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Research Article

FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF ZOLMITRIPTAN

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ABSTRACT

Introduction: Zolmitriptan is used to treat migraine headache, and it works only when a migraine attack has started, it will not stop from getting an attack. Zolmitriptan is rapidly and well absorbed, the absolute bioavailability is approximately 40%.
Objective: The present study is to formulate and evaluate an Orodispersible tablet for Zolmitriptan to treat migraine headache with rapid onset of action and also to improve the bioavailability by avoiding the first pass hepatic metabolism.
Material and Methods: Orodispersible tablets containing the Zolmitriptan by using different diluents such as Avicel, Spray dried lactose, Pearlitol and Starlac and different super disintegrant such as SSG, L-HPC, CCS and Crospovidone. Tablets were prepared by direct compression method and sublimation method by using Menthol and Camphor as subliming agent and their pre and post compression parameters were determined. The dissolution studies were performed at 37°C±5°C and at 50 rpm in pH 6.8 phosphate buffer.
Results: The drug content of all the formulations was within the acceptable limits. The tablets containing Avicel as diluents with L-HPC as super disintegrate showed less disintegration time with maximum drug release. So we used Avicel for sublimation method by using Menthol and Camphor as subliming agent and found Menthol as the better subliming agent.
Conclusion: Formulation with insoluble diluents and disintegrants were found to be better than tablets containing soluble diluents and disintegrants. By sublimation method, menthol was found better than camphor in disintegration and drug release.

Keywords: Orodispersible tablets, diluents, disintegrants, Zolmitriptan.

INTRODUCTION

Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage form is tablet[1].

Orodispersible tablets (ODT) are not only indicated for people who face difficulty in swallowing, but are also ideal for active people. Orodispersible tablets are also called as mouth dissolving tablets, melt-in mouth tablets, fast dissolving tablets, rapimelts, and porous tablets, quick dissolving tablets etc. Orodispersible tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolves or disperses in the saliva without the need of water or chewing[2]. Most Orodispersible drug delivery systems must include substances to mask the taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients. The faster the drug into solution, quicker is the absorption and onset of clinical effect. The advantage of Orodispersible dosage forms are increasingly being recognized in both, industry and academics. The ODT should disperse/disintegrate in less than three minutes[3]. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. The technologies used for manufacturing Orodispersible tablets are freeze drying, spray drying, tablet molding, sublimation, sugar-based excipients, tablet compression, and disintegration addition[4].

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[5]. Literature reveals the alternative formulations of Zolmitriptan as nasal spray and sublingual tablets prepared by direct compression with different polymers [6, 7].

MATERIALS AND METHODS

Zolmitriptan was received as a gift sample from Apotex Research Private Limited, Bangalore. Croscarmellose sodium, Sodium starch glycolate, Sodium Stearyl Fumarate was procured from DMV, Fonterra excipients, India. Menthol, Camphor and Low Substituted Hydroxypropylcellulose was obtained from S.D. Fine Chem. Ltd. Avicel PH 102, spray dried lactose were procured from Alpha chemika Mumbai. Pearlitol SD procured from Roquette Chemicals, France. Starlac obtained from Signet chemical pvt. Ltd. Crospovidone obtained from BASF, Germany.

ANALYTICAL METHOD

2.5 mg of Zolmitriptan was dissolved in small amount of pH 6.8 phosphate buffer and the volume was made up to 100 ml using the same buffer which is called as stock -I solution. 1 ml of the above solution is diluted to 10 ml with the same buffer solution, which is called as Stock-II solution. From this stock-II solution serial dilutions were made to obtain solutions of the drug in the concentrations ranging from 2, 4, 6, 8, and 10µg/ml. The absorbance of the solutions was measured at 222 nm using UV-visible spectrophotometer. A graph of concentration vs absorbance was plotted.

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.

Melting point determination: Melting point of Zolmitriptan was determined by Capillary Method.

Compatibility study: Compatibility of the drug with the excipients is determined by subjecting the physical mixture of the drug and the excipients to infrared absorption spectral analysis (FTIR). Any changes in chemical composition of the drug after combining it with the excipients were investigated with I.R. spectral analysis.

Procedure: Drug or physical mixture of drug with excipient was mixed with potassium bromide in the ratio of 1:100. The mixture was taken and compressed under 10-ton pressure in a hydraulic press to form a transparent pellet. The pellet was scanned by IR spectrophotometer.

FORMULATION OF ORODISPERSIBLE TABLETS OF ZOLMITRIPTAN

The Orodispersible tablets of Zolmitriptan were prepared by direct compression method using 2.5 mg of the drug, diluents, lubricant, sweetening agent, subliming agent or super disintegrants.

