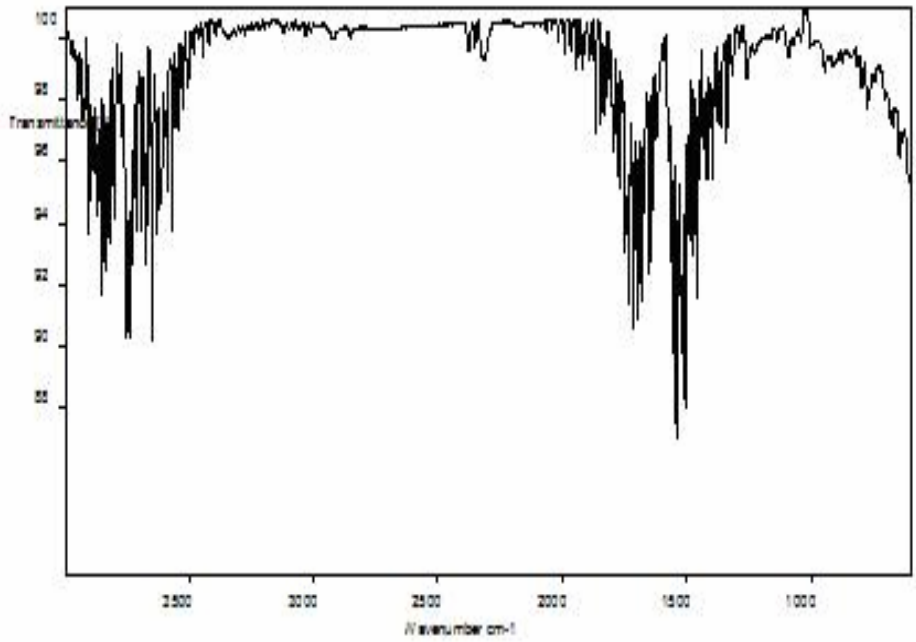

Figure 2. The identification of drug performed by FTIR

Drug - Excipient Compatibility Study by DSC

Drug excipient compatibility study was also carried out by differential scanning calorimeter. DSC thermogram of zolmitriptan is shown in **Fig. 3** and its physical mixture is shown in **Fig. 4** respectively.

