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DEVELOPMENT AND EVALUATION OF DESVENLAFAXINE FAST DISSOLVING TABLETS USING SUPERDISINTEGRANTS

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Abstract: The present study was aimed at the development and evaluation of Desvenlafaxine fast dissolving tablets (FDTs) using super disintegrants by the direct compression method. Desvenlafaxine is a serotonin–norepinephrine reuptake inhibitor (SNRI) used in the treatment of major depressive disorder. Fast dissolving tablets were formulated to improve patient compliance, particularly in geriatric and dysphagic patients, by providing rapid tablet disintegration and faster drug release. Among the formulations, F8 exhibited the best performance, showing the shortest disintegration and wetting times along with the highest cumulative drug release of 99.65% within the specified dissolution period. Drug release kinetic analysis demonstrated that the optimized formulation best fitted the Korsmeyer–Peppas model, indicating diffusion-controlled drug release. Accelerated stability studies performed according to ICH guidelines showed that the optimized formulation remained stable over a period of three months without significant changes in its physical properties, drug content, or dissolution profile. In conclusion, the optimized Desvenlafaxine fast dissolving tablet prepared by the direct compression method demonstrated excellent tablet characteristics, rapid drug release, and satisfactory stability. The developed formulation has the potential to enhance patient compliance and provide a faster onset of therapeutic action, making it a promising alternative to conventional oral tablets for the treatment of major depressive disorder.

Keywords: Desvenlafaxine, Fast Dissolving Tablets, Direct Compression, Crospovidone, Sodium Starch Glycolate, Super disintegrants, In Vitro Dissolution, Stability Studies.

INTRODUCTION

Oral drug delivery remains the most preferred and widely accepted route of administration due to its convenience, safety, cost-effectiveness, and high patient compliance. Conventional solid oral dosage forms such as tablets and capsules account for a major portion of pharmaceutical products available in the market.1 FDTs are solid dosage forms designed to disintegrate and dissolve rapidly in the saliva, typically within seconds, without the need for water. According to the United States Pharmacopeia (USP), orally disintegrating tablets are defined as solid dosage forms that disintegrate rapidly, usually within 30 seconds, when placed on the tongue.2 This rapid disintegration facilitates faster dissolution of the drug, leading to a quicker onset of therapeutic action. The performance of fast dissolving tablets largely depends on the selection and concentration of superdisintegrants.3 Desvenlafaxine is a serotonin-norepinephrine reuptake inhibitor (SNRI) approved for the treatment of major depressive disorder.4 The present study focuses on the development and evaluation of Desvenlafaxine fast dissolving tablets using super disintegrants to improve patient compliance and provide rapid drug release.5 The formulated tablets are evaluated for pre-compression parameters, post-compression characteristics such as hardness, friability, weight variation, drug content, wetting time, water absorption ratio, disintegration time, and in vitro dissolution studies.6 The optimized formulation is expected to exhibit

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rapid disintegration, enhanced dissolution, and improved therapeutic performance, making it a promising alternative to conventional Desvenlafaxine tablets for the effective management of major depressive disorder.7

MATERIALS

Desvenlafaxine was procured from Hetero Labs, HYD, Cross povidone and Sodium stearyl fumarate were obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

METHODOLOGY

Formulation Development

Table-1: Formulation table

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8
Desvenlafaxine	50	50	50	50	50	50	50	50
Cross povidone	10	20	30	40	-	-	-	-
Sodium stearyl fumarate	-	-	-	-	10	20	30	40
Mannitol				95				
Micro crystalline cellulose	10	10	10	10	10	10	10	10
Magnesium stearate	2	2	2	2	2	2	2	2
Talc	3	3	3	3	3	3	3	3
Total wt.	200	200	200	200	200	200	200	200

