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# FORMULATION AND EVALUATION OF DESVENLAFAXINE HYDROCHLORIDE DISPERSIBLE TABLETS FOR MAJOR DEPRESSIVE DISORDER

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## ABSTRACT

The present study aimed to formulate and optimize dispersible tablets of Desvenlafaxine using the direct compression method, focusing on achieving rapid disintegration and enhanced dissolution. Desvenlafaxine served as the active pharmaceutical ingredient, while Crospovidone and Pharmaburst were employed as disintegrants and co-processed excipients. All other excipients used were of analytical grade. Preformulation studies, including infrared spectral analysis, were conducted to assess drug-excipient compatibility. A $3^2$ full factorial design was utilized to evaluate the impact of varying concentrations of Crospovidone and Pharmaburst on critical tablet properties. Nine formulations (F1–F9) were developed and assessed for parameters such as weight variation, hardness, friability, disintegration time, and dissolution profile. All formulations complied with Pharmacopeial standards, with disintegration times under 2 minutes and F8 and F9 disintegrating in under 30 seconds. Drug release was rapid, with F8 achieving over 90% release in 10 minutes, even with minimal disintegrant. The factorial design was statistically significant for both disintegrants, and the optimized batch P9 exhibited excellent physicochemical characteristics and stability over time. The findings confirm that dispersible tablets of Desvenlafaxine can be effectively developed using direct compression, and the optimized formulation P9 presents a promising candidate for rapid onset antidepressant therapy.

**KEYWORD:-** Desvenlafaxine, Crospovidone, Pharmaburst, Factorial design, Direct Compression.

## INTRODUCTION

The development of drug delivery systems (DDS) aims to provide safe and effective therapies, with oral administration being the most preferred and widely used route due to ease of use, high dose accuracy, stability, and production efficiency. Among oral dosage forms, dispersible tablets have gained attention as they offer a patient-friendly solution, especially for populations with swallowing difficulties such as the elderly, children, and mentally ill patients. Dispersible tablets are uncoated or film-coated tablets designed to disperse in water (5–15 ml) within three minutes at 15–25°C, forming a homogenous dispersion suitable for easy administration. Their dispersion must pass through a 710 µm mesh, and dispersion efficiency can be enhanced by acid/base pairs generating carbon dioxide. These tablets possess ideal characteristics such as ease of disintegration in liquids, taste masking, high drug loading capacity, environmental resistance, and portability. However, several formulation challenges exist, including maintaining mechanical strength without compromising disintegration time, effective taste masking of bitter drugs, environmental sensitivity to humidity and temperature, and ensuring pleasant mouthfeel without grittiness. Additional formulation issues include aqueous solubility of drugs, which may lead to eutectic mixtures, and the need for appropriate organoleptic properties, including flavor and texture, to ensure patient compliance. Hygroscopicity is another concern, requiring specialized moisture-resistant packaging to preserve tablet integrity. Moreover, dispersible tablet production must remain cost-effective despite advanced technologies like Zydus and Orasolv, which increase manufacturing costs due to special packaging and processing needs. Thus, while dispersible tablets offer numerous advantages for oral drug delivery, their development demands careful consideration of formulation and patient-centric design parameters.[3,6]

## MATERIALS AND METHODS

Desvenlafaxine was used as the active ingredient, with Crospovidone and Pharmaburst as disintegrants and co-processed excipients; all other excipients were of

analytical grade. Tablets were formulated using direct compression, and drug-excipient compatibility was confirmed via IR spectral analysis. A $3^2$ full factorial design was applied to study the impact of Crospovidone and Pharmaburst concentrations on tablet properties. Nine formulations (F1–F9) were evaluated for weight variation, hardness, friability, disintegration time, and dissolution. Formulation P9 was selected as optimal based on statistical analysis and overall performance.

**Selection of excipients**

The formulation of dispersible tablets requires careful selection of excipients, especially when dealing with drugs that are highly water-soluble, weakly compressible, and hygroscopic, as these present significant manufacturing challenges. To ensure high compressibility and desirable tablet characteristics, appropriate excipients must be chosen. Binders or fillers, particularly in direct compression methods, play a crucial role in enhancing the flowability and compressibility of the blend. Disintegrants are essential for promoting rapid tablet disintegration in water; superdisintegrants such as crospovidone and sodium starch glycolate are preferred due to their exceptional water absorption and swelling capacity. Diluents or fillers contribute to the bulk and strength of tablets and are selected based on the drug's physicochemical properties like solubility, hygroscopicity, and compressibility; common combinations include mannitol with microcrystalline cellulose. Although lubricants like magnesium stearate are hydrophobic and may produce an unattractive scum in dispersible formulations, they are still widely used in commercial products for their excellent lubrication properties.[7][8]

**Drug excipients compatibility study**

Compatibility studies are crucial to ensure that selected excipients do not degrade the drug or generate impurities, thus ensuring patient safety. FT-IR spectroscopy was used to assess compatibility by comparing spectra of the pure drug with its 1:1 physical mixtures with excipients. Samples were prepared with dried potassium bromide, compressed into pellets, and scanned from 4000–400 $cm^{-1}$ using a Shimadzu FTIR Spectrophotometer. A UV-Visible spectrophotometric method was also developed for accurate drug estimation. The λmax was determined by scanning diluted drug solutions (200–400 nm). A calibration curve was prepared using standard solutions (2–12 µg/ml) in 0.1N HCl, with absorbance measured at λmax. Linearity and reproducibility were confirmed through repeated studies.[9]