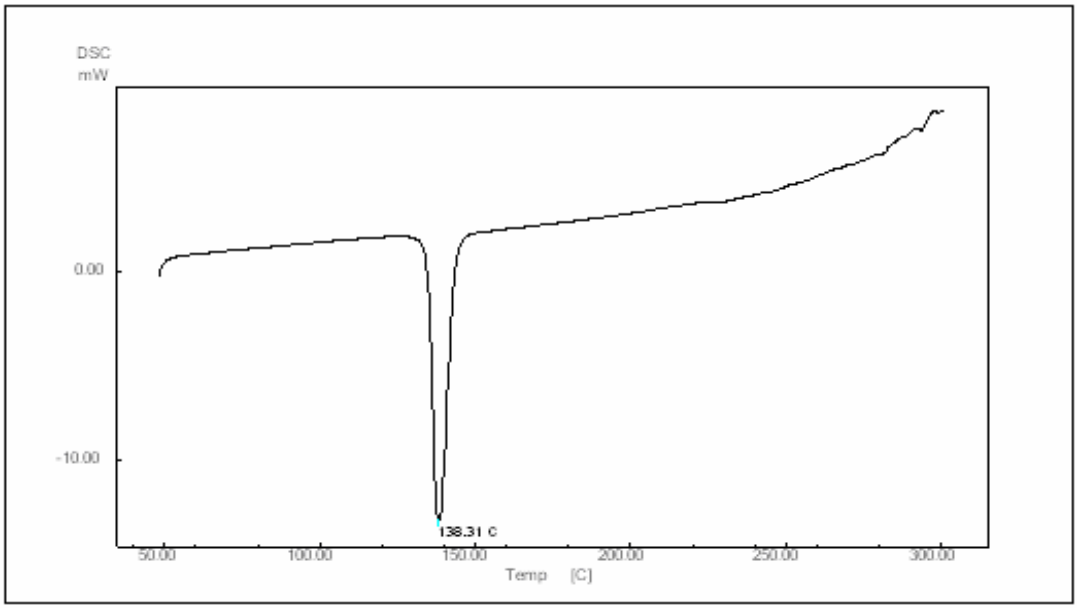

Figure.3 DSC thermogram of zolmitriptan

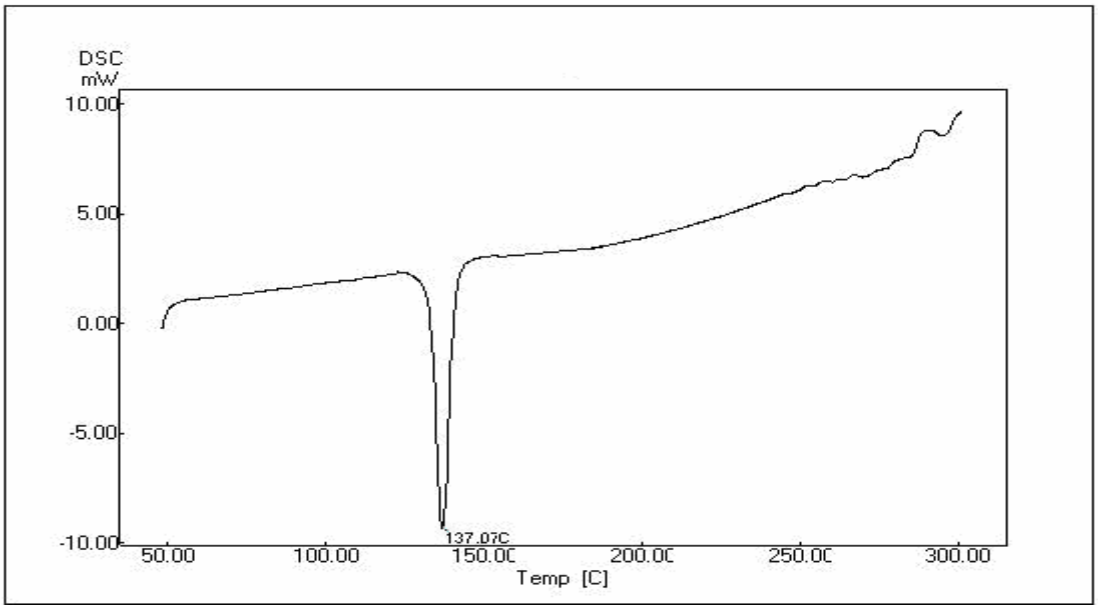

Figure.4 DSC thermogram of zolmitriptan and excipient

Method of Preparation of Fast dissolving Tablet

The fast dissolving tablets of zolmitriptan were prepared by direct compression method. Micro crystalline cellulose (MCC PH 102) and mannitol were used as diluents, guar gum (4000) was used as a disintegrating agent, starch was used as a binder and disintegrating agent, magnesium stearate was used as a lubricating agent talc and colloidal silica were used as flow promoter and aspartame was added as a sweetening agent. All ingredients separately were passed through sieve no.22. They were mixed according to geometric dilution method and after the powder blend were mixed by powder blander for sufficient time (approximate 20 min.). The mixed powder bland was compressed in to tablet using 6 mm punches on 8 station rotary tablet compression machine (Hardik engineers, Ahmadabad).

Table 1. Composition of Zolmitriptan formulation by direct compression method

S.n.	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Zolmitriptan	5	5	5	5	5	5	5	5	5
2	Starch	5	5	5	7.5	7.5	7.5	10	10	10
3	Avicel (pH-102)	30	30	30	30	30	30	30	30	30
4	Guar gum	2	5	8	2	5	8	2	5	8
5	Magnesium stearate	1	1	1	1	1	1	1	1	1
6	Talc	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
7	Colloidal silica	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
8	Mannitol	55.5	52.5	49.5	53	50	47	50.5	47.5	44.5
9	Aspartame	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
10	Total weight (mg)	100	100	100	100	100	100	100	100	100

All ingredients are in mg/tablet

Evaluation of pre compression parameters of powder and granules [2, 9]

a) Angle of Repose

Angle of repose indicates the flow property of granules. The angle of repose was calculated by following formula.

$$\theta = tan^{-1}\frac{h}{r} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

Where, θ is the angle of repose.
h is the height in cm.
r is the radius in cm.

b) Bulk Density and Tapped Density

Bulk density and tapped density were determined by using bulk density apparatus.