Preparation of Zolmitriptan tablets using super disintegrant addition method

Zolmitriptan Orodispersible tablets were prepared by direct compression method according to formulae given in the tables 1 to 5. Blend can be prepared by passing the ingredients through 40-mesh sieve separately and collected. Super disintegrants were added in 5 and 10% concentrations. The drug and other ingredients except sodium stearyl fumarate were mixed in geometrical order in poly bag and sodium stearyl fumarate passed 60-mesh sieve, lubricated for 2 min and the blend was compressed using shallow concave punch of 6.3 mm diameter to get a tablets of 100 mg weight using ten station Rimek tablet compression machine (Karnavati Engineering Ltd. Ahmadabad, India)[8].

Preparation of tablets using Sublimation method:

Specified quantity of Zolmitriptan and other excipients along with subliming agents like camphor or menthol were added in different percentages according to formulae given in the tables. The ingredients were weighed and passed through 40 # screen prior to mixing. All the materials were transferred into a mortar and triturated till it was mixed uniformity and # 60 meshes passed sodium stearyl fumarate was added and lubricated for 2 min. The resulting powder mixture was compressed into tablets using 6.3 mm punch to get tablets of weight 100 mg. The tablets were dried at 60°C in oven till constant weight was obtained.

Table1: Composition of different Orodispersible tablets of Zolmitriptan using Avicel pH 102 as diluents.

Ingredients	A1	A2	A3	A4	A5	A6	A7	A8	A9
Zolmitriptan	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Avicel PH 102	95.5	90.5	90.5	90.5	90.5	85.5	85.5	85.5	85.5
Sodium starch glycolate	0	5	0	0	0	10	0	0	0
Croscarmellose sodium	0	0	5	0	0	0	10	0	0
Crospovidone	0	0	0	5	0	0	0	10	0
L-HPC	0	0	0	0	5	0	0	0	10
Sodium stearyl fumarate	1	1	1	1	1	1	1	1	1
Aspartame	1	1	1	1	1	1	1	1	1
Total	100	100	100	100	100	100	100	100	100

Table2: Composition of different Orodispersible tablets of Zolmitriptan using Pearlitol SD as diluent.

Ingredients	P1	P2	P3	P4	P5	P6	P7	P8	P9
Zolmitriptan	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Pearlitol SD	95.5	90.5	90.5	90.5	90.5	85.5	85.5	85.5	85.5
Sodium starch glycolate	0	5	0	0	0	10	0	0	0
Croscarmellose sodium	0	0	5	0	0	0	10	0	0
Crospovidone	0	0	0	5	0	0	0	10	0
L-HPC	0	0	0	0	5	0	0	0	10
Sodium stearyl fumarate	1	1	1	1	1	1	1	1	1
Aspartame	1	1	1	1	1	1	1	1	1
Total	100	100	100	100	100	100	100	100	100

Table 3: Composition of different Orodispersible tablets of Zolmitriptan using Spray dried lactose as diluent.

Ingredients	S1	S2	S3	S4	S5	S6	S7	S8	S9
Zolmitriptan	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Spray dried lactose	95.5	90.5	90.5	90.5	90.5	85.5	85.5	85.5	85.5
Sodium starch glycolate	0	5	0	0	0	10	0	0	0
Croscarmellose sodium	0	0	5	0	0	0	10	0	0
Crospovidone	0	0	0	5	0	0	0	10	0
L-HPC	0	0	0	0	5	0	0	0	10
Sodium stearyl fumarate	1	1	1	1	1	1	1	1	1
Aspartame	1	1	1	1	1	1	1	1	1
Total	100	100	100	100	100	100	100	100	100

Table 4:.Composition of different Orodispersible tablets of Zolmitriptan by using Starlac as diluent and L-HPC as super disintegrant.

Ingredients	SC1	SC2
Zolmitriptan	2.5	2.5
Starlac	90.5	85.5
L-HPC	5	10
Sodium stearyl fumarate	1	1
Aspartame	1	1
Total	100	100

Table 5: Composition of different Orodispersible tablets of Zolmitriptan by using Avicel PH 102 as diluents and Menthol and Camphor as subliming agents.

Ingredients	ME1	ME2	CA1	CA2
Zolmitriptan	2.5	2.5	2.5	2.5
Avicel pH 102	92.5	89.5	92.5	89.5
Menthol	3	6	0	0
Camphor	0	0	3	6
Sodium stearyl fumarate	1	1	1	1
Aspartame	1	1	1	1
Total	100	100	100	100

EVALUATION OF ZOLMITRIPTAN ORODISPERSIBLE TABLETS[9]:

Weight variation test: Twenty tablets were selected randomly and average weight was determined. Then individual tablets were weighed and was compared with average weight. If the variation is within the I.P limits, the tablets pass the weight variation test.

Tablet hardness: The hardness of each batch of tablet was checked by using Monsanto hardness tester. The hardness was measured in terms of kg/cm^2. 3 tablets were chosen randomly and tested for hardness. The average hardness of 3 determinations was recorded.

