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Zolmitriptan Mouth Dissolving Tablets: Development of Formulas and Invitro Evaluation

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Abstract

Pharma Burst ODT super disintegrants were used in different concentrations to manufacture Zolmitriptan fast dissolving tablets by a direct compression method. With a 28° angle of repose, there is good flow. The densities for bulk and tapped materials are 0.410 (g/ml) and 0.500 (g/ml), respectively. The compressibility index and Hausner ratio have values of 19.05 and 1.24, correspondingly. According to IP standard, weight variation test results range from 121.4 mg to 126.1 mg. Friability: Less than 0.31%, according to the data, means that the percentage losses did not exceed 1.0% (complies with IP requirements). The thickness of the tablets ranges from 2.90 mm to 2.99 mm. Based on the results, it can be packed. There was a range of 98.62% to 100.3% content homogeneity. It was discovered that the tablet's hardness ranged from 4 to 4.6 kg/cm2. The outcomes show that the tablets are within limit and have a solid mechanical structure. The disintegration time of the pills was found to be within a 30-second range, ranging from 0'11 to 0'16 seconds. For formulations FZ1, FZ2, FZ3, ZF4, FZ5, ZF6, FZ7, FZ8, and FZ9, a dissolution investigation was conducted in 6.8 pH phosphate buffer between 0 and 15 minutes. For formulations FZ9 and commercial product, a comparative dissolving analysis was conducted in phosphate buffer with a pH of 6.8. Tablet storage conditions: For 0, 30, 60, and 90 days, tablets were kept at 45°C ± 2°C/75%. The hardness of the tablets gradually increased over time, but it was always within the permissible range. Disintegration time: varies depending on storage circumstances, but never exceeds 20 seconds, or less than 30 seconds (IP standard). The dissolving data of the formulations both at the beginning and after the designated storage period did not significantly alter, according to dissolution studies.

Keywords: Zolmitriptan, fast dissolving tablets, direct compression method, disintegration time, dissolution studies

INTRODUCTION

Mouth Dissolving Tablets (MDTs), an ideal substitute for traditional oral dose forms including tablets and capsules, have drawn a lot of attention during the last three decades. A solid dose form known as an MDT dissolve and disintegrates in the mouth (on the tongue, under the tongue, or in the buccal cavity) without the need for water in 60 seconds or less. Its absorption occurs systemically, bypassing the need for prior metabolism. The dissolved material can flow down gently with the aid of saliva, so those who struggle with swallowing or chewing can handle it with ease. An oral dose form that is currently in use is bioequivalently extended with an MDT.

To enhance porosity, sublimating agents are utilised, while superdisintigrants are used for quick dissolving [1–5]. The application of statistical

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design as part of an optimisation technique to the development of pharmaceutical formulations would offer an effective and affordable way to gather the data required to comprehend the relationship between controllable (independent) variables and performance or response (dependent) variables [6–9]. Swallowing difficulties, or dysphagia, affect people of all ages, but the old and young are especially vulnerable because of physiological changes in those groups. The mentally ill, the recalcitrant, and patients experiencing motion sickness, nausea, abrupt allergic reactions, coughing fits, or nausea are among groups that have trouble taking normal oral dosage forms. When there isn't enough water available, it can occasionally be challenging to swallow conventional items. These issues prompted the creation of an innovative class of solid oral dosage form known as an orodispersible tablet, which quickly dissolves in saliva without the need for a glass of water.

These tablets are a common dosage form in the market today because of their advantages in terms of patient compliance, quick onset of action, higher bioavailability, and superior stability. Certain medications have a bioavailability that is noticeably higher in these situations than it is in dose forms that are typically tablets.

Using superdisintegrants is the fundamental method utilised in the creation of ODTs. To make ODTs, numerous methods have been devised. Lyophilization, moulding, direct compression, and vacuum drying are a few of them. For making tablets with adequate mechanical strength, the direct compression approach is practical and reasonably priced. The new class of serotogenic agonists, zolmitriptan, has a strong symptomatic antimigraine action and a high oral absorbability. Zolmitriptan is a 5-HT1 B/D receptor selective agonist.

Polymers called Pharmabusrst, Pearlitol Flash, and Panexcea ODT are used in the current study to create Zolmitriptan orodispersible tablets. acidic materials such as sodium stearyl fumarate and citric acid is shown in Table 1 [10–14].

MATERIALS AND MEHODS

Constructing a pH 6.8 buffer (phosphate buffer) using the Zolmitriptan Standard Curve

A solution of sodium hydroxide (0.1 N) was made by dissolving 27.218 grams of potassium dihydrogen orthophosphate in 1000 milliliters of clean water. After that, 112 ml of 0.1 N sodium hydroxide solutions and 250 ml of potassium dihydrogen orthophosphate solution were combined. Finally, make 1000 ml using distilled water.

Table 1. Materials used in formulations.

S.N.	Ingredients	Manufacturer
1.	Zolmitriptan USP	Aurobindo Pharma
2.	Pharmaburst	SPI Pharma
3.	Pearlitol Flash	RoquettePharma
4.	PanExcea ODT	Avantor Performance Materials
5.	Peppermint Flavour 501500 TP0504	FirmenichPharma
6.	Citric Acid Anhydrous, USP	Avantor Performance Materials

Standard Curve Preparation for Zolmitriptan

A 100 ml volumetric flask was filled to capacity with buffer after 100 mg of Zolmitriptan, precisely weighed, was dissolved in a little amount of pH 6.8 phosphate buffer. This is the main solution that is in stock. A precisely measured 10 ml portion was taken out of the main stock solution and put into a 100 ml volumetric flask. After that, buffer was used to raise the volume to 100 ml. A series of 10 aliquots containing 2–10 mcg (2 ml, 4 ml, 6 ml, 8 ml, and 10 ml) were pipetted out of the secondary stock solution using buffer. At 248 nm, the absorbance of the above-set solutions was compared to a

blank of phosphate buffer pH 6.8. Following that, a calibration curve was created, showing concentration on the X-axis and absorbance on the Y-axis.