Where, M is the mass of granules or powder and V_b is the bulk volume of the granules and powder.

$$Bulkd\ density = \frac{Mass\ of\ granules\ or\ powder}{Bulk\ volume\ of\ granules\ or\ powder} \ldots\ldots\ldots (2)$$

$$Tapped\ density = \frac{Mass\ of\ granules\ or\ powder}{Tapped\ volume\ of\ powder\ or\ granules} \ldots\ldots (3)$$

Where, M is the mass of granules or powder and V_t is the tapped volume of the granules and powder.

c) Carr's Index: The index is subjected to flow property of powder and granules and it was calculated by following formula.

$$Carr\ sindex = \frac{Tapped\ density - bulk\ dencityX100}{Tapped\ density} \ldots\ldots\ldots\ldots\ldots (4)$$

Where, D_t is the tapped density of the granules and powder and D_b is the bulk density of the granules or powder.

d) Hausner's Ratio: Hausner's ratio is also subjected to flow property of powder and granules. The Hausner's ratio was calculated by following formula.

$$Hausner's\ ratio = \frac{Tapped\ density}{Bulk\ density} \ldots\ldots\ldots (5)$$

Evaluation of Tablets

All the tablets were evaluated for different parameters such as thickness, hardness, friability, weight variation, wetting time and disintegration time.

a) Size and Shape

The length, thickness, and width of 20 tablets were measured with the help of thickness Tester vernier caliper.

b) Hardness

The hardness or tablet crushing strength of tablets was determined by diametric compression using Monsanto hardness tester

c) Weight variation

Twenty tablets were randomly selected from each batch and individually weighed. The average of these selected tablets was calculated and compared the individual tablet weight with average tablet weight [10].

d) Friability

Friability of the tablet was determined using Roche friabilator. Pre weighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) was calculated by the following formula.

$$Fraibility = \frac{(Initial\ weight - final\ weight)X100}{Initial\ weight} \ldots\ldots\ldots (6)$$

$W_{initial}$ is the weight of 20 tablets before rotation and W_{final} is the weight of 20 tablets after rotation.

e) Wetting time

The wetting time of the tablets was measured using a simple procedure. Five circular tissue papers of 10-cm diameter were placed in a Petri dish with a 10-cm diameter. Ten millilitres of water containing eosin, a water-soluble dye was added to the Petri dish. A tablet was carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablets was noted as the wetting time [11].

f) Disintegration time

The tablet was carefully put in to the measuring cylinder containing 10 ml of phosphate buffer (6.8) and the time for the tablet to completely disintegrate into fine particles was noted [12].

g) Drug Content

The ten tablets were weighed and average weight was calculated. Tablets were crushed into powder in a mortar.

Taken powder equivalent to average weight was added in 100 ml 6.8 phosphate buffer solution and stirred on a magnetic stirrer for a period of 2 hr .The solution was filtered through whatmann filter paper no.42 and 1 ml of the filtrate was diluted to 20 ml using a phosphate buffer. Absorbance of resultant solution was measured at 224 nm using phosphate buffer as a blank [12].

h) In vitro dissolution study

The dissolution studies were performed using eight basket dissolution test apparatus U.S.P.II **(Electro Lab).** The release rate of drug from Fast dissolving tablet was determined using USP Dissolution Testing Apparatus II (Paddle type). The dissolution test was performed using 900 ml of 0.1 HCl at 37±0.5^{0}C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at every time point and the samples were replaced with fresh dissolution medium. The sample removed was filtered, diluted and analyzed by UV at 224 nm. Dissolution method was obtained from the USFDA, CDER [12, 13]

i) Stability Studies

A stability study was performed according to ICH guideline. The optimized formulations of all methods were stored in stability chamber at 45°C ± 2 temperature and 75 % ± 5% relative humidity for three months; the tablets were tasted for their contents and dissolution behavior monthly [14].