**Formulation of dispersible tablets**

The required quantities of drug, Pharmaburst 500/Ludiflash/Pearlitol, Crospovidone/Croscarmellose Sodium/Sodium Starch Glycolate, Avicel pH 102, Sucralose, and Colloidal Silicon Dioxide were sifted through #40 mesh, while Talc and Magnesium Stearate were passed through #60 mesh. The sifted materials were blended in a Double Cone Blender at 20 RPM for 15 minutes. Magnesium Stearate was then added and the blend was lubricated for 5 minutes at the same speed. The final blend was evaluated for pre-compression parameters and subsequently compressed using a Multipunch Tablet Compression Machine (Minipress) with 5.0 mm round punches. The resulting tablets were assessed for post-compression parameters of orodispersible tablets.[11]

**Optimization of nanoemulsion by response variables effects ($3^2$ factorial design)**

Based on the batches results, statistical design was applied for optimization of final formulation. It was observed that the amount of Superdisintegrant and the directly compressible excipient is critical and the physicochemical parameters was depends on the both factors. Hence, factorial design was applied by taking crospovidone and Pharmaburst 500 as an independent variable. $3^2$ factor 3 level factorial design was applied as per below;

**Table 1: Factorial design table.**

| Independent Variable | Low (-) | Center Point (0) | High (+) |
|---|---|---|---|
| $X_1$-Pharmaburst 500 | 140 | 150 | 160 |
| $X_2$-Crospovidone | 35 | 40 | 45 |
| ***Dependent Variable*** | | | |
| $Y_1$=Drug Release at 6 min (%) | | | |
| $Y_1$=Disintegration Time (sec) | | | |

**Table 2: Formulation table for factorial batches.**

| Ingredients (mg) | P1 | P2 | P3 | P4 | P5 | P6 | P7 | P8 | P9 |
|---|---|---|---|---|---|---|---|---|---|
| Drug | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 |
| Pharmaburst 500® | 140 | 140 | 140 | 150 | 150 | 150 | 160 | 160 | 160 |
| Crospovidone | 35 | 45 | 55 | 35 | 45 | 55 | 35 | 45 | 55 |
| Avicel pH 102 | 56 | 46 | 36 | 56 | 46 | 36 | 46 | 36 | 26 |
| Sucralose | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| Colloidal Silicon Dioxide | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| Talc | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Magnesium Stearate | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| Total | 270 | 270 | 270 | 270 | 270 | 270 | 270 | 270 | 270 |

**Evaluation parameters**
Evaluation of factorial batches was done as per trial batches and the results were recorded in results and discussion chapter.

**Weight variation**
Weight variation was performed to ensure dosage uniformity. The test was carried out by weighing the 20 tablets individually using analytical balance, then calculating the average weight, and comparing the individual tablet weights to the average. The percentage of weight variation was calculated by using the following formula.[12]

**Table 3: Weight variation.**

| Sr. No. | Average Weight of tablets (mg) | Maximum % difference allowed |
|---|---|---|
| 1 | 80 mg or less | + 10% |
| 2 | 80-250 mg | + 7.5% |
| 3 | >250 mg | + 5% |

**Thickness**
The thickness of a tablet influences its physical appearance and is largely determined by the compressibility of the formulation blend and the desired hardness. It is usually expressed in millimeters (mm).

**Hardness**
Tablet hardness, also known as crushing strength, refers to the amount of force required to break a tablet when it is placed on its edge. This property ensures the tablet can withstand mechanical stress during manufacturing, packaging, transportation, and handling by patients. Hardness is measured in units such as Newton (N), kilograms per square centimeter ($kg/cm^2$), or kilonewtons (kN). It is considered a **Critical Quality Attribute (CQA)** as it must maintain an optimal balance between **Disintegration Time** and **Friability**.

**Friability**
Friability measures a tablet's resistance to abrasion or breakage due to mechanical stress during handling, packaging, and transport. It is defined as the percentage of weight loss after the tablets are subjected to a standardized mechanical agitation.

**Disintegration time**
Disintegration time is a key **Critical Quality Attribute** for orodispersible tablets. It indicates how quickly the tablet breaks down into smaller particles under specific test conditions. The test is carried out using a digital disintegration apparatus. One tablet is placed in each of the six tubes of the basket rack, with a disc added to each tube. The rack is submerged in a 1-liter beaker containing water maintained at 37 ± 2°C. The basket assembly moves vertically at a rate of 28–32 cycles per minute through a distance of 5–6 cm. The time required for complete disintegration is recorded.

**Wetting Time and Water Absorption Ratio**
To simulate the conditions inside the mouth, wetting time and water absorption ratio are determined. Six tablets are tested using a petri dish lined with a folded Whatman filter paper. Ten milliliters of water, containing 0.1 g of Rhodamine B dye, is poured into the dish. The tablet is gently placed on the filter paper at time zero, and the time taken for the dye to completely color the tablet (indicating full wetting) is recorded as the **Wetting Time**.

The wetted tablet is then weighed, and the **Water Absorption Ratio (AR)** is calculated.

**Percentage drug content**
The uniformity of active pharmaceutical ingredient (API) content in the tablets is assessed by analyzing a sample of ten tablets. The average tablet weight is calculated, after which the tablets are crushed and a powder equivalent to 25 mg of API is dissolved in 250 ml of phosphate buffer (pH 6.8). The solution is shaken for 20 minutes, filtered, and appropriately diluted. The absorbance is then measured spectrophotometrically against a blank solution, and the drug content is determined accordingly.

