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Research Article

Formulation and *in vitro* Evaluation of Frovatriptan Succinate Oral Disintegrating Tablets by Direct Compression Technique

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Abstract

The aim of present study was to formulate Frovatriptan Succinate (FS) as Orally disintegrating tablets (ODT) using various concentrations of super disintegrents like, Sodium Starch Glycolate (SSG), croscarmellose sodium (CCS), crospovidone (CPV) by direct compression. To enhance its bioavailability and to fasten its onset of action in comparison to its conventional tablets. Standard calibration curve of FS was obtained in pH 6.8 phosphate buffer by spetrophotometric method, drug-excipient compatibility studies were carried by isothermal stress studies and confirmed by FT-IR studies. All the Formulations were evaluated for pre-compression, post-compression studies. Accelerated stability studies up to 6 months were conducted for the optimized formulation (F9). The drug-excipient compatibility studies reveals that all the excipients used are compatible with FS. Pre & post compression parameters were within the acceptable limits for all formulations. An *in vitro* dissolution kinetic study indicates the release rate of FS from ODT increases as the concentration of super disintegrents increases. Among all super disintegrents formulations with CPV are having faster release profiles and the order of super disintegrants to enhance dissolution rate in the formulations of FS ODT is CPV > CCS > SSG. Formulation F9 (8% w/w CPV) released 100 % of drug with in 6 min was considered as the optimal ODT among all the nine formulations tested in this study. Optimized formulation (F9) passed the test for stability in its in final pack. Hence, an effective FS ODT dosage form for treating acute migraine attack was formulated by direct compression technique.

Keywords: Frovatriptan Succinate (FS), Orally disintegrating tablets (ODT), Sodium Starch Glycolate (SSG), croscarmellose sodium (CCS), crospovidone (CPV), direct compression, *In vitro* dissolution study

Introduction

The most preferred route for administration of dosage forms is oral route, due to its potential advantages like ease of administration, convenient dosing, self-medication, no pain and patient compliance. Hence tablets and capsules are the most popular dosage forms [1]. But important drawback of these dosage forms is dysphasia [2]. The above-mentioned problem can be solved by developing a fast disintegrating/dissolving drug delivery, i.e. oral disintegrating / dissolving tablet, disintegrates and dissolves rapidly in the saliva, within a few sec without the need of drinking water or chewing [3]. In pharmaceutical sciences, disintegration usually means the process by which a solid dosage form breaks up when it comes in contact with aqueous medium absorption and thus promotes rapid release of drug for faster absorption [4]. A rapid disintegration process is the prerequisite for a good bioavailability [5]. Orally disintegrating tablets (ODT) provides ease of administration, immediate action, convenient dosing, self-medication, no pain and increases patient compliance [6]. Frovatriptan succinate (FS), a selective 5-hydroxytryptamine$_{1B/1D}$ (5-HT$_{1B/1D}$) receptor subtype agonist. FS is indicated for the acute treatment of migraine attacks with or without aura in adults. FS is incompletely absorbed in the GI tract and undergoes extensive hepatic metabolisin due to cytochrome P450 1A2. The absolute bioavailability of an oral dose of frovatriptan 2.5 mg in healthy subjects is about 20% in males and 30% in female [7]. Clinically, orotransmucosal drug delivery is reported to be the most promising alternative approach for enhancing the bioavailability and fastening the onset of action in comparison to its conventional tablets because it has high blood supply, a very thin membranous barrier (190 μm), and an ability to bypass hepatic first pass metabolism [8]. Therefore, ODT could be a promising dosage form for the administration of FS for treating acute migraine attack.

Materials and methods

Materials

Frovatriptan Succinate (FS) is a gift sample received from Natco Pharma Ltd, Hyderabad, India.

Sodium Starch Glycolate, croscarmellose sodium (Ac-Di-Sol), crospovidone (Polyplasdone XL-10), dicalcium phosphate, aspartame, magnesium Stearate, talc and colloidal silicon dioxide (AEROSIL) are received as gift samples from Glochem pharma Ltd, Hyderabad India. All the excipients used in study are of pharmaceutical grade.