j) In-Vivo Studies

The optimized formulations of all methods were subjected to in vivo release studies using rabbit as animal model. Six male rabbits weighing 1.3 kg and 12 months old were selected for the study. They were divided into two groups of 3 in each and the study was conducted as single dose randomized parallel design. The animals were housed individually under (23 ± 2°C, 55 ± 5 % RH, 12 hours light/dark cycle) environmental conditions. The rabbits were fasted overnight and allowed free access to tap water only. The optimized formulations were administered to the rabbits by gastric intubation method after calculating the animal dose70. 1 ml of blood samples were withdrawn from the marginal ear vein of rabbit at 0.25, 0.50, 0.75, 1, 2, 3, 4 and 6 hrs. The plasma samples were separated by centrifugation and the drug was extracted. The drug was analyzed by UV spectrophotometer [15].

Area under the curve (AUC)

Amount of drug that has been absorbed is known as AUC. The area under the curve can be calculated by numerical method known as "Trapezoidal rule'' frequently used in pharmacokinetics to calculate the area under the plasma drug concentration –verses-time curve, called the area under the curve. The area between time intervals is the area of a trapezoid and can be calculated with the following formula.

$$\int_{tn-1}^{tn} AUC = \frac{Cn-1 + Cn(tn + tn-1)}{2}$$

Where AUC = area under the curve

t_n = time of observation of drug concentration

c_n and t_{n-1} = time of prior observation of drug concentration corresponding to C_{n-1}. [16]

RESULT AND DISCUSSION

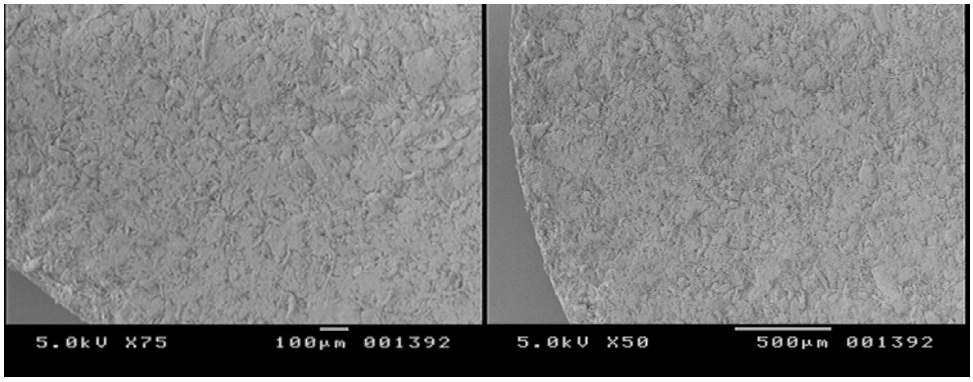

Figure 5. SEM of tablet surface

The pictures **sem studies** are shown in fig 5 the images are showing smooth surface of tablet that was prepared by dry granulation.

Fast dissolving tablets each containing 5mg zolmitriptan, were prepared by direct compression method employing starch and guar gum (4000) as super disintegrants in different concentration. Directly compressible excipients, avicel pH 102 and mannitol were used as diluents to enhance mouth feel. A total of ten formulations were designed and evaluated.

Table 2. Micromeritics of powder

S.n.	Parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Angle of repose(º)	21.21 ±0.06	22.23 ±0.06	20.32 ±0.04	24.69 ±0.03	23.29 ±0.05	21.69 ±0.07	23.56 ±0.05	22.84 ±0.07	21.84 ±0.06
2	Bulk density (gm/ml)	0.514 ±0.02	0.515 ±0.27	0.507 ±0.04	0.513 ±0.06	0.512 ±0.05	0.509 ±0.04	0.518 ±0.06	0.514 ±0.08	0.511 ±0.06
3	Tapped density (gm/ml)	0.570 ±0.04	0.542 ±0.07	0.531 ±0.03	0.557 ±0.05	0.581 ±0.04	0.569 ±0.02	0.549 ±0.07	0.561 ±0.04	0.554 ±0.03
4	Carr's index (%)	9.82 ±0.05	4.98 ±0.03	4.51 ±0.02	7.89 ±0.06	11.87 ±0.05	10.54 ±0.07	5.64 ±0.07	8.37 ±0.06	7.76 ±0.05
5	Hausner's ratio	1.10 ±0.04	1.06 ±0.03	1.05 ±0.04	1.08 ±0.05	1.13 ±0.06	1.11 ±0.05	1.12 ±0.06	1.09 ±0.04	1.08 ±0.05