Wetting time[10]: Five circular tissue papers of 10 cm diameter are placed in a petri dish with a 10 cm diameter. 10 ml of water was poured on the tissue paper placed in the petri dish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as the wetting time.

Water Absorption Ratio[10]: A piece of tissue paper folded twice was placed in a small petri dish (diameter. of 6.5 cm) containing 6 ml of distilled water. A tablet was put on the paper, and the time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, was determined using equation:

$$\text{Water absorption ratio} = \frac{Wa - \text{Wb}}{Wa} \times 100$$

Where,

Wb = weight of the tablet before water absorption

Wa = weight of the tablet after water absorption

Disintegration time: Tablet disintegration is an important step in drug absorption. The test for disintegration was carried out in Electrolab USP disintegration test apparatus. It consists of 6 glass tubes which are 3 inches long, open at the top, and held against a 10 mesh screen, at the bottom end of the basket rack assembly. To test the disintegration time of tablets, one tablet was placed in each tube and the basket rack was positioned in a 1 liter beaker containing pH 6.8 buffer solution at 37°C ± 1°C such that the tablet remains 2.5 cm below the surface of the liquid. The time taken for the complete disintegration of the tablets was noted.

Tablet friability: Five tablets were weighed and the initial weight of these tablets was recorded and placed in Roche friabilator and rotated at the speed of 25 rpm for 100 revolutions. Then tablets were removed from the friabilator, dusted off the fines and again weighed and the weight was recorded. Percentage friability was calculated by using the formula:

$$\%\text{Friability} = \frac{\text{Initial weight of the tablets} - \text{Final weight of the tablets}}{\text{Initial weight of the tablets}} \times 100$$

Thickness: The thickness of tablets was measured using Vernier calipers, which permits accurate measurements and provides information of the variation between tablets.

Assay: Ten tablets were weighed and taken in mortar and crushed to make powder. A quantity of powder weighing equivalent to 2.5 mg of Zolmitriptan was taken in 100 ml volumetric flask and phosphate buffer pH 6.8 was added. Then the solution was filtered using whatmann filter paper and then the solution was diluted up to 10 µg/ml and absorbance was measured at 222 nm. Then the amount of drug present was calculated using standard graph.

Drug content uniformity: Five tablets were weighed individually and powdered, from the powder the drug was extracted in 100 ml of phosphate buffer pH 6.8 filtered and diluted to 10µg/ml, content of drug was determined by measuring the absorbance at 222 nm.

Dissolution studies: In Vitro dissolution studies for all the prepared tablets was carried out using USP paddle method at 50 rpm in 900 ml of phosphate buffer pH 6.8 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 222 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.

Stability studies of Zolmitriptan tablet[11, 12]: Stability studies were carried out at 40°C and 75% RH for the following selected formulations for 45 days. The selected formulations were packed in bottles, which are tightly plugged with cotton and capped. They were then stored at 40°C / 75% RH for 45 day and evaluated for their, physical appearance, hardness, disintegration time and drug content.

RESULTS AND DISCUSSION

ANALYTICAL METHOD

The calibration curve in pH 6.8 buffer was linear in concentration range between 2–10 µg/ml at 222 nm. Results were plotted in Figure No. 1. The R^2 and average slope were found to be 0.9973 and 0.1189 respectively.

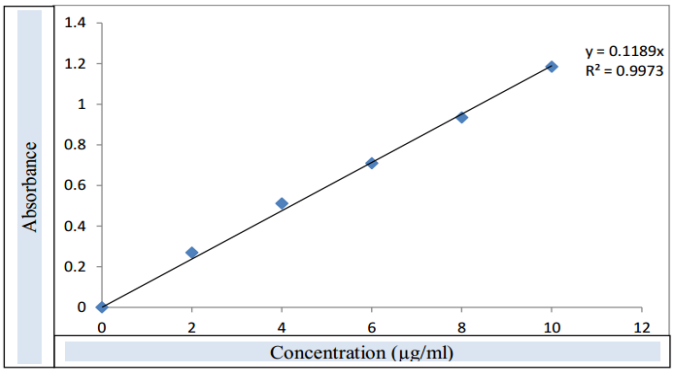

Fig. 1: Standard calibration curve for Zolmitriptan in pH 6.8 buffer

PREFORMULATION STUDIES:Melting point determination: The melting point of Zolmitriptan was found to be 139°C to 141°C, thus indicating purity of the obtained drug sample. The observed melting point was in accordance with the literature[13].

FTIR compatibility studies: From the spectra of pure drug and the combination of drug with excipients, it was observed that all the characteristic peaks of Zolmitriptan were present in the combination spectrum, thus indicating compatibility of the drug and excipients.

