Original Research Article

Formulation and evaluation of fast dissolving tablet containing domperidone ternary solid dispersion

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Abstract

Introduction: Fast dissolving tablet containing domperidone ternary solid dispersion was developed to improve the dissolution of drug and stability of solid dispersion. **Materials and Methods:** Binary and ternary solid dispersions were prepared by fusion method. They were characterized by solubility study, *in vitro* dissolution, dissolution efficiency, and stability study. The solid state properties of solid dispersions were characterized by differential scanning calorimetry (DSC), Fourier transform infrared spectroscopy (FTIR), and X-ray diffraction (XRD). Ternary solid dispersion was successfully incorporated into fast dissolving tablet by direct compression method. Tablets were characterized for pre-compression parameters, post-compression parameters, and stability study. **Results:** Optimized ternary solid dispersion containing ratio 1:2:1.5 of drug: Gelucire 50/13: Poloxamer 188 gave maximum dissolution. The FTIR, DSC, and XRD studies of solid dispersions were confirmed the formation of solid dispersion. Ternary solid dispersion was more stable compared to binary solid dispersion at accelerated environment conditions for one month as confirmed by DSC study. Crospovidone as a superdisintegrant (4%) showed good result with disintegration time of 19 s and dissolution near to 100% in 0.1N HCL at 30 min. **Conclusion:** The studies indicated that the dissolution of drug and stability of solid dispersion was improved in the presence of ternary agent (surfactant) as compared to binary solid dispersion. It was concluded that fast dissolving tablet containing ternary solid dispersion was stable at accelerated environmental conditions for 1 month.

Key words: *Fast dissolving tablet, fusion method, gelucire 50/13, poloxamer 188, stability, ternary solid dispersion*

INTRODUCTION

Domperidone has low aqueous solubility and dissolution (biopharmaceutical classification system [BCS] class II drug); hence it exhibits poor *in vivo* bioavailability. Several techniques are commonly used to improve dissolution and bioavailability of poorly water soluble drugs, such as size reduction, the use of surfactants, and the formation of solid dispersions. The latter are defined as dispersions of one or more active ingredients in an inert carrier in the solid state.[1,2] Mechanisms involved include increased wettability, solubilization of the drug by the carrier

at the diffusion layer, and reduction or absence of aggregation and agglomeration. Moreover, transformation of the crystalline drug to the amorphous state upon solid dispersion increases the dissolution rate since no lattice structure has to be broken down for dissolution to take place. Formation of solid dispersions is one of the most widely studied dissolution-enhancing strategies. Nonetheless, only few marketed products rely on this concept.[3,4] The main reason for this discrepancy is the possible physical instability of these structures. Phase separation, crystal growth, or conversion from the amorphous to the crystalline state during storage inevitably leads to reduced dissolution rates. To prevent recrystallization, carriers that reduce molecular mobility are added. Moreover, hydrophilic polymers are able to enhance drug supersaturation. In addition, to enhance drug supersaturation, surfactants decrease aggregation, improve wetting, and increase dissolution of drug.[5-7]

Vomiting is a common problem for all age groups. Pediatric, geriatric, and bedridden patients suffer from dysphasia, which results in high evidence of ineffective therapy. During travelling, the water availability chances may be less and also vomiting occurs in some people. In these conditions, fast dissolving tablet are gaining prominence as new drug delivery systems. These dosage forms dissolve or disintegrate in the oral cavity within a matter of seconds without the need of water or chewing.[8,9]

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Domperidone does not readily cross the blood-brain barrier. Domperidone is, therefore, more advantageous than any other antiemetic drug. As per BCS, domperidone is class II drug with poor water solubility and erratic absorption in the stomach and possess several dissolution problem thus, it has poor bioavailability (15%).[10]

The aim of the present study was two-fold: First, a ternary solid dispersion was developed made up of ternary agent (surfactant) and polymer, thus, combining the advantages of both excipients on drug release and stability. The polymer will be selected based on preliminary screening. Few research articles have reported on ternary solid dispersion systems using conventional carriers.[11-14] Only few new carriers have been developed in the last decade due to increasing regulatory demands. It is, therefore, recommended to build up new carrier systems made up of a combination of two or more well-known excipients. Second, fast dissolving tablet was developed using ternary solid dispersion.