***Data are expressed as mean± SD (n=3)**

Table 2 depicts the characterization of formulation was done for the flow property of powder, determined the bulk density, angle of repose, compressibility index, hausner`s ratio. Bulk density depends on the particle size, shape, size and tendency of particles to adhere together. The bulk and tapped density of mixed blend power varied from 0.507±0.04 to 0.518±0.06 and 0.531±0.03to 0.581±0.04 gm /ml respectively. The result was indicating good packaging capacity of tablet. The flow ability of the powder also evaluate by the angle of repose and Carr's index. The angle repose and Carr's index were found between 20.32±0.04 to 24.69±0.03 and 4.51±0.02to 11.87±0.05 respectively, shown excellent flow properties of granules.

Table 3. Evaluation parameter of tablet

S.n.	Parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Weight variation(mg)	101.2 ±0.7	100.6 ±0.9	100.9 ±1.1	99.8 ±0.9	100.2 ±1.2	101.7 ±0.8	99.7 ±1.2	101.7 ±0.9	100.8 ±0.9
2	Hardness (Kg/cm^2)	3.5 ±0.10	3.5 ±0.14	4.0 ±0.13	3.5 ±0.15	4.5 ±0.17	5.0 ±0.14	5.0 ±0.13	5.5 ±0.15	6.5 ±0.14
3	Thickness (mm)	0.63 ±0.3	0.64 ±0.2	0.64 ±0.3	0.64 ±0.1	0.63 ±0.3	0.63 ±0.2	0.63 ± 0.1	0.64 ±0.2	0.63 ±0.4
4	Friability (%)	1.31 ±0.2	1.26 ±0.4	0.86 ±0.2	0.55 ±0.1	0.5 ±0.2	0.57 ±0.3	0.4 ±0.2	0.3 ±0.1	0.37 ±0.2
5	Wetting time (Sec.)	10 ± 0.4	11 ± 0.3	8.0 ± 0.4	10 ± 0.5	12 ±0.6	9.0 ±0.3	10.0 ± 0.4	9.0 ± 0.4	7.0 ± 0 .5

S.n.	Parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
6	Disintegration time (sec.)	34 ±0.5	20 ±0.8	18 ±0.3	28 ±0.2	16 ±0.4	15 ±0.5	26 ±0.6	15 ±0.5	13 ±0.6

***Data are expressed as mean± SD (n=3)**

Table 3 depicts all the formulation parameters were evaluated.The The thickness of the prepared tablets was found to be in the range of 0.63±0.1 to 0.64± 0.3 mm, while the weight of all the tablet was found to be in the range of 99.8±0.9 to 101.7 ±0.8 mg. Hardness of tablets was found to in the range of 3.5 ±0.10 to 6.5 ±0.14 kg/cm^2 and percentage weight loss in the friability test was less than 1% in all the batches, which was an indication of good mechanical resistance of the tablets. Wetting time is an important criteria for understanding the capacity disintegrants to swell in the presence of little amount of water was found to be in the range of 7±0.5 to 12±0.6 seconds. All the formulations disintegrated rapidly in vitro within 13±0.6 to 34±0.5 seconds**.** The guar gum concentration was mainly affecting disintegration time. The P- value was found to be 0.0035 at 95% confidence interval which was less than 0.05(Software used prism version 3.0). The P-value indicates that the guar gum concentration is giving a highly significant effect on disintegration time of tablet.