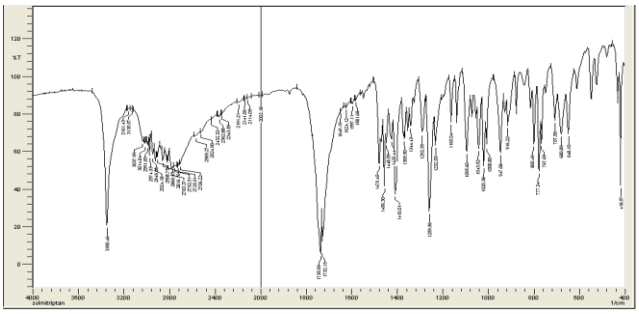

Fig. 2: IR spectra of pure drug Zolmitriptan

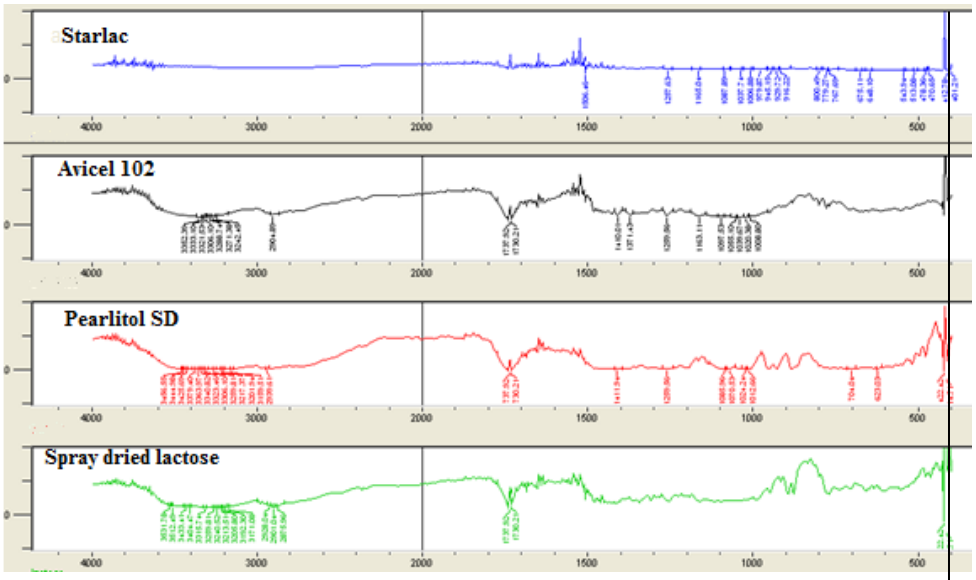

Fig. 3: IR spectra of Zolmitriptan with Starlac, Avicel PH 102, Pearlitol, Lactose as diluents

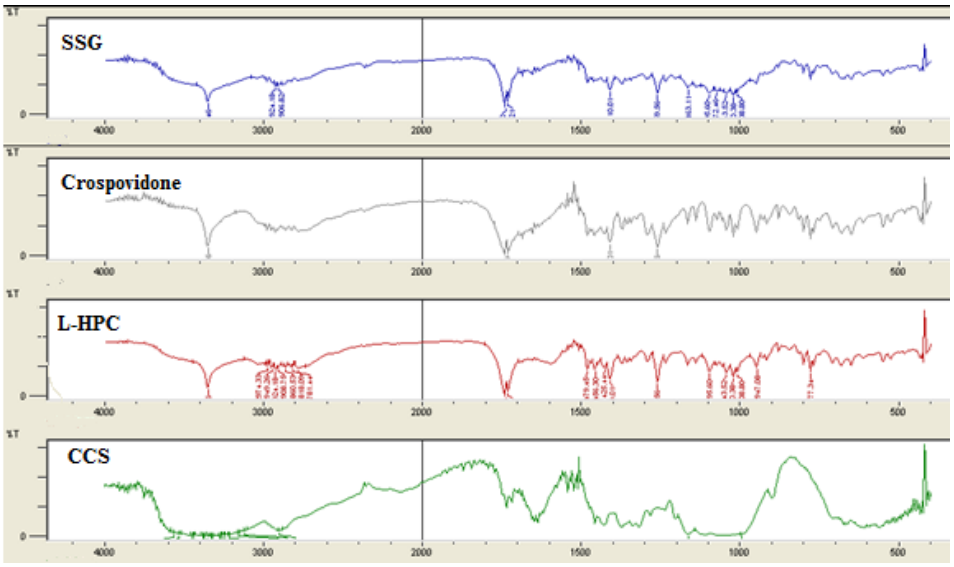

Fig. 4: IR spectra of Zolmitriptan with SSG, Crospovidone, L-HPC, CCS as superdisintegrants