Preformulation

It is the initial phase of the methodical creation of medication dosage forms. Preformulation testing is the process of examining a medicinal ingredient's physical and chemical properties both on its own and in conjunction with excipients. In order to help formulators develop stable, bioavailable dosage forms that are scalable for mass manufacturing, preformulation testing seeks to supply them with information. Preformulation studies are intended to find those excipients and physicochemical characteristics that might affect the final product's pharmacokinetic and biopharmaceutical qualities as well as its formulation design and manufacturing process.

Preformulation Parameters

Ethyl Cellulose-Zolmitriptan Mixture Preparation Technique for Taste Masking

- The API is precisely weighed before being filtered through #40 mesh.
- The proper ratio of 5:1, 5:2, and 5:3 is used to dissolve ethyl cellulose in isopropyl alcohol, which is precisely weighed shown in Table 2.
- After granulating the ethylcellulose solution, the API is first allowed to air dry before being dried quickly with a fast drier.
- The dried mixture is taste-tested orally to assess its organoleptic character. If the taste is deemed satisfactory, the concentration of ethyl cellulose is increased in relation to the API.

Table 2. Composition of unit dose of Zolmitriptan – ethylcellulose mixture for taste masking formulations

S.N.	• Composition	Ratio (API: Ethyl cellulose: IPA)	Inference form organoleptic evaluation by selected volunteers
1	Zolmitriptan	5 : 1 : 1	Bitterness was not efficiently. asked
	Ethyl cellulose		
	Iso propyl alcohol		
2	Zolmitriptan	5 : 2 : 1	Comparatively low, but bitterness still found.
	Ethyl cellulose		
	Iso propyl alcohol		
3	Zolmitriptan	5 : 3 : 1	Comparatively better taste.
	Ethyl cellulose		
	Iso propyl alcohol		

Method for Tablet Formulation and Compression (for Formulations Fz1, Fz5, Fz6, Fz7, Fz8, and Fz9)

- The formula was followed to the exact weight of each ingredient.
- The blend was geometrically enhanced by adding the API combination while sifting and combining it with the other excipients. Initially, all of the materials were filtered through #40 mesh.
- Transfer the sieved materials into a 5L Double Cone Blender and process at 15 RPM for 5 minutes.
- Empty the combined ingredients and resift through #40 mesh.
- Reload the sifted ingredients into the 5L Double Cone Blender, and mix at 15 RPM for 20 minutes.
- Combine the blended and sifted components in a 5L Double Cone Blender and run it at 15 RPM for 5 minutes.

- Use #60 mesh to strain the sodium stearyl fumarate and colloidal silicon dioxide.
- Use 7.15 mm round flat-faced, bevel-edged plain tooling to compress the combined materials.

Method for Tablet Formulation and Compression (for Formulation FZ2, FZ3, and FZ4)

- The formula was followed to the exact weight of each ingredient.
- To begin with, #40 mesh was used to sift all of the ingredients specified.
- The API mixture was added to the blend in a geometrical manner while sifting by combining with the other excipients.
- Put the sifted components into a 5L High Shear Mixture Granulator, and for three minutes, granulate the mixture at high speed using an impeller and chopper while using pure water.
- Until it reaches the LOD of 2.5%, quickly dry it in the dryer.
- After unloading the dried materials, filter through #40 mesh once more.
- Transfer the sifted ingredients and the excess granular material to the 5L Double Cone Blender. For 20 minutes, blend at 15 RPM.
- Use a #60 mesh screen to strain sodium stearyl fumarate and colloidal silicon dioxide, if applicable.
- For 5 minutes at 15 RPM, combine the blended materials and sifting components in a 5L Double Cone Blender.
- Compress the combined materials using 7.15 mm Round Flat Faced Bevel Edged Plain Tooling.

Formulation and their Composition

Table 3 below shows the unit concentration of the substances utilized in the various batches that were planned and carried out.

Table 3. Composition of unit dose of various formulations characteristics of final blend

S. No	Ingredients	Fz1 (mg)	Fz2 (mg)	Fz3 (mg)	Fz4 (mg)	Fz5 (mg)	Fz6 (mg)	Fz7 (mg)	Fz8 (mg)	Fz9 (mg)
Intragranular Portion										
1	Zolmitriptan	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00
2	Ethyl cellulose	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00
3	Iso propyl alcohol	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
4	Mannitol	109.00	109.0	104.0	99.00	-	-	-	-	-
5	Purified Water	-	10.00	10.00	10.00	-	-	-	-	-
6	Pearlitol Flash	-	-	-	-	109.0	-	-	-	-
7	Pharma Burst	-	-	-	-	-	109.0	-	-	-
8	Pan Excea ODT	-	-	-	-	-	-	109.0	107.7	106.5
9	Orange flavour	1.25	1.25	1.25	1.25	-	-	-	-	-
10	Peppermint Flavour	-	-	-	-	1.25	1.25	1.25	1.25	1.25
11	Citric Acid Anhydrous, USP	4.00	4.00	4.00	4.00	4.00	4.00	4.00	4.00	4.00
12	Sucralose	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00
Extragranular portion										
13	Polyplasdo neXL 10	-	-	5.00	10.00	-	-	-	-	-
14	Colloidal Silicon Dioxide (Aerosil 200)	-	-	-	-	1.25	.25	1.25	2.50	.50
15	Sodium Stearyl Fumarate (Pruv)	1.25	1.25	1.25	1.25	1.25	1.25	1.25	.25	2.50

16	Total	125.00	125.00	125.00	125.00	125.00	125.00	125.00	125.00	125.00

RESULTS AND DISCUSSION

Zolmitriptan Characteristics

Bulk density	:	0.34 g / mL
Tapped density	:	0.42 g / mL
Compressibility index	:	19.05
Hausner ratio	:	1.24
Loss on Drying (105°C / Automode)	:	3.18%
PSD by Malvern master Sizer		
d10	:	6 microns
d50	:	11 microns
d90	:	16 microns
Drug Manufacturer	:	Aurobindo Pharma, Hyderabad.
Batch No	:	ZIP1004110

Calibration Curve Data for Zolmitriptan

Zolmitriptan calibration curve data in 0.1N HCL and FTIR spectra are displayed in Table 4 and Figure 1 below:

Table 4. Calibration curve data for Zolmitriptan in 0.1N HCL.