MATERIALS AND METHODS

Materials

Domperidone (Nirlife Healthcare, Ahmedabad, India); Gelucire 44/14 and Gelucire 50/13 (Gattefosse India Private Limited); Poloxamer 188 and Poloxamer 407 (BASF chemical company, Germany); Polyethylene glycol 4000 (PEG 4000), Polyethylene glycol 6000 (PEG 6000) and polyvinyl pyrrolidone K30 (PVP K30) (S. D. Fine Chemical Limited, Mumbai, India); Mannitol (Sigma Aldrich, product of China); Sodium starch glycolate and crospovidone (Chemdyes corporation, Ahmedabad, India); crosscarmellose sodium (Yarrow chem., Mumbai), and other chemicals and reagent used in the study were obtained commercially and used as received. All other materials and chemicals used were of either pharmaceutical or analytical grade.

Methods
Preparation of physical mixture

Physical mixture of domperidone with carrier was prepared by thoroughly mixing the accurately weighed quantity of drug and the carrier in a glass mortar with the help of the pestle. This mixture was then subsequently passed through 80# sieve and stored in a dessicator for 24 h.

Solubility study

Solubility study was conducted as per the method reported by Higuchi and Connors.[15] Excess quantity (50 mg) of the drug was taken for study. The solubility of domperidone and physical mixture was determined in different media (0.1N HCL and distilled water). Drug and carrier as per the specified drug: Carrier ratio was weighed accurately and added to 10 ml of water in screw-capped bottles. All the bottles were shaken in an incubator shaker at 37°C and 24°C for 24 h. Then, the solutions were filtered, and concentration of drug was determined by ultraviolet (UV) spectrophotometer.

Preparation of solid dispersion

For the optimization of drug: Polymer ratio, solid dispersions were prepared by the fusion method. In this method, carriers were melted above 5°C than its melting point in porcelain dish and to this a weighed amount of domperidone was added with continuous stirring until homogenization. Solidification was allowed to occur at room temperature. The product was stored in a dessicator for 24 h and then pulverized using a glass mortar and pestle. The pulverized powders were passed through 80# sieve. The assay for drug content was carried out before and after preparation of solid dispersion to check the possible degradation effect of heating. The powder equivalents to 10 mg domperidone were evaluated for *in vitro* dissolution study.

Selection of the carrier for binary solid dispersion

For the selection and optimization of drug: Polymer ratio, different physical mixtures were prepared with the different polymers in the ratio of 1:1 and 1:2. Six polymers were taken for screening of polymer for binary solid dispersion. They were gelucire 50/13, gelucire 44/14, PVP K30, mannitol, PEG 6000, and PEG 4000. Twelve batches of physical mixtures were prepared and evaluated for solubility study [Table 1]. The optimized ratio of drug: Polymer was found to be 1:2 of drug: Gelucire 50/13. Solid dispersion of drug: Gelucire 50/13 (1:2) was prepared by fusion method and evaluated for solubility study, assay, and *in vitro* dissolution study. Percentage dissolution efficiency (% DE) was also calculated.

Selection of ternary agent for ternary solid dispersion

For the selection of ternary agent, poloxamer 188, and poloxamer 407 were taken as ternary agents in a fixed ratio of 1:2:0.5 of drug: Gelucire 50/13: Ternary agent. The ternary solid dispersions were prepared by fusion method. The batch for poloxamer 188 was coded as L1 and for poloxamer 407 was coded as L2 as shown in

Table 1: Solubility study of physical mixtures in distilled water and 0.1N HCL

Batches	Ratio	Solubility in media (mg/ml) (*n* = 3)	
		Distilled water	**0.1N HCL**
D	—	0.00095±0.00004	0.423±0.004
50G1	1:1	0.094±0.002	2.233±0.005
50G2	1:2	0.134±0.004	3.815±0.014
44G1	1:1	0.063±0.002	1.476±0.013
44G2	1:2	0.089±0.005	1.835±0.05
P1	1:1	0.053±0.005	1.433±0.008
P2	1:2	0.058±0.003	1.589±0.007
M1	1:1	0.064±0.007	1.154±0.004
M2	1:2	0.034±0.004	1.296±0.005
S1	1:1	0.051±0.005	1.542±0.007
S2	1:2	0.053±0.003	1.667±0.005
N1	1:1	0.036±0.005	1.371±0.01
N2	1:2	0.074±0.006	1.767±0.023
Solubility study for optimization of the ratio for preparation of binary solid dispersion			
Batches	Ratio	Distilled water	0.1N HCL
50G3	1:3	0.131±0.002	3.807±0.004
50G4	1:4	0.127±0.003	2.916±0.005