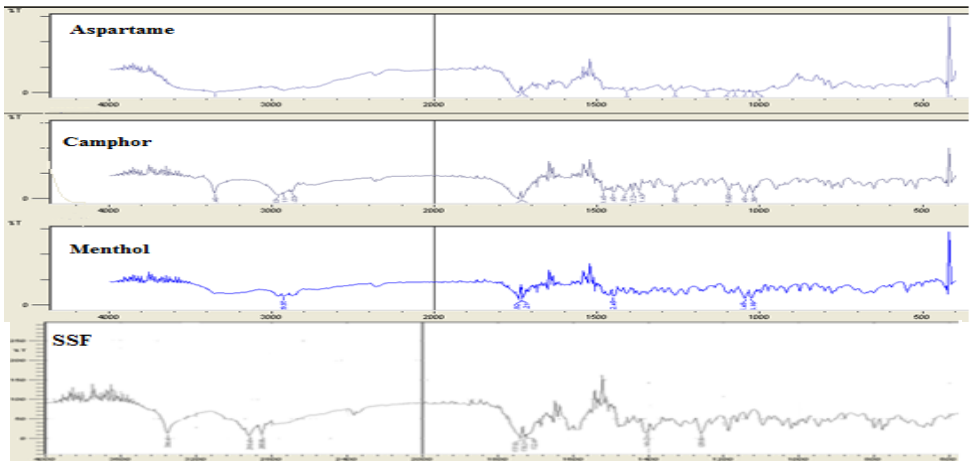

Fig. 5: IR spectra of Zolmitriptan with Aspartame,Camphor,Menthol and Sodium stearyl fumarate

Compatibility studies were performed using FTIR spectrophotometer. The FTIR spectrum of pure drug and physical mixture of drug and excipients were studied. The characteristic absorption peaks of Zolmitriptan were obtained at 3350 cm^{-1} due to NH Stretching, 1735 cm^{-1} due to C=O stretching ,1259cm^{-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 Zolmitriptan and the excipients used. From the IR spectrum Fig No.1-4, it was observed that there were no changes in these main peaks in IR spectra of mixture of drug and excipients, 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.

EVALUATION OF COMPRESSED TABLETS OF ZOLMITRIPTAN

Tablets of Zolmitriptan were punched and subjected to evaluation studies such as weight variation, hardness, friability, and thickness, wetting time, disintegration time and drug content. The results of the evaluation studies are shown in Table 6-10

Table 6: Evaluation of Physical Parameters of Orodispersible tablets of Zolmitriptan by using Avicel as diluents

Formula	Hardness (Kg/cm2)*	Thickness (mm)*	Friability (%)	Wetting time (sec)	Water absorption ratio (%)*	Disintegration Time (sec)*	Content uniform (mg)*
A1	5.2±0.29	3.17±0.02	0.478	28±0.9	0.051±1.3	60.53	2.51±0.2
A2	5±0.22	3.15±0.04	0.326	16±0.1	0.61±0.35	19 ±0.48	2.53±0.7
A3	5.1±0.19	3.14±.07	0.498	19±0.1	0.54±0.43	22 ±1.01	2.56±0.5
A4	5±0.29	3.14±0.04	0.671	17±0.1	0.68±0.32	15 ±0.29	2.49±0.6
A5	4.2±0.32	3.12±0.03	0.634	11±0.1	0.75±1.21	10 ±0.38	2.61±0.2
A6	5±0.27	3.12±0.02	0.356	15±0.1	0.65±0.28	15 ±0.13	2.45±0.5
A7	4.9±0.39	3.16±0.05	0.444	20±0.1	0.73±0.78	16 ±0.65	2.48±0.4
A8	5.1±0.31	3.11±03	0.521	12±0.1	0.81±0.16	10 ±0.29	2.65±0.2
A9	4.3±0.25	3.11±0.02	0.327	10±0.1	0.87±0.22	8 ±0.78	2.48±0.1

*** Mean ± S.D., n=3 (All the values are the average of three determination)**

Table 7: Evaluation of Physical Parameters of Orodispersible tablet of Zolmitriptan by using Pearlitol SD as diluents

Formula	Hardness (Kg/cm2)*	Thickness (mm)*	Friability (%)	Wetting time (sec)*	Water absorption ratio (%)*	Disintegration time (sec)*	Content uniform (mg)*
p1	5.2±0.53	2.63±0.04	0.498	300±30	0.03±1.39	260.81±1.03	2.31±0.4
p2	5±0.23	2.81±0.02	0.543	180±10	0.16±0.98	180.65±0.58	2.42±0.9
p3	5.1±0.78	2.82±.03	0.462	120±11	0.26±0.88	180.58±0.51	2.69±0.2
p4	4.2±0.46	2.75±0.02	0.580	120±52	0.29±0.96	180.56±0.62	2.54±0.1
p5	4.5±0.18	2.79±0.07	0.553	120±45	0.4±1.23	120.1±0.34	2.55±0.3
p6	5.2±0.58	2.82±0.05	0.648	120±15	0.2±1.29	60.23±0.39	2.35±0.4
p7	5±0.28	2.81±0.03	0.327	120±10	0.18±0.86	60.19±0.21	2.38±0.4
p8	5±0.33	2.79±0.02	0.438	120±80	0.29±0.77	60.15±1.01	2.39±0.7
p9	5±0.52	2.74±0.06	0.378	57±0.1	0.43±0.89	60.05±0.29	2.52±0.6