**Dissolution test**
To evaluate drug release from dispersible tablets, the dissolution study is performed using the USP Dissolution Apparatus II (paddle method). The test involves 900 ml of phosphate buffer (pH 6.8) as the dissolution medium, maintained at 37 ± 0.5°C and stirred at 50 rpm. At predefined time intervals (5, 10, 15, 20, and 30 minutes), 5 ml samples are withdrawn, filtered using a 0.45 µm membrane, and analyzed for absorbance at 226 nm using a UV spectrophotometer. The cumulative percentage of drug release is calculated using the standard calibration curve.

**Stability Study**
Stability testing is carried out following **ICH guidelines** to determine the formulation's shelf life and storage conditions. The most promising formulation is packed in aluminum foil and stored in a controlled humidity chamber set at 40 ± 2°C and 75 ± 5% RH for one month. After the storage period, samples are evaluated for drug content, disintegration time, and in vitro drug release to assess any changes in performance.

## RESULT AND DISCUSSION

### Preformulation study

The outcomes and conclusions from the Preformulation studies of the Active Ingredient are presented below.

### Melting point determination

The melting point of the Active Ingredient was found to be **142°C**, which matches the reported melting point of the pure drug, confirming the **purity** of the material.

### Physical characterization of drug

The physical properties of the drug were evaluated, and the results are summarized in the table below:

**Table 4: Physical characterization results.**

| Sr. No. | Test | Result | Inference |
|---|---|---|---|
| 1 | Angle of Repose | 47.8 | Poor Flow |
| 2 | Bulk Density (g/cc) | 0.15 | - |
| 3 | Tapped Density (g/cc) | 0.21 | - |
| 4 | Hausner's Ratio | 1.40 | Poor Flow |
| 5 | Carr's Consolidation Index | 28.6 | Poor Flow |

The Angle of Repose, Hausner's Ratio, and Carr's Index values indicate that the drug powder exhibits poor flow properties, which suggests that flow aids or granulation may be required during formulation.

### Solubility studies

Solubility testing of the pure drug was carried out in various media. Results are shown below:

**Table 5: Solubility data.**

| Sr. No. | Media | Solubility (mg/ml) |
|---|---|---|
| 1 | Purified Water | 1.02 |
| 2 | pH 1.2 HCl Buffer | 0.99 |
| 3 | pH 4.5 Acetate Buffer | 1.00 |
| 4 | pH 6.8 Phosphate Buffer | 0.98 |

The drug showed moderate solubility in water and across various pH conditions, indicating it is sparingly soluble.

### Analytical method for estimation

### UV Absorption

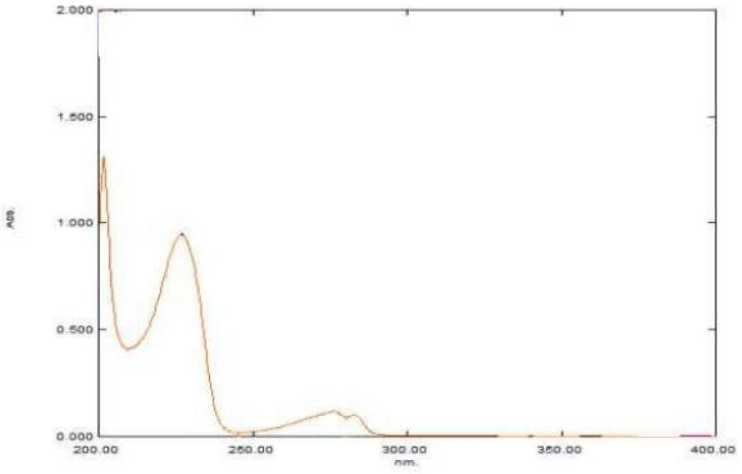


**Fig. 1: λmax of drug.**

Scanning the stock solution showed that the λmax of drug was 226 nm and all further analysis will be done at this particular wavelength.

### Standard calibration curve

The calibration curve was found to be linear in the concentration range of 2-12 µg/ml In 6.8 phosphate buffer at its λmax, 226 nm. The coefficient of correlation ($R^2$) was found to be $R^2$= 0.998 with slope of

0.100.