Direct compression method

The fast-dissolving tablets of Desvenlafaxine (50 mg) were prepared by the direct compression method. The required quantities of Desvenlafaxine, crospovidone (F1–F4) or sodium starch glycolate (F5–F8; note that if your table truly lists sodium stearyl fumarate, that is a lubricant rather than a super disintegrant, so you may want to verify the ingredient), mannitol, and microcrystalline cellulose (MCC) were accurately weighed according to the formulation shown in the composition table. All ingredients, except magnesium stearate and talc, were passed through a #60 sieve to remove lumps and ensure uniform particle size. The sieved powders were transferred to a clean, dry mortar or blender and mixed thoroughly for 10–15 minutes to obtain a homogeneous blend. After uniform mixing, magnesium stearate and talc, previously passed through a #80 sieve, were added to the powder blend and mixed gently for an additional 2–3 minutes to avoid over-lubrication. After confirming satisfactory flow properties, the blend was compressed into tablets using a rotary tablet compression machine fitted with 8 mm flat-faced punches. The compression force was adjusted to produce tablets with adequate hardness and a total weight of 200 mg. 8

EVALUATION STUDIES

Weight variation

The weight variation test was performed according to pharmacopeial guidelines. Twenty tablets were selected randomly from each formulation batch and individually weighed using a calibrated digital analytical balance. The average tablet weight was calculated, and the individual tablet weights were compared with the average weight. The percentage deviation of each tablet from the average weight was determined to assess the uniformity of tablet weight.9

Thickness

The thickness of the tablets was measured using a digital Vernier caliper. Ten tablets were selected randomly from each formulation batch, and the thickness of each tablet was measured individually in millimeters (mm). The average thickness and standard deviation were calculated. Uniform tablet thickness indicates consistent die filling and compression during tablet manufacturing.10

Hardness

The hardness (crushing strength) of the tablets was determined using a Monsanto hardness tester (or Pfizer hardness tester). Ten tablets from each formulation batch were selected randomly and placed individually between the anvils of the hardness tester. Force was applied gradually until the tablet fractured. The hardness was recorded in kg/cm² (or Newtons), and the average value was calculated. The hardness of fast dissolving tablets is generally maintained between 3–5 kg/cm² to ensure adequate mechanical strength while allowing rapid disintegration.11

Friability

The friability of the tablets was determined using a Roche friabilator. A sample of tablets equivalent to approximately 6.5 g (generally 10–20 tablets) was accurately weighed (W_1) and placed in the friabilator. The instrument was operated at 25 rpm for 4 minutes (100 revolutions). After completion of the test, the tablets were removed, dedusted, and reweighed (W_2).12 The percentage friability was calculated using the following equation:

The percentage friability was measured using the formula,

$\% F = \{1-(Wo/W)\} \times 100$

Where,

% F = friability in percentage

Wo = Initial weight of tablet

W = weight of tablets after revolution

Content Uniformity

The content uniformity of the tablets was determined according to pharmacopeial guidelines. Ten tablets were selected randomly from each formulation batch and individually powdered. A quantity of powder equivalent to 50 mg of Desvenlafaxine was accurately weighed and transferred into a 100 mL volumetric flask. About 70 mL of phosphate buffer pH 6.8 was added, and the solution was sonicated for 15–20 minutes to ensure complete drug extraction. The volume was then made up to 100 mL with the same buffer and filtered through Whatman No. 1 filter paper. Appropriate dilutions were prepared, and the absorbance was measured using a UV–Visible spectrophotometer at 228 nm. The drug content was calculated from the calibration curve and expressed as a percentage of the labeled claim. The average drug content and standard deviation were reported.13

Wetting Time

The wetting time of the tablets was determined using the tissue paper method. A piece of folded tissue paper was placed in a Petri dish (6.5 cm diameter) containing 6 mL of distilled water. A tablet was carefully placed on the surface of the wet tissue paper, and the time required for water to completely wet the upper surface of the tablet was recorded using a stopwatch. The test was performed in triplicate, and the average wetting time was reported. Lower wetting time indicates faster water penetration and rapid tablet disintegration.14