n: Number of replicates, HCL: Hydrochloric acid

Table 2. They were evaluated for assay and *in vitro* dissolution study. % DE was also calculated. The screened ternary agent was found to be poloxamer 188; hence, it was taken for further study.

Selection of drug: Gelucire 50/13: Poloxamer 188 ratio

For screening of drug: Gelucire 50/13: Poloxamer 188 ratio, amount of poloxamer 188 was increased from 1:2:1 to 1:2:2. Three batches were prepared (1:2:1, 1:2:1.5, and 1:2:2). The batches were coded as M1, M2, and M3 as shown in Table 3. These ternary solid dispersions were prepared by fusion method. They were evaluated for assay and *in vitro* dissolution study. From the *in vitro* dissolution study, no much difference in dissolution between 1:2:1.5 and 1:2:2 ratios was found. Hence, 1:2:1.5 ratio of drug: Gelucire 50/13:Poloxamer 188 was selected as optimized ternary solid dispersion.

Evaluation of solid dispersions

For the determination of % drug content, accurately weighed solid dispersion equivalent to 10 mg of domperidone was transferred to 100 ml of volumetric flask and diluted to 100 ml with methanol and sonicated for 30 min for complete solubilization of the drug. The solution was filtered through a 0.45 μ filter and measured at 287 nm in double beam UV spectrophotometer (UV 1800, Shimadzu, Kyoto, Japan). Concentration of domperidone was determined using the calibration curve of the drug in methanol.

The *in vitro* dissolution study of solid dispersions was performed using USP apparatus type I fitted with a basket (75 rpm) at 37°C ± 0.5°C using 0.1N HCL as dissolution medium. At the pre-determined time intervals, 10 ml samples were withdrawn, filtered through a 0.45 μm membrane filter and assayed at 284 nm using a double beam UV spectrophotometer. Cumulative percentage drug (CPR) release was calculated using an equation obtained from a calibration curve. From the CPR, DE at 30 min was calculated. DE represents the area under the dissolution curve at time t (measured using the trapezoidal rule) and expressed as a percentage of the area of the rectangle described by

100% dissolution in the same time.[16] It is calculated by following equation. Where, *y* is the drug percent dissolved at time *t*.

$$D.E. = \frac{\int_{0}^{t} y \times dt}{y_{100} \times t} \times 100\% \tag{1}$$

Fourier transform infrared spectroscopy study

Fourier transform infrared spectroscopy has been used to study the physical and chemical interactions between drug and the excipients used. Fourier transform infrared spectroscopy (FTIR) spectra of drug and physical mixture were recorded using KBr mixing method on FTIR instrument available at central instrument laboratory of the institute (FTIR-1700, Shimadzu, Kyoto, Japan).

Differential scanning calorimetry study

For checking the solid state property of the drug, polymers, and solid dispersions, differential scanning calorimetry (DSC) study was carried out using DCS 60 (Shimadzu, Kyoto, Japan). Samples were placed in pierced aluminum pans and scanned at a heating rate of 10°C/min from 30°C to 300°C in a nitrogen atmosphere.

X-ray diffraction study

Physical natures of solid dispersions were analyzed by X-ray diffraction (XRD). XRD patterns of the powdered samples of the drug and the solid dispersion were recorded using X-ray powder diffractometer (Phillips X-Pert MPD, The Netherlands) with a copper tube anode over the interval 1-40° $2\theta^{-1}$. The operational parameters were as follows: Generator tension (voltage) of 45 kV; generator current of 40 mA; scan step time of 9/s, and scan step size of 0.008° (2θ).