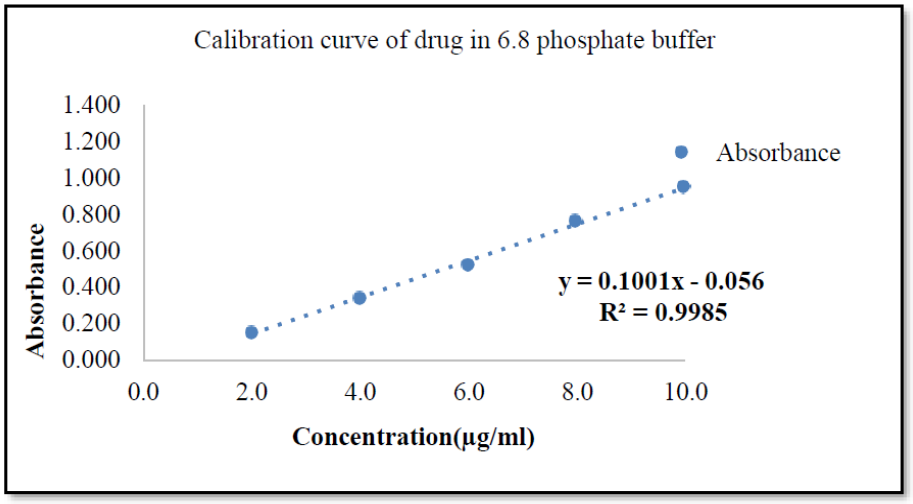


**Fig. 2: Calibration curve of drug.**

**Drug Excipient compatibility IR studies**

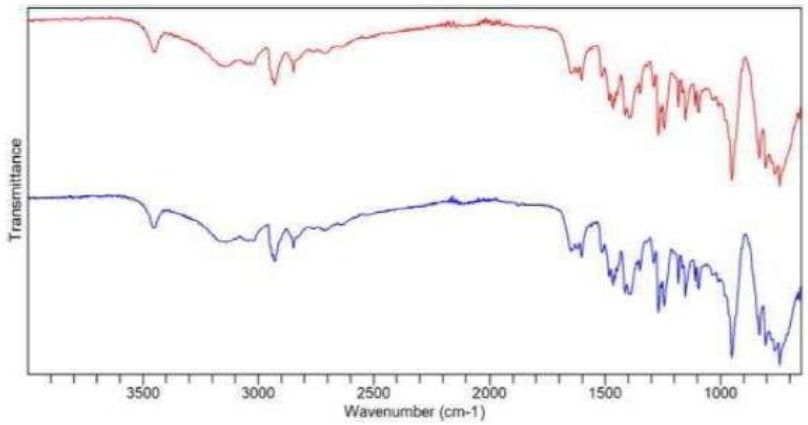


**Fig. 3: FT-IR Spectrumof pure drug and formulation mixture.**

The graph is evident of the fact that all the functional groups of drug are maintained in the spectrum of drug + excipients. Hence it can be concluded that all the excipients used in the formulation of DT are compatible with the drug.

**Table 6: FTIR Interpretation.**

| Functional group | FTIR Region | Observed frequency in Pure Drug ($cm^{-1}$) | Observed frequency in Formulation ($cm^{-1}$) | Conclusion |
|---|---|---|---|---|
| C-H | 2960-2850 | 2809 | 2922 | *No Interaction* |
| C=O | 1700-1725 | 1705 | 1705 | |
| O-H | 1200-1500 | 1279 | 1280 | |
| N-H | 1500-1700 | 1448 | 1448 | |

**Evaluation of trial batches formulation**

**Pre-Compression parameters**

Pre-compression parameters of blends (F1–F9) were evaluated. No major difference was observed in flowability and compressibility due to similar excipients used. Results are tabulated below:

**Table 7: Pre-Compression Parameters.**

| Batch | Angle of Repose (θ) (n=3) | Bulk Density (g/ml) (n=3) | Tapped Density (g/ml) (n=3) | Hausner's Ratio (n=3) | Carr's Consolidation Index (%) (n=3) |
|---|---|---|---|---|---|
| F1 | 22.8 ± 0.3 | 0.311 ± 0.004 | 0.482 ± 0.003 | 1.550 ± 0.021 | 35.477 ± 0.035 |

| | | | | | |
|---|---|---|---|---|---|
| F2 | 23.9 ± 0.5 | 0.350 ± 0.001 | 0.468 ± 0.004 | 1.337 ± 0.011 | 25.214 ± 0.024 |
| F3 | 25.0 ± 0.7 | 0.341 ± 0.002 | 0.480 ± 0.001 | 1.408 ± 0.023 | 28.958 ± 0.032 |
| F4 | 27.4 ± 0.4 | 0.372 ± 0.002 | 0.489 ± 0.003 | 1.315 ± 0.020 | 23.926 ± 0.014 |
| F5 | 26.3 ± 0.6 | 0.339 ± 0.004 | 0.479 ± 0.001 | 1.413 ± 0.011 | 29.228 ± 0.031 |
| F6 | 24.5 ± 0.5 | 0.352 ± 0.003 | 0.457 ± 0.002 | 1.298 ± 0.013 | 22.976 ± 0.025 |
| F7 | 25.7 ± 0.5 | 0.361 ± 0.002 | 0.469 ± 0.001 | 1.299 ± 0.031 | 23.028 ± 0.017 |
| F8 | 22.0 ± 0.3 | 0.340 ± 0.005 | 0.472 ± 0.002 | 1.388 ± 0.022 | 27.966 ± 0.031 |
| F9 | 23.4 ± 0.4 | 0.345 ± 0.003 | 0.461 ± 0.003 | 1.336 ± 0.010 | 25.163 ± 0.031 |

(Mean ± SD)

**Post-Compression Parameters**

Post-compression evaluation showed acceptable results for weight variation, hardness, friability, disintegration, wetting time, and drug content.

**Table 8: Post-Compression Parameters (Weight, Thickness, Hardness, Friability).**

| Formulation | Weight Variation (mg) (n=20) | Thickness (mm) (n=3) | Hardness (kg/cm²) (n=3) | Friability (%) |
|---|---|---|---|---|
| F1 | 271 ± 2.6 | 3.80 ± 0.23 | 5.3 ± 0.9 | 0.39 |
| F2 | 271 ± 3.1 | 3.78 ± 0.31 | 4.1 ± 1.2 | 0.31 |
| F3 | 270 ± 3.7 | 3.76 ± 0.11 | 7.4 ± 0.8 | 0.41 |
| F4 | 269 ± 2.1 | 4.08 ± 0.20 | 6.9 ± 1.1 | 0.30 |
| F5 | 272 ± 3.3 | 4.05 ± 0.17 | 5.5 ± 0.4 | 0.32 |
| F6 | 271 ± 2.0 | 4.03 ± 0.11 | 4.9 ± 0.3 | 0.34 |
| F7 | 273 ± 3.0 | 4.05 ± 0.22 | 4.7 ± 0.4 | 0.31 |
| F8 | 269 ± 2.4 | 4.09 ± 0.15 | 5.5 ± 0.3 | 0.29 |
| F9 | 272 ± 2.9 | 4.00 ± 0.11 | 4.9 ± 0.1 | 0.28 |

(Mean ± SD)