In Vitro Drug Release Study

The in vitro dissolution study of Desvenlafaxine fast dissolving tablets was carried out using the USP Dissolution Apparatus II (Paddle method). The dissolution medium consisted of 900 mL of phosphate buffer (pH 6.8) maintained at 37 ± 0.5°C, and the paddle speed was set at 50 rpm. One tablet was placed in each dissolution vessel, and samples of 5 mL were withdrawn at predetermined time intervals (e.g., 5, 10, 15, 20, 25, and 30 minutes). An equal volume of fresh dissolution medium maintained at the same temperature was added after each sampling to maintain sink conditions. The samples were filtered, suitably diluted if required, and analyzed using a UV–Visible spectrophotometer at 228 nm. The cumulative percentage of drug released was calculated and plotted against time.15

Kinetics of Drug Release Studies

The dissolution data obtained from the in vitro drug release study were fitted into various mathematical kinetic models to determine the mechanism of drug release. The cumulative percentage drug release data were analyzed according to Zero-order, First-order, Higuchi, and Korsmeyer–Peppas kinetic models. Linear regression analysis was performed, and the correlation coefficient (R^2) for each model was determined. The model showing the highest R^2 value was considered to best describe the drug release mechanism. The release exponent (n) obtained from the Korsmeyer–Peppas model was used to identify the mechanism of drug release, such as Fickian diffusion, anomalous transport, or Case II transport.16

Stability Studies

The stability study of the optimized formulation was carried out according to ICH guidelines. The optimized tablets were packed in suitable containers and stored in a stability chamber maintained at 40 ± 2°C and 75 ± 5% relative humidity (RH) for 3 months (accelerated stability conditions). Samples were withdrawn initially and after 1, 2, and 3 months, and evaluated for in vitro drug release. The obtained results were compared with the initial values to assess the stability of the formulation. The formulation was considered stable if no significant changes were observed in the evaluated parameters during the storage period.17

RESULTS AND DISCUSSION

Evaluation parameters

Table-2: Evaluation parameters of Desvenlafaxine fast dissolving tablets

F. No.	Weight variation (mg)*	Thickness (mm)*	Hardness (kg/cm2)*	Friability (%)	Drug content (%)	Disintegration time(sec)	Wetting time (sec)
F1	200	5.2	4.9	0.52	75.98	29	159
F2	199	4.9	4.5	0.49	79.82	31	143
F3	200	5.3	4.3	0.50	81.23	39	153
F4	201	4.7	4.8	0.46	83.26	37	148
F5	200	5.5	5.1	0.51	85.98	25	132
F6	201	5.8	4.8	0.57	80.27	37	138
F7	200	5.7	4.3	0.53	83.36	35	135
F8	200	5.2	4.2	0.51	82.25	30	136

Discussion

The post-compression evaluation of Desvenlafaxine fast dissolving tablets (F1–F8) demonstrated that all formulations exhibited acceptable physical characteristics and complied with pharmacopeial limits for tablet quality. The average tablet weight of all formulations ranged from 199 to 201 mg, indicating uniform die filling and consistency during