*** Mean ± S.D., n=3 (All the values are the average of three determination)**

Table 8: Evaluation of Physical Parameters of Orodispersible tablet of Zolmitriptan by using Spray dried lactose as diluents

Formula	Hardness (Kg/cm2)*	Thickness (mm)*	Friability (%)	Wetting time (sec)*	Water absorption ratio (%)*	Disintegration time (sec)*	Content uniform (mg)*
S1	4.5±0.23	2.69±0.02	0.329	300±0.1	0.03±0.88	300.32±1.33	2.24±0.5
S2	4.1±0.43	2.62±0.03	0.324	58±0.16	0.12±1.21	45±0.67	2.38±0.8
S3	4±0.95	2.67±0.05	0.456	53±0.19	0.54±0.89	32±0.34	2.68±0.6
S4	4±0.65	2.61±0.04	0.433	47±0.20	0.51±0.77	20±0.31	2.58±0.9
S5	4±0.24	2.64±0.03	0.372	120±0.3	0.23±0.29	60.55±0.29	2.59±0.2
S6	4.3±0.33	2.75±0.02	0.298	39±0.16	0.56±0.33	120.10±0.21	2.43±0.3
S7	4.1±0.35	2.65±05	0.199	35±0.14	0.24±0.76	48±0.57	2.58±0.1
S8	4.2±0.42	2.66±0.07	0.234	33±0.19	0.45±0.39	15±0.22	2.66±0.5
S9	4±0.28	2.63±0.04	0.411	180±0.2	0.25±0.26	60.10±0.26	2.71±0.7

*** Mean ± S.D., n=3 (All the values are the average of three determination)**

Table 9: Evaluation of Physical Parameters of Orodispersible tablet of Zolmitriptan by using Starlac as diluents

Formula	Hardness (Kg/cm2)*	Thickness (mm)*	Friability (%)	Wetting Time (min)*	Water absorption ratio (%)*	Disintegration time (sec)*	Content uniform (mg)*
SL1	4±0.18	2.69±0.02	0.234	22±0.3	0.56±0.19	360±23	2.49±0.3
SL2	4.3±0.12	2.62±0.05	0.330	19±0.2	0.59±0.21	360±10	2.48±0.2

*** Mean ± S.D., n=3 (All the values are the average of three determination)**

Table 10: Evaluation of Physical Parameters of Orodispersible tablet of Zolmitriptan by using Menthol & Camphor as subliming agents

Formula	Hardness (Kg/cm)*	Thickness (mm)*	Friability (%)	Wetting Time (sec)*	Water absorption ratio (%)*	Disintegration Time (sec)*	Content uniform (mg)*
ME1	4±0.48	2.69±0.03	0.432	42±0.1	0.47±0.45	35±0.22	2.54±0.2
ME2	4±0.28	2.62±0.09	0.444	38±0.2	0.48±0.38	15±0.19	2.48±0.4
CA1	4.1±0.21	2.75±0.04	0.654	42±0.2	0.54±0.35	50±0.12	2.39±0.2
CA2	4.5±0.09	2.65±0.02	0.731	30±0.1	0.59±0.19	30±0.32	2.48±0.5

*** Mean ± S.D., n=3 (All the values are the average of three determination)**

Thickness of tablets: The thickness of the all formulation was found to be between 3.91 mm- 4.51mm as shown in Table 6-10

Hardness test: The measured hardness of tablets of different batches ranged between 4-5.2 kg/cm^2 of formulations shown in Table No.6-10. This ensures good handling characteristics of all batches. When Starlac was used as diluents, hardness was not increased beyond 2 - 2.5 kg/cm^2 with Croscarmellose sodium, Crospovidone & Sodium starch glycolate used as disintegration. L-HPC was used as a binder and disintegrants & compressed[14].

Hardness of the tablets prepared by sublimation method (3.96 to 4.36 kg/cm^2) was less than those prepared by superdisintegrant addition method (4.83 to 5.14 kg/cm^2) because of their porous structure.

Friability Test: The values of friability test were tabulated in Table 6-10 it is ranging from 0.1990 to 0.7310 the % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable.

Weight Variation Test: The percentage weight variations for all formulations were tabulated in Table 6-10 it is ranging from 98.7 to 101.8 % all the formulated tablets passed weight variation test, as the % weight variation was within the pharmacopoeia limits of 7.5% of the average weight. The weights of all the tablets were found to be uniform with low standard deviation.