The tablet containing an appropriate amount of guar gum 4000 and starch showed the better result in respect of disintegrate of tablet. The formulation containing 5% w/w guar gum (4000) and 10% w/w starch showed the minimum disintegration time (15 ±0.5) sec. Nevertheless, all other formulations prove to be very effective disintegrants. DSC studies indicated that the drug is compatible with all the excipients.The DSC studies showed the no difference of melting point of drug conforming that no interaction of drug occurred to the components of the formulation. The IR spectroscopic studies also indicated that the drug is compatible with all the excipients. The IR spectra of the formulations showed all the characteristic peaks of drug, thus conforming that no interaction of drug occurred.

As seen from Table 3, the assay revealed that the tablets to contain zolmitriptan between 99.0 ±0.43 to 100 ±0.92 % of the labeled claim. All the tablets subjected to uniformity of the drug content, were found to contain zolmitriptan within 100±5% of the labeled claim .Zolmitriptan release was significantly faster from all the prepared formulations as compared to marketed conventional tablet formulation.

Table 4. Results of cumulative % drug release of tablet in 0.1HCl

Time(min.)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	Marketed preparation
0	0	0	0	0	0	0	0	0	0	0
2	62.67±0.9	74.21±1.1	65.19±0.7	68.25±0.8	77.58±0.8	70.29±0.3	68.56±0.9	85.78±1.2	73.65±0.7	76.64±0.9
4	75.38±0.5	94.37±0.3	78.39±0.6	83.56±0.7	99.15±0.5	82.39±0.8	79.38±0.6	99.23±0.8	92.38±0.4	88.28±0.7
6	88.39±0.7	99.64±0.8	91.26±0.4	94.68±0.5		97.67±1.2	92.67±0.7		99.69±1.1	97.35±0.8
8	96.28±0.9		99.47±0.8	99.16±0.2		99.88±0.5	98.65±0.6			99.29±0.9
10	99.62±0.8									

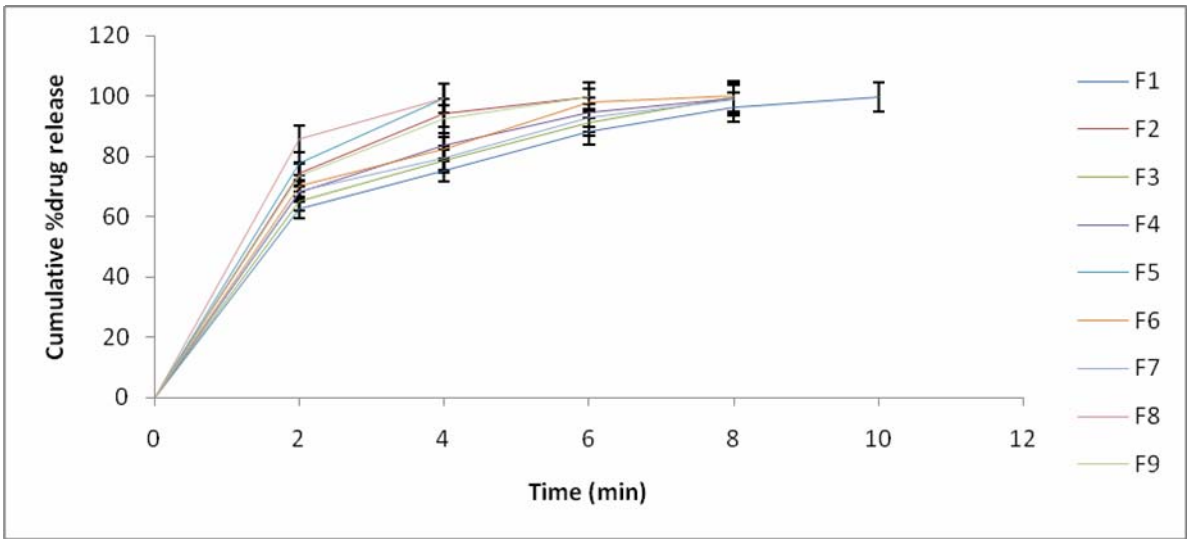

Figure 6. Dissolution of formulations

Release rate of zolmitriptan from the formulations F_2, F_5, F_8, and F_9 was found to be faster than F_1, F_3, F_4, F_6, and F_7 respectively. The batches F_2, F_5, F_8, and F_9 subjected to T_{50} and $T_{90,}$ the all four batches release the 50% drug within 1min 25 sec. and 90% drug within 3 min 55 sec which showed faster release with respect to marketed preparation.