Methods

Standard calibration curve of FS in pH 6.8 phosphate buffer [9]

It was obtained at the λmax 291 nm using a UV-Visible spectrophotometer (UV-1700, Shimadzu, Mumbai, India) and represented in Figure 1, which was further used for drug release calculations of *in vitro* dissolution studies and assay.

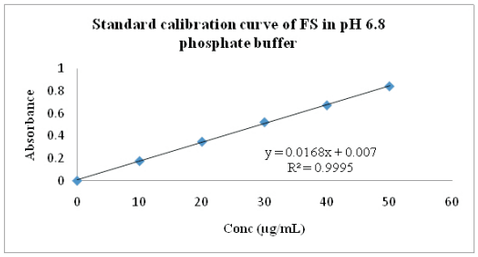

Figure 1: Standard calibration curve of FS in pH 6.8 phosphate buffer

Drug-excipient compatibility / isothermal stress studies [10]

These were performed in order to evaluate the integrity and compatibility of the drug with various excipients used in the formulation. The physical mixtures of drug and excipients (1:1 ratio), were sealed in 4 mL glass vial using a teflon-lined screw cap and

stored at 50°C (Hot air oven, Universal, Narang Scientific, India). These samples are monitored on weekly basis, for a period of 3 weeks and examined for any unusual color change. Drug–excipient blends stored in refrigerator served as controls. The drug-excipient with unusual color change indicates incompatibility and vice versa.

Preparation of FS ODT [11]

All the formulations were prepared by direct compression method, by keeping the amount of FS constant as 3.91 mg, equivalent to 2.5 mg of frovatriptan base per tablet. The composition of other excipients are varied as mentioned in Table 1.

Table 1: Formulation table of FS ODT

Ingredients*	F1	F2	F3	F4	F5	F6	F7	F8	F9
Frovatriptan Succinate	3.91	3.91	3.91	3.91	3.91	3.91	3.91	3.91	3.91
Sodium Starch Glycolate	4	-	-	6	-	-	8	-	-
Croscarmellose sodium	-	4	-	-	6	-	-	8	-
Crospovidone	-	-	4	-	-	6	-	-	8
Aspartame	1	1	1	1	1	1	1	1	1
Powder vanilla flavor	1	1	1	1	1	1	1	1	1
Collidal silicon dioxide	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium striate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Di calcium phosphate	86.59	86.59	86.59	84.59	84.59	84.59	82.59	82.59	82.59
Total (mg)	100	100	100	100	100	100	100	100	100

*Quantities of ingredients per each tablet were expressed in mg, Avg. wt. of a tablet is100 mg.

In the formulations, Sodium Starch Glycolate (SSG), croscarmellose sodium (CCS), crospovidone (CPV) are used as superdisentigrents, di calcium phosphate (DCP) is a directly compressible diluent, aspartame is an artificial sweetener, powder vanilla flavor as flavoring agent, magnesium stearate is a lubricant, talc and colloidal silicon dioxide (AEROSIL) are glidants. FS and all the other excipients excluding magnesium stearate and talc were co- sifted though Sieve No. # 40 (ASTM), blended uniformly in a poly bag for 10 min and lubricated with Sieve No. # 60 (ASTM) passed magnesium stearate and talc and mixed in a poly bag for additional 2–3 min. Tablets were compressed on a tabletting machine (16 station, Cad mach Pharma Machinery Pvt. Ltd., India) fitted with a 8 mm standard round punches with an average wt. of 100 mg and hardness of 3-4 kg/cm^2.

Precompression studies [12]

The directly compressible tablet blends were evaluated for precompression studies.

Angle of Repose (θ)

It was determined by funnel method, the blend was poured through the walls of a funnel, which was fixed at a position such that its lower tip was at a height of exactly 2 cm above hard surface. The blend was poured till the time when upper tip of the pile surface touched the lower tip of the funnel.