Drug Content Uniformity: The percentages of drug content were found to be 2.24 mg to 2.71 mg of Zolmitriptan which indicates that the drug was uniformity mixed with excipients. The results were shown in Table 6-10

Disintegration test: Orodispersible tablet of Zolmitriptan was prepared using Avicel, Pearlitol, Spray dried lactose, Starlac as diluents using different superdisintegrants like sodium Starch glycolate, Crospovidone, croscarmellose sodium & L-HPC in 5% and 10% concentration levels.

Crospovidone is a cross-linked polyvinylpyrrollidone (PVP), which is insoluble but highly hydrophilic due to its high molecular weight and cross-linked structure. It does not swell significantly, but it is a very good disintegrant also at low concentration, Croscarmellose sodium (CCS) is soluble in water and because of the fibrillar structure highly hydrophilic, Low-substituted hydroxypropyl cellulose (L-HPC) is Insoluble in water, Rapidly swells in water. Grades LH-11 and LH-21 exhibit the greatest degree of swelling. Certain grades can also provide some binding properties while retaining disintegration capacity[15]. Sodium Starch Glycolate (SSG) Absorbs water rapidly, Rapid and extensive swelling with minimal gelling. Effective Concentration is 4-6%. Above 8%, disintegration times may actually increase due to gelling and its subsequent viscosity producing effects[16].

Formulations with Avicel (A1-A9) were found to be best as the disintegration time with the all disintegrants was not beyond 22 sec.

Formulation prepared using Pearlitol SD (P1-P9) as diluents exhibited disintegration time between 60.05 sec to 180.65 sec, similarly Spray dried lactose (S1-S9) as diluents the disintegration time was found to be 15 sec to 120.10 sec.

At last Starlac (SL1&SL2) when used as diluents (except L-HPC) hardness was not developed & so formulations were not developed with other disintegrants. Only with L-HPC 5% and 10 % was compressed, disintegration time was found between 6.10 min to 6.23 min.

Among all diluents, the disintegration time was found to be in order Avicel < Spray dried lactose < Pearlitol < Starlac. when we cheek the solubility of diluents it was observed that starlac and pearlitol & spray dried lactose were soluble diluents and Avicel are totally insoluble diluents so insoluble diluents may promote faster disintegration time than soluble diluents, Investigations show that superdisintegrants have a greater effect on disintegration time in an insoluble system than in a soluble or partially soluble system. With soluble compounds the viscosity of penetrating fluid increases and pores of tablet widen rapidly. This reduces the effectiveness of strongly swelling disintegrating agents[17].

As Avicel was found to be the best diluents we planned sublimation method using Menthol & Camphor as subliming agent. Disintegration time for Menthol was between 15 sec to 35 sec and similarly for Camphor disintegration time was found to be between 30 sec to 50 sec. Therefore among subliming agent Menthol < Camphor in disintegration time so Menthol was better subliming agent.

Wetting time: The wetting time for all the formulation was tabulated in Table 6-10 The value lies between 10 sec to 180 sec, except Starlac which is take long time around 19 min to 22min in wetting time.

Water Absorption Ratio: The water absorption ratio for all the formulation was tabulated in table No.6-10 value lies between 0.12 % to 0.87 %.

In-vitro dissolution study: All the formulations of prepared Orodispersible tablets of Zolmitriptan were subjected to in vitro release studies using dissolution apparatus in pH 6.8 buffer. The release data obtained for all the formulations were tabulated in Table No.6-10 and Fig No.4-8 shows the plot of % drug released as a function of time for different formulations.

In the formulation A1 to A9 formulation containing Avicel shows the better drug release of 108.03% at the end of 4 min. indicating good bioavailability of the drug from this formulation. The rapid drug dissolution might be due to easy breakdown of particles and rapid release of drugs into the dissolution medium. When spray dried lactose is used with sodium starch glycolate, the dissolution and disintegration time decreased when the disintegrant concentration level was increased. As per the literature the recommended concentration of Sodium starch glycolate in a formulation is 2-8%, with the optimum concentration about 4% although in many cases 2% is sufficient[18]. So when we increase the concentration beyond 5% the increase in the disintegration time and dissolution is not observed.