Concentration(µg/ml)	Absorbance
1	0.130±0.003
2	0.264±0.001
3	0.385±0.002
4	0.495±0.001
5	0.640±0.002
6	0.758±0.004
7	0.877±0.001
8	0.979±0.003

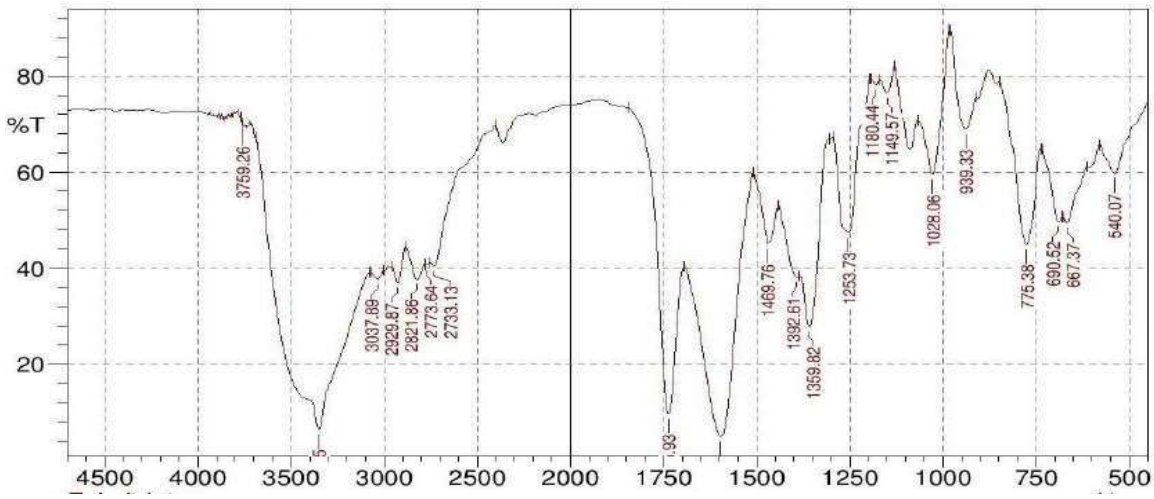

Figure 1. FTIR spectra of the zolmitriptan.

FTIR Spectra for Zolmitriptan

Compatibility studies of the improved formulation between the drug and excipient

The graphic displayed each of the Zolmitriptan optimised formulation's distinct IR spectra. The IR Spectral analysis revealed the principal peaks listed in Table 5.

In the infrared spectra of the rug and the optimised formulation (FZ9), the observed principle peaks were the same. Therefore, there was no contact between the medicine and the excipient in this study, either chemically or physically.

Table 5. The principle peaks were observed from IR spectra of Zolmitriptan.

S.N.	Wave Number in cm^{-1}	Characteristic bands
1.	3551.32	O – H stretching
2.	3402.32	N – H stretching
3.	2931.47	C – H stretching
4.	1622.30	C = C stretching
5.	1455.80	C – H Bending
6.	1142.94	C – O stretching Ether
7.	1018.19	C – O stretching
8.	873.33, 766.75, 669.19,	C – H (OOP) For Aromatic rings
9.	465.97, 450.74, 444.88,	C – X stretching

IR spectra of bands

Bulk density, tapped density, angle of repose, and loss on drying were among the metrics used to characterize the final blend for each batch. The results are compiled and displayed in Table 6.

Table 6. Result for bulk density, tapped density, angle of repose and loss on drying.

S.	Parameters	FZ1	FZ2	ZF3	FZ4	FZ5	FZ6	FZ7	FZ8	FZ9
1	Bulk Density(gm/mL)	0.33	0.35	0.36	0.34	0.38	0.38	0.41	0.39	0.41
2	Tapped Density (gm/mL)	0.38	0.39	0.4	0.38	0.48	0.48	0.51	0.49	0.50
3	Angle of Repose (°C)	33	31	31	32	31	31	29	29	28
4	Loss on Drying (%)	2.93	3.19	3.18	3.14	2.04	2.04	3.12	2.98	2.86

Particle Size Distribution

Table 7 displays the findings of the particle size distribution analysis that was done on the final blend of the trial batches.

Table 7. Particle size distribution results for the final blend.

S.N.	Sieve size#	FZ 1	FZ2	ZF3	FZ4	FZ5	FZ6	FZ7	FZ8	FZ9
1	20	0	0	0	0	0	0	0	0	0
2	40	0	2	1	1	1	0	0	0	0
3	60	5	10	11	12.1	12	7.5	15	15	11.1
4	80	30	5	6	7.2	5.5	5	5	20	13.9
5	100	10	5	7.5	9.4	9	17.5	5	17.5	19.4
6	140	10	43	46	43.8	42	5	20	20	27.8
7	200	7.5	20	17.5	15.4	17.6	17.5	20	17.5	16.7
8	Pan	27.5	15	11	11.1	12.9	37.5	35	10	11.1

Blend Uniformity

Percentage content of samples from final blend of trial batches were analyzed and the results are tabulated shown in Table 8.

Table 8. Results of Blend uniformity samples of final blend.

S. No	Fz1	Fz2	Fz3	Fz4	Fz5	Fz6	Fz7	z8	Fz9
1	95.7	96.7	94.6	96.6	96.8	98.7	96.7	97.6	98.9
2	96.9	96.8	95.7	96.8	99.7	98.3	100.6	98.7	99.5
3	96.9	97.1	95.9	97.2	99.5	98.8	96.7	97.4	99.9
4	97.1	97.8	96.8	97.5	94.7	99.1	99.8	99.6	99.6
5	97.3	97.9	97.2	97.9	98.1	99.8	99.6	98.9	99.8
6	97.5	98.3	97.6	98.1	97.4	98.9	99.3	99.6	99.1
7	97.9	98.5	97.9	98.5	98.9	99.1	98.1	100.2	98.1
8	98.3	98.7	98.5	98.7	99.7	99.3	100.9	100.1	99.6
9	98.5	99.1	98.9	99.2	100.2	99.5	97.9	100	100.8
10	98.6	99.2	98.9	99.8	97.1	99.6	98.7	99.1	101.2
AVG	97.47	98.01	97.2	98.03	98.21	99.11	98.83	99.12	99.65
Min	95.7	96.7	94.6	96.6	94.7	98.3	96.7	97.4	98.1
Max	98.6	99.2	98.9	99.8	100.2	99.8	100.9	100.2	101.2
%RSD	0.92	0.93	1.49	1.06	1.76	0.46	1.50	1.00	0.89

Tablet Characterization

Weight Variation

Weight variation of all the batches were evaluated and the results are tabulated shown in Table 9.