In order to describe the kinetics of the release process of drug in all formulations, zero order, first order rate equations and higuchi model were used. Zero order rate equation describes the systems where the release rate is independent of the concentration of the dissolved species, the first order equation describes the release from systems where dissolution rate is dependent on the concentration of the dissolving species while the higuchi model describes the diffusion of drug from tablet surface.

It is evident from valve of $R^{2,}$ that the drug released process was not zero order in nature. This indicates that the dissolution rate of the drug is not independent of the amount of drug available for dissolution and diffusion from the matrix. The dissolution data of all formulations when fitted in accordance with the first order equation, it was evident that a linear relationship was obtained with R^2 (concentration coefficient) value close to unity and higher then R^2 obtained from the zero order equation for all formulations. This shows that the release is an apparent first order process and indicates that the amount of drug released is dependent on the matrix of drug loaded. With reference to higuchi model, it was observed that R^2 valve found close to linearity which indicates that the drug is diffused from the tablet surface.

With reference to T_{50} and T_{90} value of all formulation, it was observed that formulation F8 exhibiting 1min 09 sec for 50% and 3min 36 sec for 90% drug release in 0.1 HCl which is best among all formulations.

The guar gum (4000) has good swelling nature and disintegration of tablet was occurred by swelling mechanism of guar gum and it was observed that when concentration of guar gum (4000) was used up to 8%, tablets were disintegrate rapidly but concentration was used above 8 % the disintegration of tablet was taken more time it may due to increase the viscosity of medium and formation of gel layer around the tablet surface which create the problem for disintegration of tablet (libermann et al). However, guar gum (4000) and starch in formulation showed a good disintegration time of 15±0.05 sec. and complete drug release was achieved in 4min. This may be attributed to the swelling property of guar gum (4000) and synergistic activity of starch.

Short term stability studies 3 month for formulation F8 and the assay of drug contain 100.7±1.02 indicating that there was no significant difference in drug content of

labeled claim. The release rate of drug was not significantly changed during stability study andit was found 99.06±0.7, indicating stability of formulation.

The optimized batch (F_8) was chosen according to in vitro dissolution studies results by means of fast disintegration time and dissolution profile. Formulation F_8 was directly included for in vivo studies. The data are given in **Table 5.**

Table 5. Data of plasma concentration time

S.n.	Sampling time (hrs)	Control plasma concentration (µg/ml)	Test plasma concentration (µg/ml)
1	0	0	0
2	0.25	1.54±0.04	3.53±0.06
3	0.50	4.02±0.09	9.38±0.07
4	0.75	8.14±0.08	12.03±0.05
5	1	10.12±0.06	15.16±0.09
6	2	8.13±0.05	14.26±0.04
7	3	7.0 ±0.07	13.12±0.07
8	4	6.14±0.05	11.45±0.08
9	5	5.12±0.03	8.59±0.07
10	6	5.02±0.02	7.69±0.07