DISSOLUSION PROFILE GRAPHS

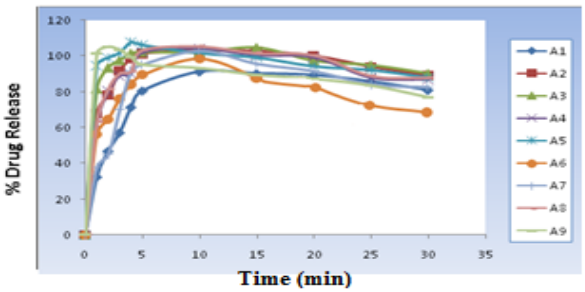

Fig. 6: Dissolution profile of Orodispersible tablets of Zolmitriptan using Avicel as diluents

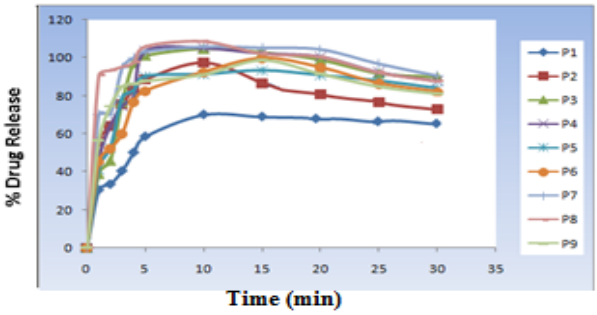

Fig. 7: Dissolution profile of Orodispersible tablets of Zolmitriptan using Pearlitol as diluents.

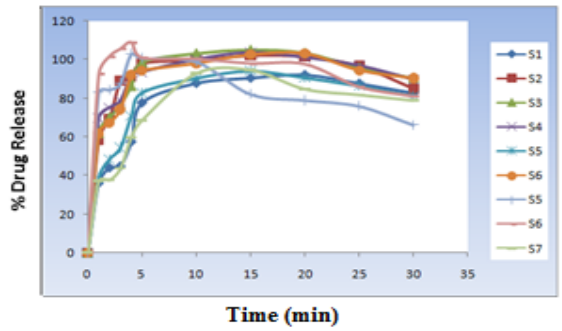

Fig. 8: Dissolution profile of Orodispersible tablets of Zolmitriptan containing Spray dried lactose as diluents.

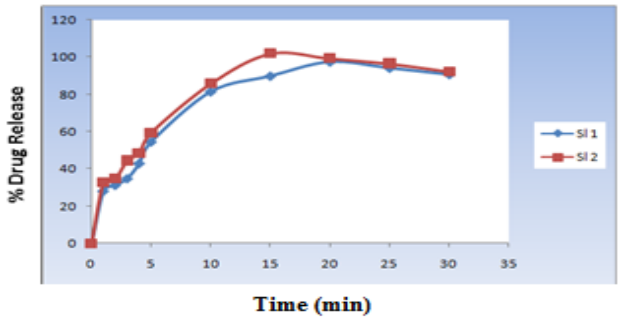

Fig. 9: Dissolution profile of Orodispersible tablets of Zolmitriptan containing Starlac as diluents.

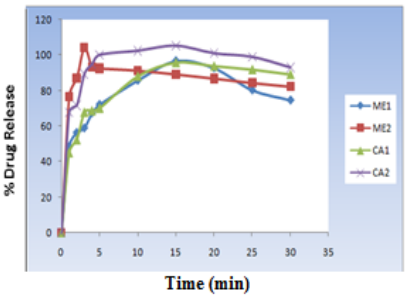

Fig. 10: Dissolution profile of Orodispersible tablets of Zolmitriptan by using Menthol & Camphor as subliming agents.

STABILITY STUDIES

Table 11 stability studies of the formulations were carried out as per the ICH guidelines. The Best formulation A5 and ME2 was subjected to stability studies at 40º±2˚C and 75±5% RH for a period of 45 days .The physical stability was assessed by the appearance and the chemical stability by change in the drug content and disintegration time and hardness. The results showed that the formulation were stable at the end of the 45th days.

TABLE 11: STABILITY STUDY DATA OF A5 & ME2

45th day

Formulations	Physical Appearance	Disintegration time (sec)	Drug content (mg)	Hardness (kg/cm 2)
A5	No change	10	2.60	4.4
Me2	No change	14	2.48	4

CONCLUSION

In present study Orodispersible tablet of Zolmitriptan were prepared by direct compression method and evaluated, drug estimation by UV spectroscopy at 222 nm was developed.

The FTIR studies showed that there were no chemical interactions between the drug and the excipients as no new peaks were observed. Formulation developed using diluents like Avicel, Spray dried lactose, Pearlitol and Starlac and using superdisintegrant such as L-HPC, Crospovidone, Sodium starch glycolate, Croscarmellose sodium at 5% and 10 % levels. Formulation were evaluated for tablet disintegration, wetting time, water absorption ratio, friability, uniformity of weight, and hardness, thickness, content uniformity, and assay. Incorporation of superdisintegrants in formulation played a critical role in dissolution enhancement. Among all formulation insoluble diluents such as Avicel promote faster disintegration time than soluble diluents like Pearlitol, Starlac. Among the formulations prepared the formulation containing Avicel as the diluents and L-HPC as superdisintegrant at 5% concentration level exhibited excellent disintegrating as well as release characteristics by direct compression method. By sublimation method formulation prepared using menthol as subliming agent were superior in tablet disintegration and drug release compared camphor formulation.

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