Table 9. Results for weight variation of the formulation.

S.N.	FZ1 (gm)	FZ2 (gm)	FZ3 (gm)	FZ4 (gm)	FZ5 (gm)	FZ6 (gm)	FZ7 (gm)	FZ8 (gm)	FZ9 (gm)
1	117.5	121.2	122.3	120.3	121.2	122.6	120.4	20.4	126.0
2	119.6	120.6	123.0	125.6	123.1	122.4	123.8	126.3	123.1
3	125.6	122.9	121.6	124.5	123.9	122.4	123.9	121.0	124.8
4	117.6	126.5	122.3	124.8	121.9	123.6	125.9	123.1	123.9
5	126.6	125.2	125.6	123.6	124.6	123.1	120.9	124.9	125.1
6	121.5	124.3	124.3	124.2	122.8	125.2	120.1	124.3	121.4
7	116.5	121.6	125.3	125.1	123.4	123.7	125.8	126.1	126.0
8	124.3	124.2	122.8	122.6	124.1	124.9	126.0	125.9	125.8
9	121.8	120.6	121.5	123.2	123.7	125.1	126.3	123.1	121.9
10	117.9	121.5	122.9	123.8	122.8	125.0	120.4	124.5	126.1
Avg	120.9	122.9	123.2	123.8	123.2	123.8	123.4	124.0	124.4
Min	116.5	120.6	121.5	120.3	121.2	122.4	120.1	120.4	121.4
Max	126.6	126.5	125.6	125.6	124.6	125.2	126.3	126.3	126.1

Thickness

Thickness of ten tablets were evaluated from each batch and tabulated in the Table 10.

Table 10. Thickness of tablets of the formulations.

S.N.	FZ1 (mm)	FZ2 (mm)	FZ3 (mm)	FZ4 (mm)	FZ5 (mm)	FZ6 (mm)	FZ7 (mm)	FZ8 (mm)	FZ9 (mm)

1	2.62	2.85	2.88	2.91	2.82	2.89	2.93	2.93	2.9
2	2.65	2.86	2.89	2.85	2.82	2.89	2.97	2.93	2.99
3	2.68	2.81	2.87	2.86	2.91	2.86	2.96	2.94	2.91
4	2.65	2.83	2.86	2.87	2.91	2.87	2.97	2.97	2.93
5	2.64	2.85	2.87	2.86	2.91	2.86	2.97	2.94	2.91
6	2.68	2.86	2.88	2.85	2.83	2.87	2.98	2.93	2.93
7	2.69	2.87	2.89	2.84	2.82	2.86	2.93	2.98	2.94
8	2.64	2.85	2.85	2.87	2.83	2.86	2.97	2.96	2.94
9	2.65	2.83	2.87	2.86	2.83	2.95	2.96	2.97	2.94
10	2.63	2.87	2.89	2.89	2.9	2.94	2.95	2.97	2.93
Avg	2.65	2.85	2.88	2.87	2.86	2.89	2.96	2.95	2.93
Min	2.62	2.81	2.85	2.84	2.82	2.86	2.93	2.93	2.90
Max	2.69	2.87	2.89	2.91	2.91	2.95	2.98	2.98	2.99

Hardness

Table 11 displays the results of the evaluation of the hardness of ten tablets from the experimental batches.

Table 11. Hardness of ten tablets and its average for the formulations.

S.N.	FZ1 (kg/cm^2)	FZ2 (kg/cm^2)	ZF3 (kg/cm^2)	FZ4 (kg/cm^2)	FZ5 (kg/cm^2)	FZ6 (kg/cm^2)	FZ7 (kg/cm^2)	FZ8 (kg/cm^2)	FZ9 (kg/cm^2)
1	3.4	3.4	4.3	4.0	3.1	3.6	4.0	4.1	3.5
2	3.6	3.5	4.0	4.8	3.8	3.8	4.0	4.5	3.9
3	3.6	3.6	3.9	4.6	3.7	3.2	3.8	4.4	3.5
4	3.8	3.5	3.8	4.7	3.6	3.8	3.6	4.6	3.6
5	3.5	4.3	3.7	4.1	3.9	4.1	3.9	4.1	3.8
6	4.3	3.7	4.4	4.2	4.1	3.9	4.1	4.3	4.5
7	3.9	3.8	4.7	4.1	4	4.3	4.8	4.5	4.6
8	3.5	4.1	4.6	3.6	4.7	4.6	4.3	3.9	4.4
9	4.1	4.2	4.8	3.9	4.5	4.5	4.9	3.8	4.1
10	4.1	4.2	3.6	3.6	4.2	4.1	3.9	3.9	4.0
Avg	3.8	3.8	4.2	4.2	4.0	4.0	4.1	4.2	4.0
Min	3.4	3.4	3.6	3.6	3.1	3.2	3.6	3.8	3.5
Max	4.3	4.3	4.8	4.8	4.7	4.6	4.9	4.6	4.6

Content Uniformity

Each batch's ten tablets were examined for content homogeneity; the findings are displayed in Table 12 as a percentage.

Table 12. Results of percentage content and %RSD of tablets of formulations.