***Data are expressed as mean± SD (n=3)**

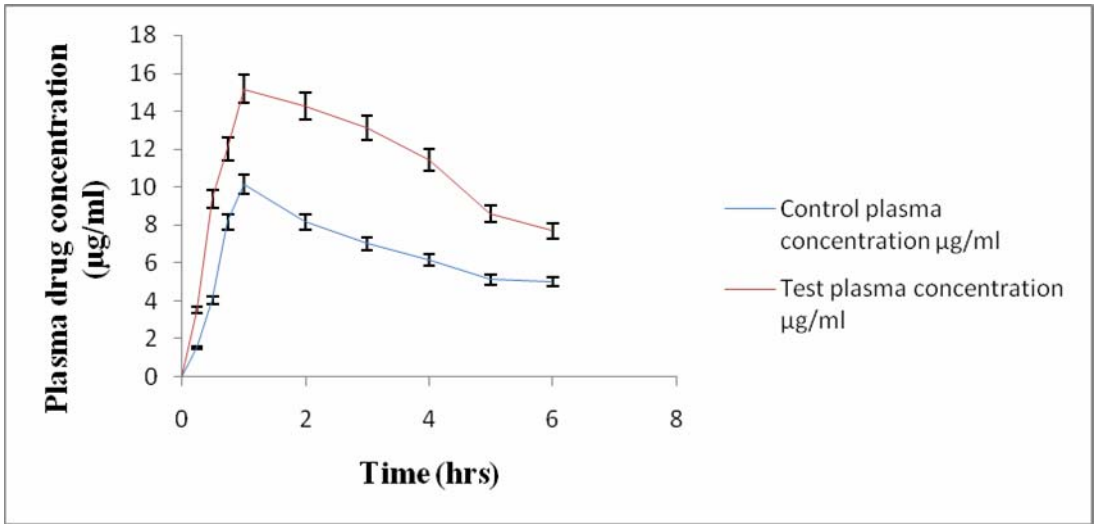

Figure 7. Graph between Plasma drug conc. v/s time.

The results were obtained from the in vivo studies of both F-8 and control formulation (without superdisintegrant). For formulation F-8, the C_{max} was found to be 15.16±0.09µg/ml and the t_{max} is 60 minutes. The AUC was found to be 66.98 µg-hr/ ml. For control formulation the C_{max} was found to be 10.12±0.06µg/ml and the t_{max} is 60 minutes. The AUC was found to be 38.65 µg-hr/ ml. The control shows a difference of percentage with that of formulation F-8. The In-vivo graph shows the increase in plasma drug concentration of test (F-8) formulation when compared to the control formulation.

The in vivo study reveals that when using of super disintegrating agent, it increases the plasma concentration of drug because, it disintegrate tablet rapidly, so the drug releases from dosage form and reach quickly in to systemic circulation resultant bioavailability is increased.

CONCLUSION

The fast dissolving tablet prepared by direct compression method using 5% guar gum and 10% starch concentration was effective. F-8 formulation was optimized with related to all tablet characteristics, in vitro, in vivo study and stability study. The In-vivo graph shows the increase in plasma drug concentration of test (F-8) formulation when compared to the control formulation, so it can be concluded that using of super disintegrating agent (using 5% guar gum and 10% starch), it increases the plasma concentration of drug because of rapid tablet disintegration.

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دراسة تبين المدة الزمنية للتفكك وإطلاق الدواء في توليفة سريعة الذوبان على شكل اقراص لمادتي صمغ الغار والنشا في الارانب باتباع طريقة عشوائية مصممة بشكل متوازٍ باستخدام جرعة واحدة

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ملخـص

الهدف من الدراسة إيجاد تأثير النشا وصمغ الغار 4000 على مدة التفكك والسلوك الذوباني لعقار زولمتروبتان من قرص سريع الذوبان (FDT) والذي تم تحضيره بطريقة الضغط المباشر. وقد تم تقييم المعلمات قبل الضغطية بتعريضها لزاوية الاستناد وكذلك الكمية السائبة والكثافة المستغلة. وقد كانت نسبة هاوزنر ومؤشر كار ضمن الحدود المسموحة بها. وقد تم تقييم الاقراص المحضرة من حيث السمك وانتظام المحتوى والصلابة والهشاشة، وكذلك وقت الترطيب ووقت التفتت خارج الجسم واطلاق العقار داخل الجسم. وقد تم تقييم اطلاق العقار خارج الجسم باستخدام مطياف الاشعة فوق البنفسجية. وقد اظهرت الدراسة الحيوية (داخل الجسم) أن استخدام صمغ الغار (5%) والنشا (10%) في التوليفة زيادة في تركيز العقار في بلازما الدم بسبب زيادة السرعة في تفتيت الاقراص وانطلاق العقار من التوليفة الدوائية ووصوله بسرعة إلى الدورة الدموية؛ مما يعني زيادة التوافر الحيوي للمادة.

الكلمـات الدالـة: اقراص سريعة الذوبان، صمغ الغار، طريقة عشوائية مصممة بشكل متوازٍ باستخدام جرعة واحدة، زولمترتبان.

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