**Table 9: Post-Compression Parameters (Disintegration, Water Absorption, Wetting Time, Assay).**

| Formulation | Disintegration Time (sec) (n=6) | Water Absorption Ratio (%) (n=3) | Wetting Time (sec) (n=3) | Assay (%) (n=3) |
|---|---|---|---|---|
| F1 | 37 ± 3.5 | 61.7 ± 4.5 | 75 ± 5.9 | 98.9 ± 1.3 |
| F2 | 49 ± 1.9 | 48.6 ± 2.9 | 84 ± 4.8 | 99.2 ± 1.2 |
| F3 | 62 ± 2.8 | 35.3 ± 1.9 | 92 ± 6.5 | 99.3 ± 0.3 |
| F4 | 31 ± 4.6 | 68.4 ± 2.7 | 65 ± 5.4 | 99.6 ± 0.4 |
| F5 | 35 ± 3.4 | 65.9 ± 3.9 | 72 ± 3.6 | 99.4 ± 1.0 |
| F6 | 38 ± 3.7 | 57.3 ± 1.8 | 75 ± 4.8 | 99.9 ± 0.6 |
| F7 | 34 ± 4.6 | 67.9 ± 1.8 | 70 ± 4.9 | 98.1 ± 0.2 |
| F8 | 27 ± 1.9 | 75.1 ± 3.8 | 54 ± 6.1 | 98.3 ± 0.1 |
| F9 | 24 ± 3.7 | 85.3 ± 4.1 | 51 ± 2.3 | 99.4 ± 0.3 |

(Mean ± SD)

**Table 10: Dissolution study results.**

| Formulation | 5 min | 10 min | 15 min | 20 min | 30 min |
|---|---|---|---|---|---|
| F1 | 72.4 ± 8.4 | 81.3 ± 6.2 | 93.4 ± 5.0 | 98.4 ± 3.2 | 99.9 ± 1.7 |
| F2 | 69.4 ± 9.1 | 75.6 ± 7.6 | 88.9 ± 6.1 | 94.3 ± 4.2 | 98.7 ± 2.1 |
| F3 | 65.5 ± 12.3 | 71.2 ± 9.4 | 85.6 ± 7.6 | 95.1 ± 5.4 | 99.8 ± 4.2 |
| F4 | 83.4 ± 4.9 | 88.2 ± 3.2 | 97.6 ± 2.1 | 99.7 ± 1.7 | 99.8 ± 1.6 |
| F5 | 80.0 ± 4.5 | 84.7 ± 3.2 | 97.1 ± 1.4 | 99.9 ± 1.5 | 99.9 ± 1.5 |
| F6 | 78.1 ± 7.1 | 85.6 ± 4.2 | 95.5 ± 3.1 | 99.8 ± 2.7 | 99.9 ± 1.9 |
| F7 | 77.8 ± 6.2 | 84.2 ± 5.1 | 93.7 ± 3.0 | 99.9 ± 2.7 | 99.9 ± 2.2 |
| F8 | 87.8 ± 6.1 | 94.3 ± 3.9 | 99.4 ± 3.1 | 99.5 ± 1.7 | 99.9 ± 1.6 |
| F9 | 92.0 ± 3.3 | 99.7 ± 1.6 | 99.8 ± 1.5 | 99.9 ± 1.5 | 99.9 ± 1.4 |

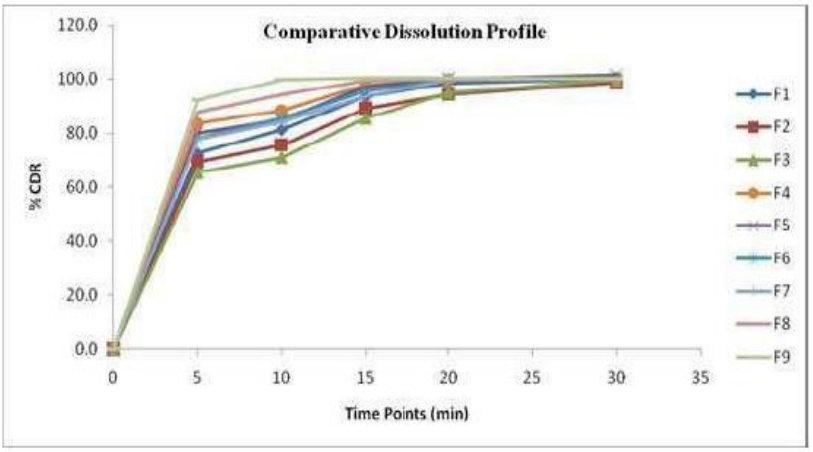


**Fig. 4: Comparative dissolution profile of trial batches.**

- **Weight variation, hardness, thickness, friability** were within acceptable Pharmacopoeial limits.
- **Disintegration time:** F8 and F9 passed ODT criteria (below 30 sec).
- **Wetting Time & Water Absorption:** F9 had fastest wetting and highest absorption.
- **Dissolution:** Rapid drug release (>90% at 10 min) observed with F8 and F9.