S.N.	FZ1	FZ2	ZF3	FZ4	FZ5	FZ6	FZ7	FZ8	FZ9
1	98.7	99.9	98.6	99.9	99.7	96.7	98.9	99.6	98.9
2	102.3	96.6	98.2	101.1	96.5	100.3	98.6	98.4	100.1
3	103.1	98.7	99.1	98.6	96.9	98.1	98.7	99.8	99.6
4	99.2	97.8	98.3	97.7	97.9	99.2	97.2	96.4	99.8
5	99.6	99.9	100.6	98.2	99.1	96.5	99.1	100.1	98.6
6	104.3	99.5	97.3	98.6	99.3	99.8	99.7	99.8	98.9

7	100.3	99.1	99.6	100.8	95.8	100	99	99.1	100.1
8	95.6	99.6	98.3	98.9	99.1	99.9	99.2	99.6	99.9
9	96.6	99.9	97.9	102.3	99.5	100.8	99.7	100	100.3
10	100.9	99.3	99.6	99.2	99.7	100.3	99.5	98.9	99.7
AVG	100.06	99.03	98.75	99.53	98.35	99.16	98.96	99.17	99.59
Min	95.6	96.6	97.3	97.7	95.8	96.5	97.2	96.4	98.6
Max	104.3	99.9	100.6	102.3	99.7	100.8	99.7	100.1	100.3
%RSD	2.74	1.09	0.99	1.47	1.49	1.55	0.74	1.12	0.59

Friability

Tablets from each batch are weighed at the beginning, end, and % of weight reduction to determine if they pass the friability test. Additionally, Table 13 displays the data in tabular form.

Table 13. Friability and its parameters for all the formulations.

Paramet ers	**FZ1**	**FZ2**	**ZF3**	**FZ4**	**FZ5**	**FZ6**	**FZ7**	**FZ8**	**FZ9**
Initial Weight (gm)	6.7504	6.8002	6.7652	6.7786	6.8412	6.7351	6.7638	6.9967	6.8011
Final Weight (gm)	6.6918	6.7804	6.7700	6.7604	6.824	6.7102	6.7449	6.9716	6.7801
Percenta ge Weight loss (%)	0.87	0.29	-0.07	0.27	0.25	0.37	0.28	0.36	0.31

Disintegration Time

Minimum and maximum time taken by the six tablets from each batch was noted and tabulated in the Table 14.

Table 14. Disintegration time of each formulation.

Parameters	**FZ1**	**FZ2**	**ZF3**	**FZ4**	**FZ5**	**FZ6**	**FZ7**	**FZ8**	**FZ9**
Minimum Time (min)	0’22	6'00	3'28"	1'45"	0’15	0’18	0’12	0’10	0’11
Maximum Time (min)	0’29	7'38"	4'45"	2'25"	0’21	0’24	0’16	0’15	0’16

Assay & Water by Kf

Results of assay and moisture content evaluated by karlfischer reagent was tabulated in Table 15.

Table 15. Assay and water by kf results of the formulations.

Parameters	**FZ1**	**FZ2**	**ZF3**	**FZ4**	**FZ5**	**FZ6**	**FZ7**	**FZ8**	**FZ9**
Assay(%)	104.2	102.3	101.2	99.6	96.7	101.0	98.7	97.9	99.2
Water by Kf (%)	5.25	5.15	5.12	5.16	4.22	4.01	4.97	4.96	4.82

Related Substance

The analytical method for related substance was performed and the highest unknown impurity and total impurity values of the respective batches were tabulated shown in Table 16.

Table 16. Highest unknown impurity and total impurities results of the respective formulations.

Parameters	**FZ1**	**FZ2**	**ZF3**	**FZ4**	**FZ5**	**FZ6**	**FZ7**	**FZ8**	**FZ9**
Highest Unknown Impurity (%)	0.09	0.77	0.33	0.11	0.23	0.39	0.03	0.02	0.03
Total Impurities (%)	2.29	2.95	3.00	3.01	3.20	3.19	0.07	0.08	0.06

DISSOLUTION

After 15 minutes of dissolving, the % release of the medication was measured, and the results for each batch were tabulated and displayed in Table 17.

Table 17. Results of dissolution data of the formulations.

Formulations	5 min	10 min	15 min
FZ1	94.3±0.16	98.9±0.78	100.2±0.06
FZ2	66.8±0.48	85.9±0.95	94.8±0.07
FZ3	78.8±0.34	88.3±0.66	96.8±0.09
FZ4	88.0±0.38	94.2±0.57	98.8±0.04
FZ5	93.2±0.62	99.5±0.12	100.2±0.08
FZ6	86.5±0.41	96.4±0.18	99.7±0.02
FZ7	92.7±0.06	99.8±0.06	100.1±0.01
FZ8	94.8±0.09	100.1±0.12	99.8±0.04
FZ9	95.8±0.09	99.9±0.02	100.3±0.02

And the graphical representation of the batches is shown in Figure 2.

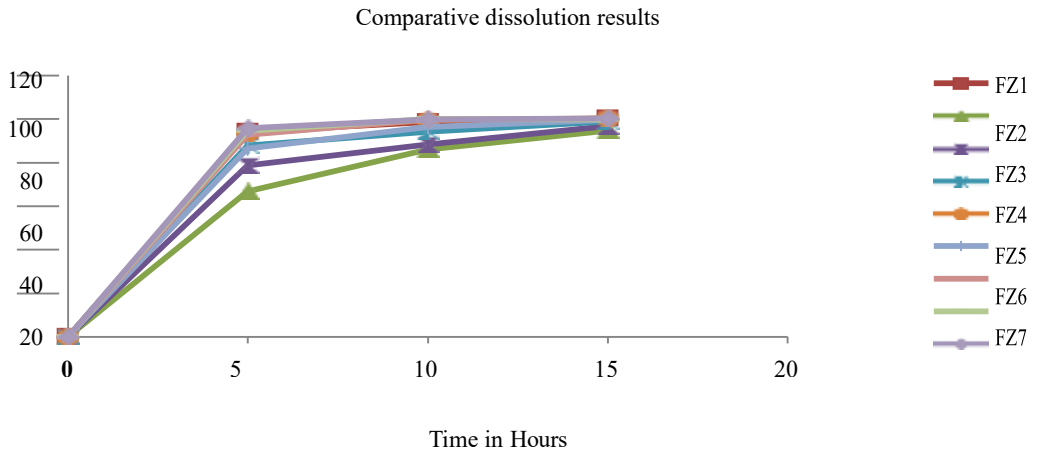

Figure 2. Graphical representation of Percentage dissolution of the formulations.