The θ is calculated by the equation.

$$\theta = \tan^{-1} h/r \qquad \text{Eq.No. (1)}$$

Where, θ = angle of repose, h = height of heap, r = radius of base of heap circle.

Density

Bulk density (BD)

A quantity of 2 g of blend from each formulation, previously lightly shaken to break any agglomerates formed, was introduced into a 10 mL measuring cylinder and the volume is noted as bulk volume. The BD was calculated by the equation.

Bulk density = weight of powder/ Bulk volume Eq.No. (2)

Tapped density (TD)

After the determination of BD, the measuring cylinder was fitted to a tapped density apparatus. The tapped volume was measured by tapping the powder for 500 times. Then the tapping was done for 750 times and the tapped volume was noted (the difference between these two volumes should be less than 2%). If it is more than 2%, tapping is continued for 1250 times and was noted. The TD was calculated by the equation.

Tapped density = Weigh of powder / Tapped volume Eq.No. (3)

Carr's Index (CI)

The percentage of CI is calculated by the equation.

Carr's index = (Tapped density-Bulk density)×100 / Tapped density Eq.No.(4)

Hausner's Ratio (HR)

It is a number that is correlated to the flow ability of a powder. It is calculated by the equation.

Hausner's Ratio = Tapped density /Bulk density Eq.No.(5)

Precompression studies of all the formulations were carried out in triplicate; the consolidated results (mean ±SD) were tabulated in Table 2.

Table 2: Precompression studies of FS ODT

F Code	Angle of repose (°)	Bulk density(gm/cm^3)	Tapped density (gm/cm^3)	Hausner's ratio	Carr's index (%)
F1	28.17 ± 0.202	0.543 ± 0.005	0.692 ± 0.001	1.19 ± 0.001	16.67 ± 0.01
F2	29.53 ± 0.465	0.538 ± 0.001	0.652 ± 0.001	1.21 ± 0.001	17.02 ± 0.06
F3	31.08 ± 0.561	0.528 ± 0.001	0.614 ± 0.001	1.16 ± 0.001	17.68 ± 0.05
F4	29.61 ± 0.206	0.509 ± 0.001	0.639 ± 0.007	1.19 ± 0.002	15.81 ± 0.07
F5	29.62 ± 0.109	0.538 ± 0.005	0.621 ± 0.005	1.21 ± 0.001	17.55 ± 0.07
F6	30.78 ± 0.117	0.541 ± 0.005	0.630 ± 0.007	1.21 ± 0.001	17.30 ± 0.01
F7	30.09 ± 0.220	0.534 ± 0.005	0.640 ± 0.007	1.18 ± 0.005	18.16 ± 0.01
F8	30.12 ± 0.476	0.521 ± 0.001	0.599 ± 0.001	1.18 ± 0.005	19.03 ± 0.22
F9	31.92 ± 0.502	0.530 ± 0.001	0.682 ± 0.005	1.24 ± 0.005	20.70 ± 0.07

Postcompression studies

Shape of tablet and general appearance was checked by magnifying lens.

Thickness of tablet

Thickness of 3 tablets of each formulation was determined using a Venire calipers (Mitutoyo Corporation, Japan). The mean± SD values were calculated.

Tablet weight variation [13]

An electronic balance (Mettler Toledo, 3-MS-S/MS-L, Switzerland) was used to accurately weigh the individual wt. of Twenty tablets from were randomly selected from each formulation. The mean± SD values were calculated.

Hardness test [13]

To evaluate diametrical crushing strength, 3 tablets of each formulation were tested using a hardness tester (Monsanto type hardness tester, MHT-20, Campbell Electronics, India). The mean± SD values were calculated.

Friability test [13]

The friability of the 20 tablets (n = 1) was tested by a friabilator (ERWEKA, TAR 120, Germany), at a speed of 25 rpm for 4 min. The tablets were then de-dusted, reweighed and percentage weight loss (friability) was calculated by the equation.