**Evaluation of Factorial Batches Formulation**

The factorial batches (P1–P9) were prepared and evaluated for pre-compression and post-compression parameters. The results are summarized below:

**Table 11. Results of Pre-Compression Parameters.**

| Formulations | Angle of Repose (θ) | Bulk Density (g/mL) | Tapped Density (g/mL) | Hausner's Ratio | Carr's Index (%) |
|---|---|---|---|---|---|
| P1 | 22.5 ± 0.4 | 0.315 ± 0.003 | 0.476 ± 0.004 | 1.511 ± 0.018 | 33.82 ± 0.032 |
| P2 | 23.6 ± 0.5 | 0.348 ± 0.002 | 0.471 ± 0.003 | 1.353 ± 0.012 | 26.13 ± 0.025 |
| P3 | 25.3 ± 0.6 | 0.339 ± 0.003 | 0.483 ± 0.002 | 1.424 ± 0.021 | 29.82 ± 0.030 |
| P4 | 27.0 ± 0.5 | 0.375 ± 0.002 | 0.492 ± 0.004 | 1.312 ± 0.017 | 23.78 ± 0.015 |
| P5 | 26.1 ± 0.4 | 0.336 ± 0.003 | 0.474 ± 0.003 | 1.411 ± 0.014 | 29.11 ± 0.029 |
| P6 | 24.8 ± 0.4 | 0.350 ± 0.002 | 0.459 ± 0.002 | 1.311 ± 0.016 | 23.75 ± 0.024 |
| P7 | 25.5 ± 0.6 | 0.358 ± 0.004 | 0.472 ± 0.001 | 1.318 ± 0.019 | 24.15 ± 0.020 |
| P8 | 22.3 ± 0.3 | 0.343 ± 0.004 | 0.468 ± 0.002 | 1.364 ± 0.023 | 26.71 ± 0.027 |
| P9 | 23.1 ± 0.4 | 0.347 ± 0.003 | 0.464 ± 0.002 | 1.337 ± 0.011 | 25.22 ± 0.030 |

(Mean ± SD)

**Table 12: Results of Post-Compression Parameters.**

| Formulations | Weight Variation (mg) (n=20) | Thickness (mm) (n=3) | Hardness (kg/cm²) (n=3) | Friability (%) |
|---|---|---|---|---|
| P1 | 270 ± 2.5 | 3.85 ± 0.05 | 5.9 ± 0.2 | 0.41 |
| P2 | 272 ± 3.2 | 3.86 ± 0.02 | 6.1 ± 0.1 | 0.39 |
| P3 | 271 ± 3.1 | 3.84 ± 0.06 | 6.2 ± 0.3 | 0.42 |
| P4 | 268 ± 2.9 | 3.85 ± 0.03 | 6.0 ± 0.2 | 0.38 |
| P5 | 270 ± 3.4 | 3.86 ± 0.04 | 5.9 ± 0.1 | 0.35 |
| P6 | 272 ± 2.1 | 3.85 ± 0.02 | 5.9 ± 0.2 | 0.38 |
| P7 | 270 ± 3.3 | 3.86 ± 0.03 | 5.7 ± 0.1 | 0.37 |
| P8 | 271 ± 2.5 | 3.84 ± 0.01 | 5.6 ± 0.2 | 0.31 |
| P9 | 270 ± 2.8 | 3.85 ± 0.02 | 5.9 ± 0.2 | 0.33 |

(Mean ± SD)

**Table 13: Results of Disintegration Time and Drug Content.**

| Formulations | Disintegration Time (sec) (n=6) | Drug Content (%) (n=3) |
|---|---|---|
| P1 | 52 ± 3 | 99.2 ± 1.2 |
| P2 | 48 ± 2 | 98.5 ± 0.7 |
| P3 | 41 ± 4 | 99.0 ± 0.2 |

| | | |
|---|---|---|
| P4 | 37 ± 5 | 98.6 ± 1.4 |
| P5 | 32 ± 4 | 97.9 ± 0.5 |
| P6 | 28 ± 3 | 98.8 ± 1.1 |
| P7 | 25 ± 4 | 99.3 ± 0.8 |
| P8 | 23 ± 2 | 97.5 ± 1.6 |
| P9 | 20 ± 3 | 98.8 ± 1.4 |

(Mean ± SD)

**Table 14: Dissolution studies of factorial batches.**

| Time (min) | P1 | P2 | P3 | P4 | P5 | P6 | P7 | P8 | P9 |
|---|---|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 39.4 | 39.9 | 33.7 | 46.8 | 42.5 | 44.5 | 49.5 | 51.9 | 65.9 |
| 4 | 52.1 | 55.4 | 50.2 | 51.2 | 53.6 | 59.6 | 68.9 | 70.8 | 82.2 |
| 6 | 80.4 | 82.3 | 84.1 | 86.3 | 87.0 | 90.0 | 92.2 | 94.0 | 99.1 |
| 8 | 85.4 | 86.9 | 89.6 | 92.5 | 91.3 | 93.5 | 95.6 | 96.8 | 99.8 |
| 10 | 89.8 | 92.9 | 93.1 | 96.4 | 94.9 | 96.8 | 97.8 | 98.9 | 99.9 |