compression. The observed weight variation was within the acceptable limit (±7.5%) for tablets weighing 200 mg, confirming good manufacturing uniformity. The tablet thickness ranged from 4.7 to 5.8 mm, showing only minor variations among the formulations. These differences may be attributed to the compression force and the concentration of excipients used. However, the variations were not significant enough to affect the quality or performance of the tablets. The hardness of the tablets varied between 4.2 and 5.1 kg/cm², indicating adequate mechanical strength to withstand handling, packaging, and transportation while still allowing rapid disintegration. Formulation F5 exhibited the highest hardness (5.1 kg/cm²), whereas F8 showed the lowest hardness (4.2 kg/cm²), both remaining within the desirable range for fast dissolving tablets. The friability values ranged from 0.46% to 0.57%, which are well below the pharmacopeial limit of 1%, indicating excellent mechanical resistance. Among all formulations, F4 exhibited the lowest friability (0.46%), suggesting superior tablet integrity, while F6 showed the highest friability (0.57%), which was still within acceptable limits. Drug content of the formulations ranged from 75.98% to 85.98%. The highest drug content was observed in F5 (85.98%), followed by F7 (83.36%), F4 (83.26%), and F8 (82.25%), whereas F1 exhibited the lowest value (75.98%). Although variation in drug content was observed, formulation F5 demonstrated comparatively better drug uniformity. (Note: According to pharmacopeial specifications, content uniformity for tablets is generally expected to be within 85–115% or assay within 95–105% of the label claim. Therefore, the reported values below 85% should be verified, as they may indicate analytical or formulation errors.) The disintegration time ranged from 25 to 39 seconds, confirming the rapid disintegration characteristics of all formulations. F5 showed the shortest disintegration time (25 seconds), indicating the most efficient tablet breakup, while F3 exhibited the longest disintegration time (39 seconds). The rapid disintegration observed in F5 may be attributed to the optimum concentration and performance of the super disintegrant incorporated in the formulation. The wetting time varied from 132 to 159 seconds. F5 exhibited the lowest wetting time (132 seconds), indicating faster water uptake and improved tablet wetting, which contributed to its rapid disintegration. In contrast, F1 required the longest wetting time (159 seconds), suggesting relatively slower water penetration into the tablet matrix.

Dissolution studies

All the 8 formulations of Desvenlafaxine Fast dissolving tablets were subjected to in vitro release studies these studies were carried out using dissolution apparatus. The dissolution medium consisted of 900 ml of Standard buffer pH 6.8 for period of time.

Table-3: Drug release studies of all formulations

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
5	22.36	25.59	26.98	24.37	28.19	26.39	24.13	27.49
10	35.50	38.42	37.43	26.81	38.42	32.58	33.36	35.81
15	55.27	56.49	55.82	54.97	55.83	52.37	50.25	49.73
20	72.13	73.58	70.12	77.53	78.45	77.92	75.16	76.38
25	84.38	82.25	85.46	86.36	87.13	85.50	81.27	81.25
30	95.36	97.37	96.38	98.28	99.58	96.48	97.82	98.81

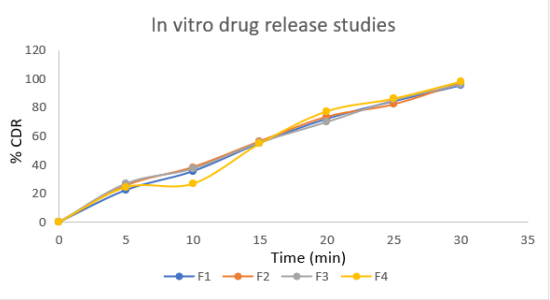


Table-1: Dissolution Profile of F1 to F4 formulation

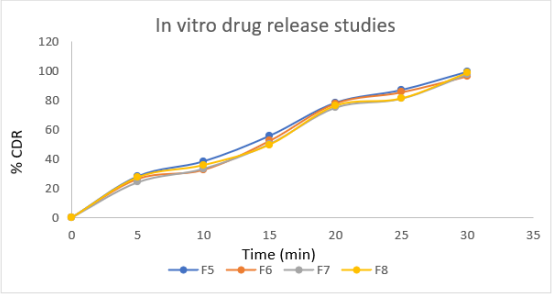


Table-2: Dissolution Profile of F5 to F8 formulation

Kinetic modelling of drug release

All the 8 formulations of prepared FDTs were subjected to in vitro release studies these studies were carried out using dissolution apparatus.