% Friability = (initial wt.- wt. after friability) × 100/initial wt. Eq.No.(6)

***In Vitro* disintegration time & fineness of dispersion [14]**

The *in vitro* disintegration time was observed by placing one tablet in a beaker containing 50 mL of pH 6.8 phosphate buffer at 37 ºC ± 1 ºC (to correlate the dispersion of tablets *in vivo*), the time required to disperse the tablets was determined. The same dispersion was passed through a sieve screen with a nominal mesh aperture of 710 mm to confirm the fineness of dispersion. It was carried out in replicates of six tablets (n=3) and mean ±SD values were recorded.

Wetting time and water absorption ratio [15]

A piece of tissue paper folded twice was placed in Petri dish having internal diameter of 5.5 cm, containing 6 mL of water. A tablet was placed on the paper and the time required for complete wetting was measured and noted as wetting time using a stopwatch. The wetted tablet was then weighed. Water absorption ratio (R) was determined using following equation.

$R = [(Wa - Wb)/Wb] \times 100$ Eq.No.(7)

Where, Wb and Wa were the weights of the tablet before and after water absorption.

Drug content [9]

To evaluate the drug content uniformity, 10 tablets of each formulation were powdered in motar & pestle. Blend equivalent to 2.5 mg of Frovatriptan was accurately weighed and transferred into a 100 mL volumetric flask. Then, the volume was made up to 100 mL with 6.8 phosphate buffer and ultrasonicated for 2 min to extract the FS from the tablet blend and filtered through 0.45μ Poly Tetra Fluoro Ethylene (PTFE) filter disc to filter the dispersion, the filtrate was suitably diluted if necessasary and its absorbance was measured by UV-Visible spectrophotometer at 291 nm.

Post compression studies of all the formulations except friability test were carried out in triplicate; the consolidated results (mean ±SD) were tabulated in Table 3.

Table 3: Post compression studies of FS ODT

F Code	Wt variation (%)	Hardness (Kg/cm2)	Thickness (mm)	*Friability (%)	Assay (%)	Disintegration Time (Sec)	Wetting time (Sec)	Water abs. Ratio (%)
F1	0.100±2.97	3.6±0.16	2.4±0.24	0.74	96.40±0.39	33.00±1.33	24.33±0.44	71.60±2.14
F2	0.101±0.97	3.7±0.24	2.3±0.16	0.66	97.73±0.22	30.66±1.78	22.00±0.66	73.45±2.54
F3	0.102±0.99	3.7±0.24	2.4±0.24	0.49	96.57±0.41	31.66±0.44	24.31±1.11	76.25±2.14
F4	0.100±1.47	3.7±0.24	2.3±0.12	0.49	95.69±0.28	29.66±0.88	20.31±0.88	73.25±1.65
F5	0.101±0.99	3.8±0.24	2.4±0.12	0.49	98.21±0.42	28.00±0.66	16.00±0.66	74.35±2.30
F6	0.101±0.48	3.9±0.16	2.3±0.16	0.66	97.02±0.37	28.00±1.33	19.00±0.66	71.26±2.89
F7	0.102±1.98	3.6±0.16	2.4±0.16	0.80	99.72±0.25	26.33±0.44	15.66±1.10	77.52±3.45
F8	0.104±2.45	3.7±0.24	2.4±0.24	0.83	99.88±0.11	22.00±1.33	13.33±0.88	76.54±3.68
F9	0.103±1.47	3.8±0.24	2.4±0.24	0.60	94.66±0.32	15.09±2.01	10.33±2.21	78.00±2.46

* Except friability test all other were performed by (n=3) and the values are represented as mean ± SD.

Comparison of disintegration time and wetting time of FS ODT were represented in Figure 2.