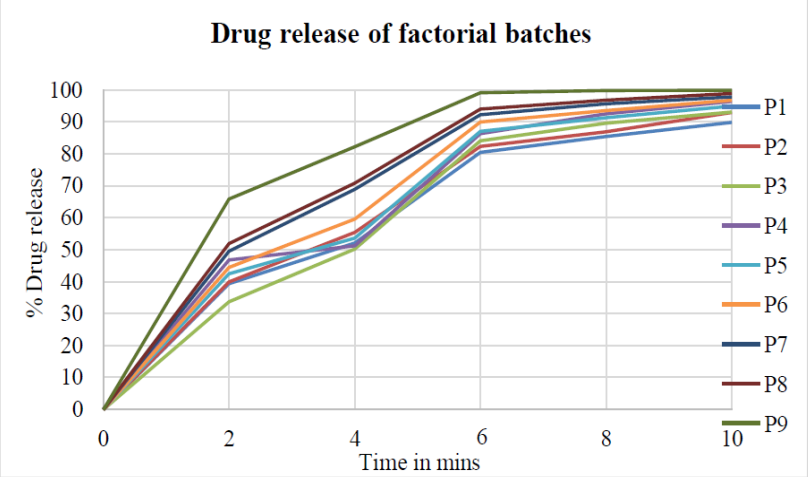


**Fig. 5: Comparative dissolution profile of factorial batches.**

**Analysis of factorial design**

**Table 15: Analysis of factorial design.**

| $3^2$ Full Factorial Design Layout | | | | |
|---|---|---|---|---|
| Batch code | Independent variable | | Dependent Variables | |
| | X1 | X2 | Y1 % Drug release at 6 min | Y2 Disintegration time (sec) |
| P1 | -1 | -1 | 80.4 | 52 |
| P2 | -1 | 0 | 82.3 | 48 |
| P3 | -1 | +1 | 84.1 | 41 |
| P4 | 0 | -1 | 86.3 | 37 |
| P5 | 0 | 0 | 87.0 | 32 |
| P6 | 0 | +1 | 90.0 | 28 |
| P7 | +1 | -1 | 92.2 | 25 |
| P8 | +1 | 0 | 94.0 | 23 |
| P9 | +1 | +1 | 99.1 | 20 |

| Translation of coded level in actual unit | | | |
|---|---|---|---|
| Independent variables | Real Value | | |
| | Low(-1) | Medium(0) | High(+1) |
| X1-Amount of Pharmaburst 500® (mg) | 140 | 150 | 160 |
| X2-Amount of Crospovidone (mg) | 35 | 45 | 55 |

- Independent variables

X1- Amount of Pharmaburst 500® (mg) (A) X2- Amount of Crospovidone (mg) (B)

- Dependent variables

Y1- % Drug release at 6 min Y2- Disintegrating time (sec)

**ANOVA for Quadratic model**
**Response 1: Drug release at 6 min (Table 16)**

| Source | Sum of Squares | df | Mean Square | F-value | p-value | |
|---|---|---|---|---|---|---|
| **Model** | 287.04 | 5 | 57.41 | 92.05 | 0.0018 | significant |
| A-Pharmaburst 500® | 247.04 | 1 | 247.04 | 396.09 | 0.0003 | |
| B-Crospovidone | 34.08 | 1 | 34.08 | 54.64 | 0.0051 | |
| AB | 2.56 | 1 | 2.56 | 4.10 | 0.1359 | |
| $A^2$ | 1.68 | 1 | 1.68 | 2.69 | 0.1992 | |
| $B^2$ | 1.68 | 1 | 1.68 | 2.69 | 0.1992 | |
| **Residual** | 1.87 | 3 | 0.6237 | | | |
| **Cor Total** | 288.92 | 8 | | | | |

Factor coding is **Coded**.
Sum of squares is **Type III - Partial**
The **Model F-value** of 92.05 implies the model is significant. There is only a 0.18% chance that an F-value this large could occur due to noise.

**P-values** less than 0.0500 indicate model terms are significant. In this case A, B are significant model terms. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

**Final equation in terms of coded factors**
Drug release at 6 min =+87.16+6.42 A+2.38 B+0.8000 AB+0.9167 $A^2$+0.9167 $B^2$
The equation in terms of coded factors can be used to make predictions about the response for given levels of each factor. By default, the high levels of the factors are coded as +1 and the low levels are coded as -1. The coded equation is useful for identifying the relative impact of the factors by comparing the factor coefficients.

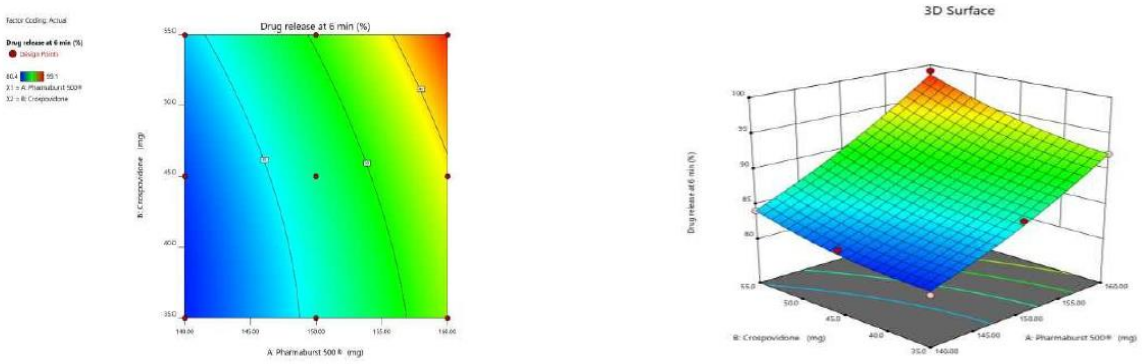


**Fig. 6: Response 1: Drug release at 6 min.**

**ANOVA for Quadratic model**
**Response 2: Disintegration time (Table 17)**

| Source | Sum of Squares | df | Mean Square | F-value | p-value | |
|---|---|---|---|---|---|---|
| **Model** | 1014.33 | 5 | 202.87 | 365.16 | 0.0002 | significant |
| A-Pharmaburst 500® | 888.17 | 1 | 888.17 | 1598.70 | < 0.0001 | |
| B-Crospovidone | 104.17 | 1 | 104.17 | 187.50 | 0.0008 | |
| AB | 9.00 | 1 | 9.00 | 16.20 | 0.0276 | |
| $A^2$ | 12.50 | 1 | 12.50 | 22.50 | 0.0178 | |
| $B^2$ | 0.5000 | 1 | 0.5000 | 0.9000 | 0.4128 | |
| Residual | 1.67 | 3 | 0.5556 | | | |
| Cor Total | 1016.00 | 8 | | | | |

Factor coding is **Coded**.
Sum of squares is **Type III - Partial**
The **Model F-value** of 365.16 implies the model is significant. There is only a 0.02% chance that an F-value this large could occur due to noise.