Organoleptic Evaluation

The organoleptic evaluation of the tablets was carried out and the observations of the respective batches were tabulated shown in Table 18.

Table 18. Organoleptic evaluation and its observation.

Formulations	Organoleptic evaluation
FZ1	Average
FZ2	Average
FZ3	Average
FZ4	Average
FZ5	Average
FZ6	Average
FZ7	Good
FZ8	Good
FZ9	Good

Accelerated Stability Studies

When the dunnage is packed in a 75cc Heavy Weight HDPE bottle with a 33mm child-resistant closure and an induction seal liner, 30 tablets containing one 1 mg molecular sieve canister and one 1g oxygen absorber canister were used as desiccants. A placebo was also loaded for analytical purposes in each condition.

Condition : 40°C/75% RH- 1st Month
Description : White to off white colored plain flat bevel edged tablets Water by Kf (%) :5.16
Assay (%) : 99.7

DISSOLUTION

Figure 3 displays the graphical representation of the dissolution profile. The percentage drug release of the stability sample (40°C/75% RH- 1st Month) was assessed, and the results were summarized in Table 19.

Table 19. Percentage drug release of Stability sample (40°C/75% RH- 1st Month)

S.N.	Time(Min)	Percentage Drug Release
1	5	96.1±0.09
2	10	99.8±0.04
3	15	100.1±0.02

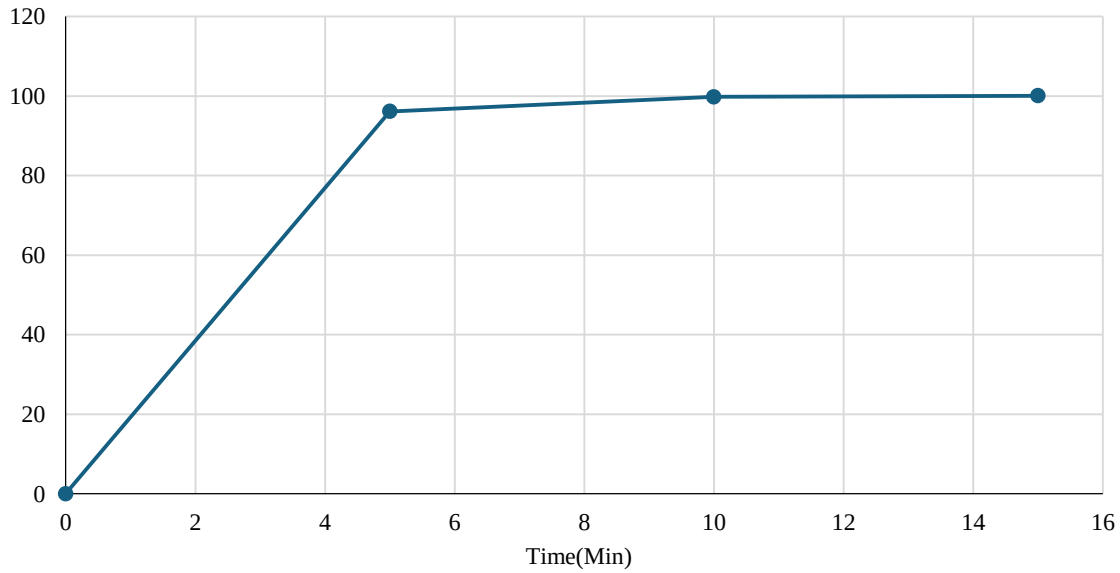

Figure 3. Percentage drug release of Stability sample (40°C/75% RH-1st Month)

Condition : 40°C/75% RH- 3rd Month
Description : White to off white colored plain flat bevel edged tablets Water by Kf(%) : 5.46
Assay (%) : 99.6

DISSOLUTION

Percentage drug release of the Stability sample (40°C/75% RH- 3rd Month) was evaluated and the results are tabulated in Table 20.

Table 20. Percentage drug release of Stability sample (40°C/75% RH- 3rd Month)

S.N.	Time (Min)	%Drug Release
1	5	97.4±0.07
2	10	99.8±0.05

3	15	100.3±0.02

And the graphical representation of the dissolution profile is shown Figure 4.

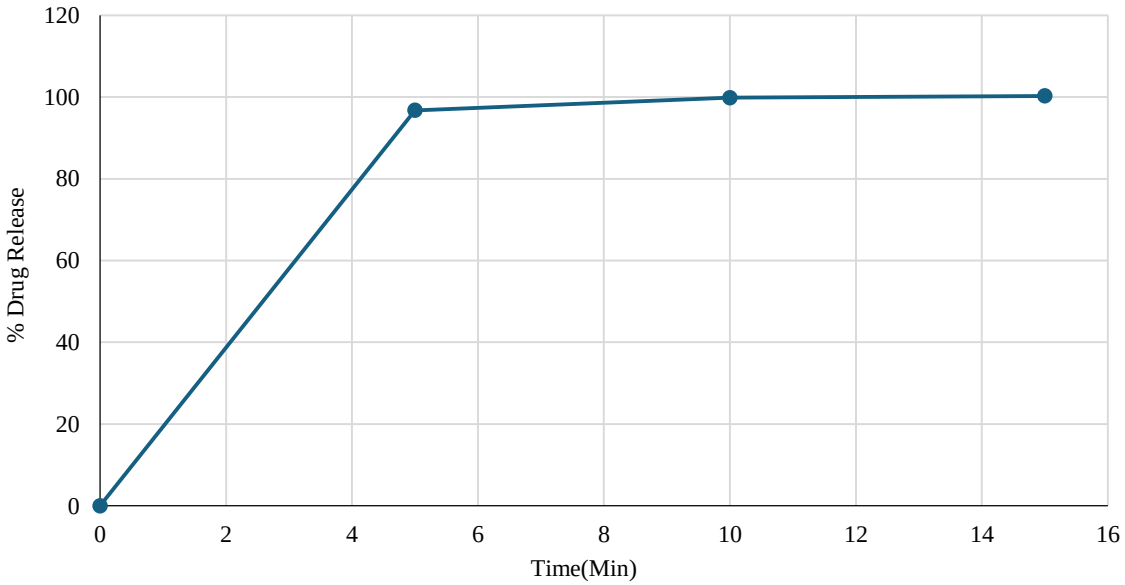

Figure 4. Percentage drug release of Stability sample (40°C/75% RH-3rd Month).