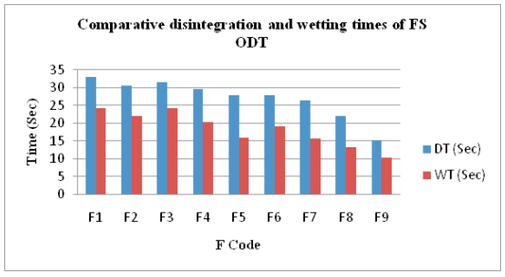

Figure 2: Comparative disintegration and wetting times of FS ODT

In Vitro dissolution Studies [9]

This was performed using the dissolution apparatus (Labindia Disso 2000, Labindia Analytical Instruments Pvt Ltd, India) with USP-II/Paddle. Each dissolution flask contains 900 mL of pH 6.8 Phosphate buffer; speed of paddle was maintained at 50 rpm, the temperature was kept stable at 37 °C ± 0.5 °C. At every time interval, 5 mL of dissolution media was withdrawn with a pipette containing 0.45μ (PTFE) filter disc, suitably diluted if necessary and its absorbance was measured by UV-Visible spectrophotometer at 291 nm. Furthermore, 5 mL of fresh pH 6.8 Phosphate buffer was replaced to the dissolution flask to keep the volume of dissolution medium constant. The dissolution tests were performed in (n=3) for each formulation and the dissolution profiles were represented graphically in Figure 3.

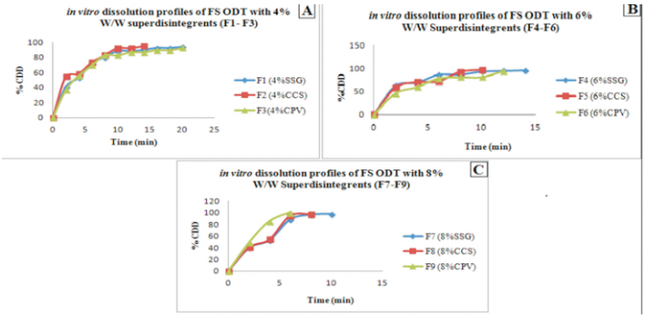

Figure 3: *In vitro* dissolution profiles of FS ODT

In vitro dissolution kinetics [16]

The *in vitro* drug release data was fitted to plot dissolution profiles (cumulative % drug dissolved Vs time) and first order plots (log % drug undissolved Vs time) as per the following equations.

Zero order: $Q_t = Q_0 + K_0 t$ **Eq.No.(8)**

First order: $\log Q_t = \log Q_0 - K_1 t / 2.303$ **Eq.No.(9)**

Where Qt is the amount of drug dissolved in time t, Q_0 is the initial amount of drug in the solution, K_0 & K_1 refers to the rate constants of zero & first order respectively.

The *in vitro* dissolution kinetic parameters: first order dissolution rate constant (K_1), regression coefficient (r^2), time for 50 % drug release (t_{50}) and time for 90 % drug release (t_{90}) were calculated. The consolidated in vitro dissolution kinetic parameters of FS ODT were tabulated in Table 4.

Table 4: *In vitro* dissolution kinetics of FS ODT

F Code	t_{50} (min)	t_{90} (min)	First order dissolution rate constant; K_1 (min^{-1})	First order regression coefficient (r^2)
F1	4	16	0.173	0.895
F2	3.2	10.5	0.22	0.854
F3	3	19.3	0.215	0.859
F4	2.2	10.5	0.31	0.833
F5	2.5	9.1	0.314	0.752
F6	3	12.5	0.257	0.855
F7	2.5	8.5	0.267	0.928
F8	2.4	6	0.463	0.948
F9	2.2	5	0.483	0.994

Accelerated stability studies [17]

Of the optimized formulation (F9), in final package (10 CC HDPE bottle) up to 6 months were carried according to International Conference on Harmonization (ICH) guidelines. 20 tablets were packed, labelled and sealed in the containers and placed in a humidity chamber (NSW-175, Narang Scientific work, India) maintained at 45°C ± 2°C and 75% ± 5% RH. At the end of 1M, 2M, 3M & 6M, the samples were withdrawn and evaluated for post compression studies. The chemical stability of drug in the 6M-accelerated stability sample of optimized FS ODT (F9), was compared with drug alone using FT-IR studies by recording in the region of 400-4000 cm^{-1} at spectral resolution of 2 cm^{-1}, using direct sampling method with isopropyl alcohol as solvent, using (Agilent technologies Cary 630 FTIR, Japan). The consolidated results of post compression studies on accelerated stability samples of optimized FS ODT (F9); except friability test were carried out in triplicate; the results (mean ± SD) were tabulated in Table 5.