Short-term stability testing of solid dispersion

The stability studies were carried out on the most satisfactory formulations as per ICH guideline Q1C. The most satisfactory formulation was filled in high-density polyethylene bottle which is sealed with aluminum packaging and kept in the humidity chamber maintained 40 ± 2°C/75% ± 5% relative humidity (RH) for 1 month. At the end of studies, samples were analyzed for the assay and *in vitro* drug release. Solid state property of solid dispersion after stability period was also characterized by DSC.

The similarity factor (f_2) given by SUPAC guidelines for a dosage form was used as a basis to compare dissolution profiles of before stability and after stability. The dissolution profiles are considered to be similar when f_2 is between 50 and 100. The dissolution profile was compared using f_2 which is calculated from following formula.[17,18]

$$f_2 = 50 \times \log\left\{[1+(\tfrac{1}{n})\sum_{t=1}^{n} w_t (R_t - T_t)^2]^{-0.5} \times 100\right\} \tag{2}$$

Where, *n* is the dissolution time and R_t and T_t are the reference (here this is the dissolution profile before stability study) and test (here this is the dissolution profile, after stability study) dissolution value at time t.

Table 2: Composition for selection of ternary agent for ternary solid dispersion

Contents (mg)	Formulation code	
	L1	L2
Drug	10	10
Gelucire 50/13	20	20
Poloxamer 188	5	—
Poloxamer 407	—	5

Table 3: Formulation for screening of drug: Gelucire 50/13: Poloxamer 188 ratio

Contents (mg)	Formulation code		
	M1	M2	M3
Drug	10	10	10
Gelucire 50/13	20	20	20
Poloxamer 188	10	15	20

Preparation of fast dissolving tablets

The ternary solid dispersion batch M2 was selected for tablet dosage forms based on its drug release profile. Three different batches of fast dissolving tablet containing a fixed concentration of superdisintegrants were prepared [Table 4] by direct compression. All the ingredients were passed through 80# sieve. Solid dispersion (45 mg is equivalent to 10 mg domperidone) was mixed with superdisintegrant (crosscarmellose sodium, crospovidone, or sodium starch glycolate), mannitol and directly compressible microcrystalline cellulose as diluents and other excipients such as magnesium stearate (1%) and talc (2%). The powder blend was directly compressed using 8 mm flat punches on a double rotary tablet compression machine (Rimek 10 station minipress).

Crospovidone was selected as more suitable superdisintegrant for fast dissolving tablet. Three batches of fast dissolving tablet containing different concentrations of crospovidone were prepared [Table 5] by the same procedure described earlier.

Evaluation of tablet properties

Prepared tablets were characterized for hardness, friability, *in vitro* disintegration time, wetting time, uniformity of weight, drug content, and *in vitro* dissolution study. The hardness of the tablets was measured using a Monsanto hardness tester (Janki Impex, India). The limits for crushing strength of the tablets were kept in the range of 3-5 kg/cm^2. The friability of the tablets was measured using a Roche Friabilator (Hicon, Grover Enterprise, Delhi, India).

Table 4: Formulation of fast dissolving tablets for selection of superdisintegrant

Ingredients (mg)	F1	F2	F3
Optimized ternary solid dispersion*	45	45	45
Crospovidone	4.5	—	—
Crosscarmellose sodium	—	4.5	—
Sodium starch glycolate	—	—	4.5
Microcrystalline cellulose	57.6	57.6	57.6
Mannitol	38.4	38.4	38.4
Talc	3	3	3
Magnesium stearate	1.5	1.5	1.5
Total	150	150	150

*Optimized ternary solid dispersion equivalent 10 mg of domperidone

Table 5: Formulation of fast dissolving tablets for screening of concentration of superdisintegrant

Ingredients	Quantity per tablet (mg)		
	P1	P2	P3
Optimized ternary solid dispersion*	45	45	45
Crospovidone	3	4.5	6
Microcrystalline cellulose	58.5	57.6	56.7
Mannitol	39	38.4	37.8
Talc	3	3	3
Magnesium stearate	1.5	1.5	1.5
Total	150	150	150

*Optimized ternary solid dispersion equivalent 10 mg of domperidone

Six pre-weighed tablets were rotated for 4 min at 25 rpm. The tablets were then weighed again, and the percentage of weight loss was calculated the limit of the percent friability was kept below 1%. The *in vitro* disintegration test was carried out on six tablets using tablet disintegration tester ED-2 L (Electrolab, Mumbai, India) in distilled water at 37°C ± 2°C and the time in second taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured in seconds.