Condition: 40°C/75% RH- 6th Month
Description : White to off white colored plain flat bevel edged tablets
Water by Kf(%) : 5.61
Assay (%) : 99.8

DISSOLUTION

Percentage drug release of the Stability sample (40°C/75% RH- 6th Month) was evaluated and the results are tabulated in Table 21.

Table 21. Percentage drug release of Stability sample (40°C/75% RH- 6th Month).

S.N.	Time(Min)	%Drug Release
1	5	95.2±0.05
2	10	98.7±0.03
3	15	99.8±0.02

And the graphical representation of the dissolution profile is shown Figure 5.

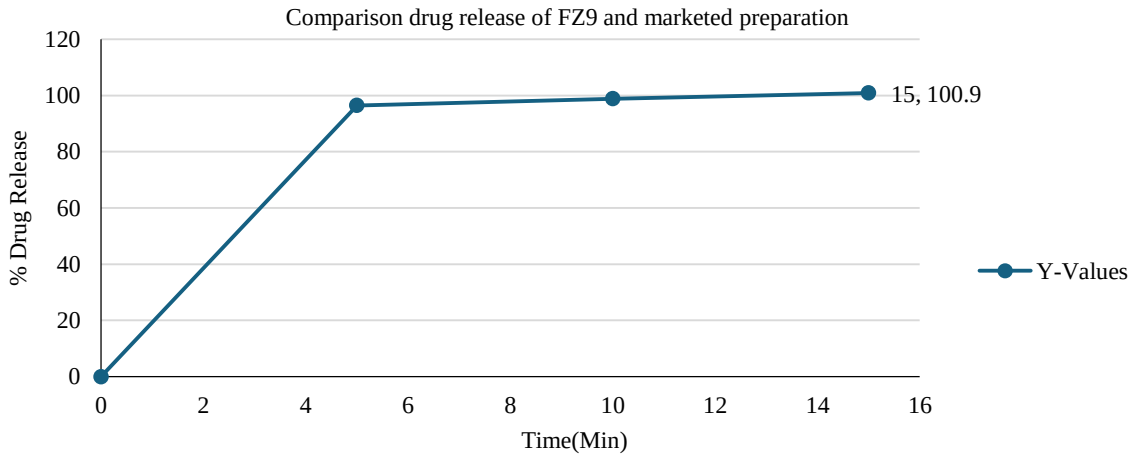

Figure 5. Percentage drug release of Stability sample (40°C/75% RH- 6th Month).

Table 22 displays the comparison drug release of the marketed preparation and the optimized formulation, while Figure 6 provides a graphic representation of this comparison.

Table 22. Comparison drug release of FZ9 and marketed preparation.

Formulations	5 min	10 min	15 min
FZ9	95.8±0.06	99.9±0.02	100.3±0.02
Marketed product	94.5±0.09	100.1±0.12	99.8±0.04

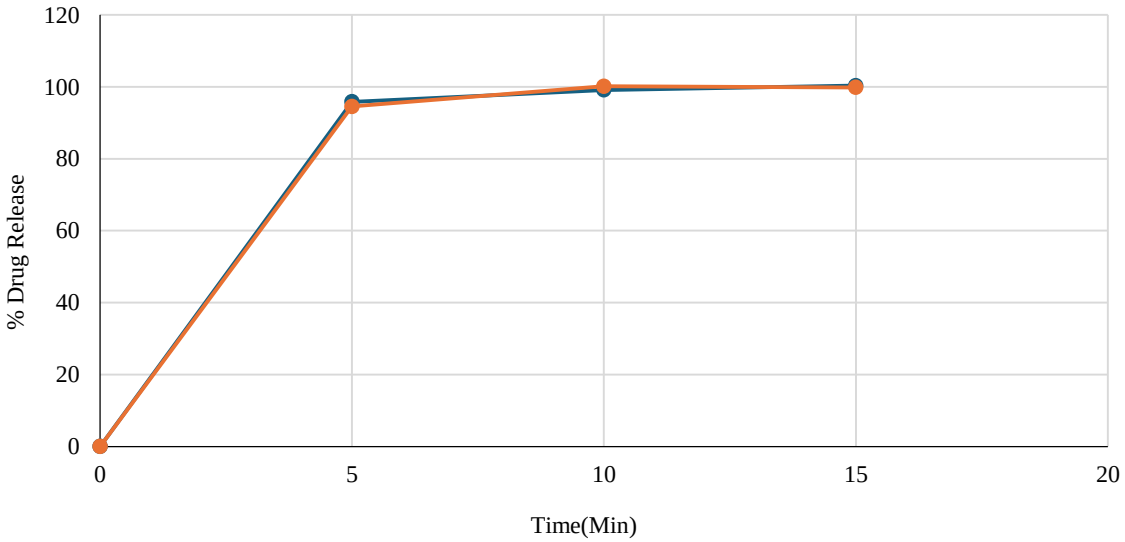

Figure 6. Comparison drug release of FZ9 and marketed preparation

Table 23. Regression values of in-vitro release kinetic study optimized Zolmitriptan immediate release Tablet (FZ9)

Regression values(R^2)	FZ9
Zero order release kinetics	0.993
First order release kinetics	0.922
Hixon-crowell cubic root kinetics	0.954
Higuchi release kinetics	0.717
Korse meyer peppas kinetics	0.991

The formulation with the highest f2 and lowest f1 values, known as FZ9, or drug release kinetic and

mechanism of release studies, was chosen. Numerous kinetic models, such as zero order, first order, Higuchi, Hixson-Crowell, and Korse Meyer-Peppas equations, were used to suit the Zolmitriptan rapid release tablet (FZ9) in vitro dissolving data. The resulting graphs were presented. As seen by their maximum regression values (0.991) for the FZ9 formulation, the Korse Mayer Peppa's kinetic graphs were determined to be reasonably linear . The optimised formulation FZ9's release exponent, 'n,' was found to be 0.991 ($0.5 < n < 1$), suggesting a possible link between the erosion mechanism and diffusion, sometimes known as anomalous diffusion. According to Peppas' release kinetic model, the in vitro drug release kinetics of Zolmitriptan instant release tablets in this investigation were anomalous diffusion combined with erosion. Table 23 displayed all of the release kinetics regression data.