Table 5: Post compression studies on accelerated stability samples of optimized FS ODT (F9)

Parameter	Initial	45°C / 75%RH 1M	45°C / 75% RH 2M	45°C / 75%RH 3M	45°C / 75%RH 6M
Weight Variation (%)	0.103 ± 1.47	0.101 ± 1.12	0.102 ± 1.23	0.101 ± 1.24	0.101 ± 1.23
Hardness (kg/cm2)	2.8 ± 0.24	2.8 ± 0.24	2.8 ± 0.24	2.8 ± 0.24	2.8 ± 0.24
Thickness (mm)	2.4 ± 0.24	2.4 ± 0.14	2.4 ± 0.11	2.4 ± 0.32	2.4 ± 0.21
*Friability (%w/w)	0.60	0.62	0.62	0.59	0.58
DT (Sec)	15.09 ± 2.01	15.11 ± 1.45	15.23 ± 1.87	15.32 ± 1.21	15.54 ± 1.12
Wetting time (Sec)	10.33 ± 2.21	11.14 ± 1.12	11.13 ± 1.24	11.24 ± 1.14	11.23 ± 1.32
Water abs. Ratio (%)	78.00 ± 2.46	78.56 ± 1.14	79.32 ± 1.32	80.00 ± 1.14	80.12 ± 1.13
Assay (%)	94.66 ± 0.32	96.32 ± 0.23	98.95 ± 0.62	97.68 ± 0.34	99.15 ± 0.52

* Except friability test all other were performed by (n=3) and the values are represented as mean ± SD.

FT-IR spectra of pure FS & 6M-accelerated stability sample of optimized formulation (F9) were represented in Figure 4. In vitro dissolution profiles of accelerated stability samples of optimized FS ODT (F9) were represented graphically in Figure 5.

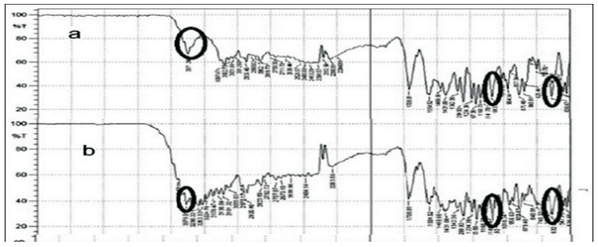

Figure 4: FT-IR spectra of a) Pure FS & b) 6M's accelerated stability sample of optimized FS ODT (F9)

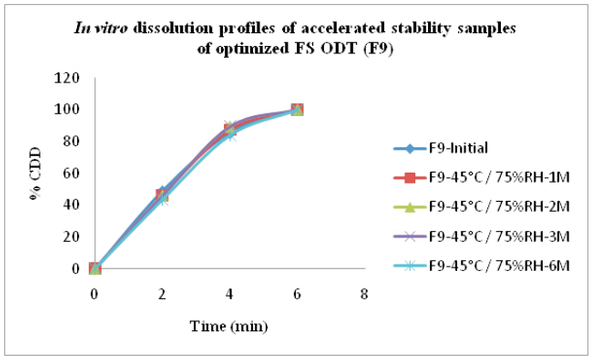

Figure 5: *In vitro* dissolution profiles of accelerated stability samples of optimized FS ODT (F9)

Results and Discussion

Standard calibration curve of FS in pH 6.8 phosphate buffer

Based on the measurement of absorbance at 291 nm in pH 6.8 phosphate buffer in the conc. Range of 10-50 μg/mL, gives a straight line with equation: $y = 0.0168 x + 0.007$ and a regression coefficient (r^2) of 0.9995 (Figure 1).

Drug-excipient compatibility / isothermal stress studies

Samples examined does not show any unusual color change, when compared with controls stored in refrigerator up to 3 weeks. Hence all the excipients employed in the study are compatible with drug.