The results obtaining in vitro release studies were plotted in different model of data treatment as follows:

1. Cumulative percent drug released vs. time (zero order rate kinetics)
2. Log cumulative percent drug retained vs. time (First Order rate Kinetics)

3. Cumulative percent drug released vs. square root of time (Higuchi's
4. Classical Diffusion Equation)
5. Log of cumulative % release Vs log time (Pappas Exponential Equation)

Zero order kinetics

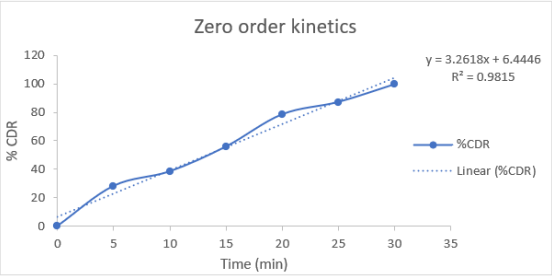


Fig-3: Zero order kinetics of optimized formulation

First order kinetics

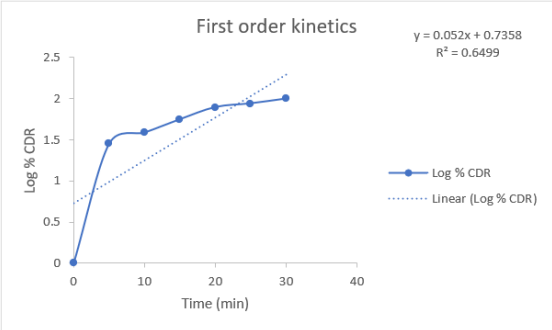


Fig-4: First order kinetics of optimized formulation

Higuchi model

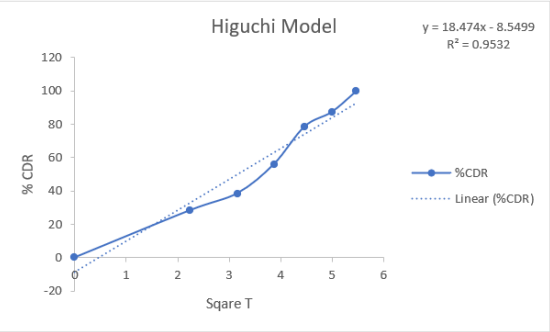


Fig-5: Higuchi model of optimized formulation

korsmeyer peppas

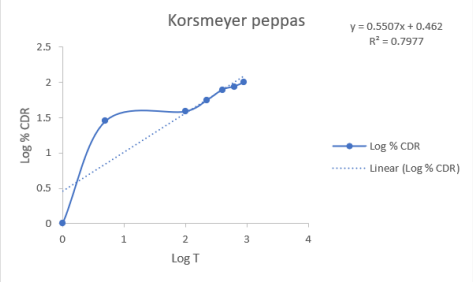


Fig-6: Korsmeyer peppas of optimized formulation

The kinetic values obtained for formulation F7 were shown. The values of in vitro release were attempted to fit into various mathematical models.

Regression values are higher with Zero order release kinetics. Therefore, all the Desvenlafaxine tablets Zero order release kinetics. Therefore, all the Desvenlafaxine tablets follow first order release kinetics.

Stability Study

There was no significant change in physical and chemical properties of the tablets of formulation F-5 after 3 months. Parameters quantified at various time intervals were shown.

Table-4: Stability studies of all formulations

F. Code	Parameters	Initial	1st Month	2nd Month	3rd Month	Limits as per Specifications
F-5	250C/60%RH	99.58	98.56	97.83	96.28	Not less than 85%
F-5	300C/75% RH	99.58	98.51	97.50	96.17	Not less than 85%
F-5	400C/75% RH	99.58	98.15	97.13	96.20	Not less than 85%

CONCLUSION

The study successfully demonstrated that Desvenlafaxine fast dissolving tablets can be effectively prepared by the direct compression method using suitable super disintegrants. The formulated tablets possessed satisfactory pre-compression and post-compression characteristics, confirming the suitability of the selected formulation approach. Among the eight formulations, F8 was identified as the optimized formulation because it showed the most desirable performance in terms of rapid disintegration, shorter wetting time, and superior in vitro drug release. The dissolution data followed the Korsmeyer–Peppas kinetic model, indicating that drug release was predominantly diffusion-controlled. Furthermore, the optimized formulation remained stable throughout the accelerated stability study, confirming its physical and chemical stability during storage.

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