**P-values** less than 0.0500 indicate model terms are significant. In this case A, B, AB, $A^2$ are significant model terms. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

**Final equation in terms of coded factors**
Disintegration time =+32.67-12.17 A-4.17 B+1.50 AB+2.50 $A^2$-0.5000 $B^2$
The equation in terms of coded factors can be used to make predictions about the response for given levels of each factor. By default, the high levels of the factors are coded as +1 and the low levels are coded as -1. The coded equation is useful for identifying the relative impact of the factors by comparing the factor coefficients.

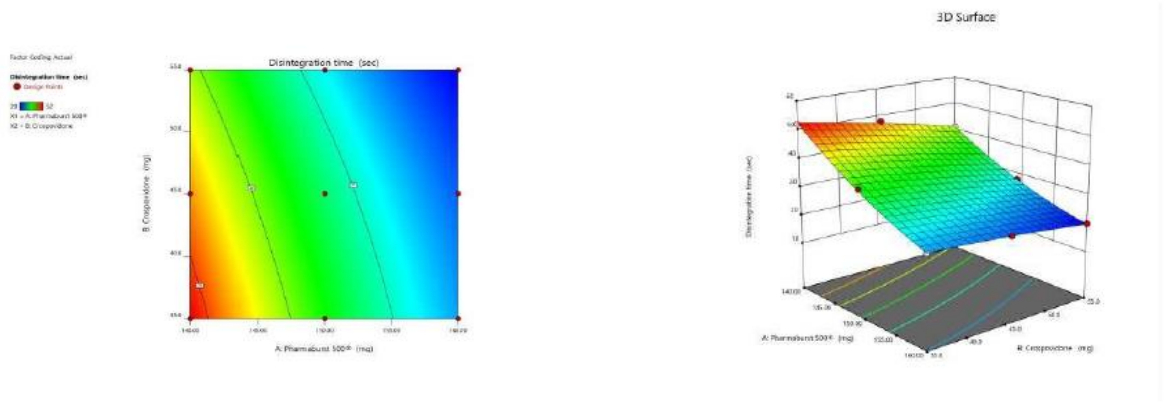


**Fig. 7: Response 2: Disintegration time.**

**Check point batch**
A checkpoint batch was created based on the desirability function, as presented in Table 6.12. To validate the predictions, checkpoint batches C1 was prepared and tested under the same conditions as the other batches. The response data was compared against the required data. The response variables obtained from the checkpoint batches were analyzed in relation to the target response parameters, and the bias between predicted and observed responses was found to be acceptable.

**Table 18: Check point batch.**

| Batch | Amount of X1 (mg) | Amount of X2 (mg) | % Drug release in 6 min | | | Disintegration time (sec) | | |
|---|---|---|---|---|---|---|---|---|
| | | | Predicted | Observed | % Bias | Predicted | Observed | % Bias |
| C1 | 150.7 | 48.7 | 88.6 | 87.9 | 1.00 | 30 | 29 | 1.03 |

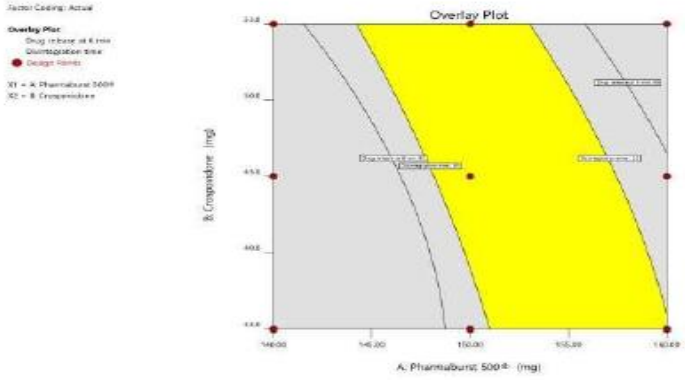


**Fig. 8: Overlay plot for checkpoint batch.**

**Stability study**
Stability study of optimized batch P9 was carried out and results recorded in following table. Formulation found stable and no any critical observation seen during stability.

**Table 19: Results of stability study.**

| Evaluation parameter | Initial | 30th day |
|---|---|---|
| Physical appearance | White colored, round tablet | White colored, round tablet |
| % Drug Content ± SD (n=3) | 98.8 ±1.4 | 98.4 ± 1.3 |
| Disintegration time ± SD (sec) (n=3) | 20 ± 3 | 22 ± 2 |
| % Drug release in 10 mins (n=3) | 99.9 ± 1.2 | 99.6 ± 1.7 |

## CONCLUSION

Desvenlafaxine dispersible tablets were successfully formulated using the direct compression method. Preformulation studies, including IR spectroscopy, confirmed compatibility between the drug and excipients. All formulations met pharmacopeial standards for weight variation, hardness, friability, disintegration time, and dissolution. Rapid disintegration (<2 minutes) and effective drug release were observed, with F8 and F9 disintegrating in under 30 seconds. F8 showed >90% drug release at 10 minutes even at a lower disintegrant level. A $3^2$ full factorial design was employed using Crospovidone and Pharmaburst as variables, and evaluation of factorial batches (P1–P9) confirmed the influence of these factors on tablet performance. Among them, formulation P9 was optimized, exhibiting excellent physicochemical properties and stability, making it the most effective and stable formulation.

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