Pre Compression studies

On directly compressible blends of all formulations, reveals that the angle of repose was found between 28°.17'to 31°.92', bulk density between 0.509 to 0.543 gm/cm3, tapped density between 0.599 to 0.692 gm/cm3, Carr's index between 16.67 to 20.70 % and Hausner's Ratio between 1.16 to 1.24. The micromeritic studies indicate better flow and compression characteristics of all formulations (Table 2).

Postcompression studies

The wt. variation of tablets of all the formulations was found to be 0.100 to 0.104 %. The average thickness of tablets was found to be 2.4 to 2.3 mm. The average hardness of the tablets was 3.6 to 3.9 Kg/cm^2, indicating satisfactory mechanical strength. The average % wt. loss in the friability test ranges from 0.49 to 0.89 %, which was less than 1% as per official requirement of IP indicating a good mechanical resistance of tablets. Assay of all the prepared batches is within 99.88 to ± 94.66 % of the labelled content, indicating content uniformity of the prepared formulations. The average wetting time of all the formulations was obtained in the range of 24.33 to 33.33 sec. As the conc. of superdisintegrants increases, there is a significant decrease in the wetting time followed by in vitro disintegration time. Wetting is related to the inner structure of the tablets, hydrophilicity of the components and swelling mechanism of superdisintegrants. Water absorption ratio was further related to the hydrophilicity of the matrix. In the view of above findings the order of superdisintegrants efficacy in the formulations of FS ODT is CPV > CCS > SSG. The formulation F9 (8% w/w CPV) showed min wetting time of 10.33 Sec and min in vitro disintegration time of 15.09 Sec is an optimized formulation. (Table 3)

In vitro dissolution studies

Dissolution profiles are represented graphically in Figure 1 and 2, indicates that the release rate increases as the concentration of super disintegrents increases. Based on first order dissolution rate constant (K1); the order of superdisintegrants to enhance dissolution rate in the formulations of FS ODT is CPV > CCS > SSG. All the ODT formulations released more than 90.0% of the drug within 20 min. Formulation F9 (8% w/w CPV) released 100 % of drug within 6 min, was considered as the optimal ODT among all the nine formulations tested in this study (Figure 2).

In vitro dissolution kinetics

ODT F9 (8% w/w CPV) had the highest first order dissolution rate constant (K1) of 0.483 min^{-1} with a regression coefficient (r^2) of 0.994, time for 50 % drug release (t_{50}) is 2.2 min and time for 90 % drug release (t_{90}) is 5 min is the optimal ODT among all the nine formulations tested in this study (Table 4).

Accelerated stability studies

As there were no significant differences in post compression and in vitro dissolution profiles of initial and accelerated stability samples up to 6 months, optimized formulation F9 passes the test for stability. A FT-IR spectrum of pure FS is having primary amide group and two secondary amino groups. Two N-H stretching bands resulting from symmetrical and asymmetrical stretching in 3400-3520 cm^{-1} correspond to primary amide group [18]. An FTIR spectrum of 6M-accelerated stability sample of optimized formulation (F9), shows the same functional groups at the corresponding frequencies as that of pure drug. Thus, indicates no significant chemical interaction and change in functional groups of FS occurred during the accelerated stability study of optimized formulation (F9). (Table 5); (Figure 4 and 3).

Conclusion

In the view of above findings all the formulations passed the pre & post compression parameters. The release rate of FS from ODT increases as the concentration of super disintegrents increases. Among all superdisintegrents formulations with CPV are having faster release profiles and the order of superdisintegrants to enhance dissolution rate in the formulations of FS ODT is CPV > CCS > SSG. Formulation F9 (8% w/w CPV) released 100 % of drug with in 6 min, was considered as the optimal ODT among all the nine formulations tested in this study. An accelerated stability study up to 6 months of optimized formulation (F9) indicates it passed the test for stability in its in final pack. Therefore, an effective FS ODT dosage form for treating acute migraine attack was formulated by direct compression techniqu. ODT will enhance the bioavailability and fastens the onset of action of FS in comparison to its conventional tablets.

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Conflict of interest

The author declares no competing interest.

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