DISCUSSION

The Zolmitriptan quick dissolving tablets were made by the direct compression process. Pharmaburst ODT superdisintegrants were used in different concentrations for this purpose.

With a 28° angle of repose, there is good flow.

The densities for bulk and tapped materials are 0.410 (g/ml) and 0.500 (g/ml), respectively. The compressibility index and Hausner ratio have values of 19.05 and 1.24, correspondingly. Table 15 displays the findings for pre-compressed parameters.

According to IP standard, weight variation test results range from 121.4 mg to 126.1 mg. Friability: Less than 0.31%, according to the data, means that the percentage losses did not exceed 1.0% (complies with IP requirements). The thickness of the tablets ranges from 2.90 mm to 2.99 mm. Based on the results; it can be packed.

There was a range of 98.62% to 100.3% content homogeneity. It was discovered that the tablet's hardness ranged from 4 to 4.6 kg/cm2. The outcomes show that the tablets are within limit and have a solid mechanical structure.

The disintegration time of the pills was found to be within a 30-second range, ranging from 0'11 to 0'16 seconds.

Results of a dissolve study for formulations FZ1, FZ2, FZ3, ZF4, FZ5, ZF6, FZ7, FZ8, and FZ9 in a pH phosphate buffer of 6.8 showed that the optimized batch's percentage test was 99.2%.

For formulations FZ9 and commercial product, a comparative dissolving analysis was conducted in phosphate buffer with a pH of 6.8. State of storage: Tablets were kept at 45°C ± 2°C/75% for 0, 30, 60, and 90 days. Over this time, the tablets' hardness increased, but it was always within the allowed range. Disintegration time: varies depending on storage circumstances, but never exceeds 20 seconds, or less than 30 seconds (IP standard). Dissolution experiments reveal that the formulations' dissolving data did not significantly alter at the beginning or after the designated storage term.

CONCLUSION

For formulations FZ9 and commercial product, a comparative dissolving analysis was conducted in phosphate buffer with a pH of 6.8.

State of storage: Tablets were kept at 45°C ± 2°C/75% for 0, 30, 60, and 90 days. Over this time, the tablets' hardness increased, but it was always within the allowed range. Disintegration time: varies depending on storage circumstances, but never exceeds 20 seconds, or less than 30 seconds (IP standard). Dissolution experiments reveal that the formulations' dissolving data did not significantly alter at the beginning or after the designated storage term.

REFERENCES

1. Aurora J, Pathak V. Oral disintegrating technologies: Oral disintegrating dosage forms: An overview. Drug Deliv Technol. 2005;5(3):50–4.
2. Bandari S, Mittapalli RK, Gannu R. Orodispersible tablets: An overview. Asian Journal of Pharmaceutics (AJP). 2008;2(1).
3. Panigrahi D, Baghel S, Mishra B. Mouth dissolving tablets: An overview of preparation techniques, evaluation and patented technologies. J Pharm Res. 2005 Jul;4(3):35–8.
4. Platteeuw J, van den Heuvel DJ, inventors; Synthon BV, assignee. Orally disintegrating tablets. United States patent application US 10/824,619. 2004 Dec 30.
5. Ghosh TK, Pfister WR. Drug delivery to the oral cavity: molecules to market. CRC Press; 2005 Feb 28.
6. Manager GS. Statistical experimental design and its application to pharmaceutical development problems. Drug Development and Industrial Pharmacy. 1986 Jan 1;12(8–9):1109–23.
7. Gohel M, Patel M, Amin A, Agrawal R, Dave R, Bariya N. Formulation design and optimization of mouth dissolve tablets of nimesulide using vacuum drying technique. AAPs PharmSciTech. 2004 Sep;5:10–5.
8. Omaima A. Sammour, Formulation and Optimization of Mouth Dissolve Tablets Containing Rofecoxib Solid Dispersion. AAPS PharmSciTech 2006; 7 (2) Article 55 .
9. Zaghloul AA, Vaithiyalingam SR, Faltinek J, Reddy IK, Khan MA. Response surface methodology to obtain naproxen controlled release tablets from its microspheres with Eudragit L100–55. Journal of microencapsulation. 2001 Jan 1;18(5):651–62.
10. Martin GR. Pre-clinical pharmacology of zolmitriptan (Zomig™; formerly 311C90), a centrally and peripherally acting 5HT1B/1D agonist for migraine. Cephalalgia. 1997 Oct;17(18_suppl):4–14.
11. Rubio-Beltrán E, Labastida-Ramírez A, Villalón CM, MaassenVanDenBrink A. Is selective 5–HT1F receptor agonism an entity apart from that of the triptans in antimigraine therapy?. Pharmacology & therapeutics. 2018 Jun 1;186:88–97.
12. Goadsby PJ, Holland PR, Martins-Oliveira M, Hoffmann J, Schankin C, Akerman S. Pathophysiology of migraine: a disorder of sensory processing. Physiological reviews. 2017 Feb 8.
13. Becker WJ. Acute migraine treatment in adults. Headache: The Journal of Head and Face Pain. 2015 Jun;55(6):778–93.
14. Feniuk W, Humphrey PP, Perren MJ, Connor HE, Whalley ET. Rationale for the use of 5-HT 1-like agonists in the treatment of migraine. Journal of neurology. 1991 Feb;238:S57-61.