The wetting time of the tablets was measured using a reported procedure. Five circular tissue papers of 9 cm diameter were placed in a petridish with a 9-cm-diameter containing 10 ml of purified water. Ten ml of water containing Eosin, a water soluble dye, was added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required to develop a red color on the upper surface of the tablet was recorded as the wetting time.

The weights were determined to within ± 1 mg by using sartorius balance (Model BT-124S). Weight control is based on a sample of 20 tablets. Determinations were made in triplicate. Drug content was determined by weighing randomly selected tablets, pulverizing to a fine powder. The weight equivalent to 10 mg domperidone was weighed and dissolved in 5 ml of methanol in volumetric flask using magnetic stirrer, the volume was adjusted to 100 ml with 0.1N HCL, and the solution was filtered. After suitable dilution, the content drug was determined spectrophotometrically at 284 nm.

In vitro dissolution study of fast dissolving tablets carried out using the USP Apparatus 2 (Paddle apparatus). The dissolution test was carried out using 900 ml of 0.1N HCL at 37°C ± 0.5°C at 50 rpm. A sample of the solution was withdrawn from the dissolution apparatus at specific time intervals and withdrawn volume was replaced with fresh dissolution media, filtered, and assayed spectrophotometrically.

Comparison of optimized formulation with marketed formulation

In vitro release study of optimized fast dissolving tablet of domperidone and marketed formulation were carried out using the USP apparatus 2 (Paddle apparatus). The dissolution test was carried out using 900 ml of 0.1N HCL at 37°C ± 0.5°C at 50 rpm. A sample of the solution was withdrawn from the dissolution apparatus at 5, 10, 20, 30, 45, and 60 min, and withdrawn volume was replaced with fresh dissolution media, filtered, and assayed spectrophotometrically.

Stability testing of optimized fast dissolving tablet

Stability study for a representative sample (P3) was carried out at 40°C ± 2°C/75 ± 5% RH for 1 month. The effect on various tablet properties such as hardness, disintegration time, wetting time drug content, and *in vitro* dissolution were measured. Similarity factor f_2 was also calculated.

RESULTS AND DISCUSSION

Solubility study

The solubility of domperidone was found to be 0.00095 mg/ml in distilled water and 0.423 mg/ml in 0.1N HCL [Table 1]. The physical mixture of drug: Gelucire 50/13 containing 1:2 ratio shows the highest solubility 0.134 mg/ml in distilled water and 3.815 mg/ml in 0.1N HCL as shown in Table 1. Hence, for further study, the ratio was increased up to 1:4. Any significant improvement in solubility was not seen, when increase the ratio of drug: Gelucire 50/13. Hence, 1:2 ratio of physical mixture was selected for preparation of binary solid dispersion. The solubility of binary solid dispersion was found to be 0.805 mg/ml in distilled water and 5.895 mg/ml in 0.1N HCL. Hence, solubility of binary solid dispersion was more compared to physical mixture. The drug content of binary solid dispersion was found to be 98.76%. The % DE of binary solid dispersion was found to be 67.82 at 30 min.

Selection of ternary agent for ternary solid dispersion

Poloxamer 188 as ternary agent in fixed ratio 1:2:0.5 of drug: Gelucire 50/13: Ternary agent shows better *in vitro* dissolution as compared to poloxamer 407 as ternary agent as shown in Figure 1. The % drug content for both solid dispersions was found to be in the range of 99-101% w/w. The % D.E. of drug: Gelucire 50/13: Poloxamer 188 in the ratio of 1:2:0.5 was found to be 76.59 at 30 min. The screened ternary agent was found to be poloxamer 188 from the study.
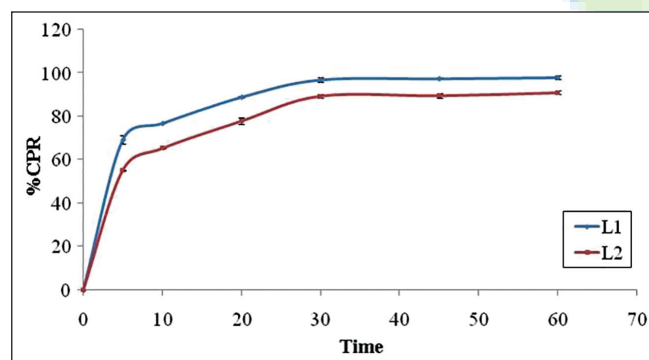
Selection of drug: Gelucire 50/13: Poloxamer 188 ratio

From the *in vitro* dissolution study, no much difference in dissolution between 1:2:1.5 ratio and 1:2:2 ratio was found as shown in Figure 2. The percentage of drug content for all batches was found to be within the range of 98.63-99.81. Hence, 1:2:1.5 ratio of drug: Gelucire 50/13: Poloxamer 188 was selected as optimized ternary solid dispersion on the basis of *in vitro* drug release profile. The percentage of D.E optimized ternary solid dispersion was found to be 91.29 at 30 min.

Comparison of ternary solid dispersion with binary solid dispersion

Dissolution studies revealed that the dissolution of the drug from ternary solid dispersion was more in comparison to binary solid dispersion as shown in Figure 3. The *in vitro* drug release from binary and ternary solid dispersions were found to be 89.576% and nearly100%, respectively. This improvement was due to the presence of ternary agent poloxamer 188, which can probably be explained by increased wettability of domperidone. Indeed, poloxamer 188 causes a decrease of the interfacial tension between the drug and the dissolution medium.

Solid state studies

The FTIR spectrum of pure drug and ternary system (1:2:0.5) with gelucire 50/13 and poloxamer 188 are presented in Figures 4 and 5, respectively. Pure drug shown sharp characteristic bands at 3122, 1720, 1677, 1488, and 1271 cm^{-1} due to stretching vibration bands of C=O, N-H, C-N, and two C-O, respectively. It was observed that there were no changes in these main bands in the FTIR spectra of the ternary system of drug with excipients. The FTIR study revealed no physical or chemical interactions of domperidone with gelucire 50/13 and poloxamer 188.
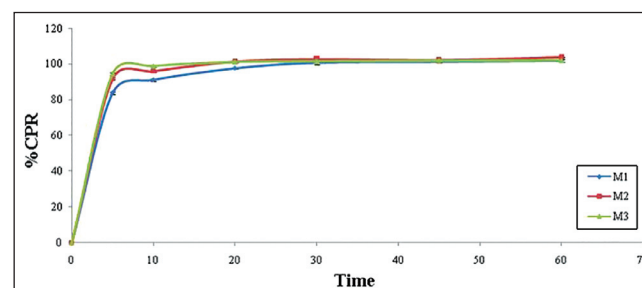

Figure 1: *In vitro* dissolution profile of L1 and L2 in 0.1N HCL

Figure 2: *In vitro* dissolution profile of batches M1, M2, and M3 in 0.1N HCL

Figure 3: Comparison of *in vitro* dissolution profile between binary and ternary solid dispersions
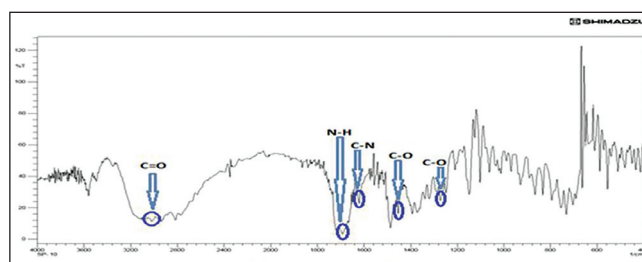

Figure 4: Fourier transform infrared spectroscopy spectrum of pure drug

The DSC thermograms of pure drug, polymer, and carrier systems are depicted in Figures 6-10. The thermogram of drug was characterized by melting endotherm at 253.79°C. As expected, DSC analysis demonstrated that the domperidone was rendered entirely amorphous in the ternary solid dispersion as compared to binary solid dispersion as indicated by the absence of the melting endothermic peak for domperidone at approximately 253.79°C.

The X-ray diffractograms of pure domperidone, binary solid dispersion, and ternary solid dispersion are shown in Figures 11-13, respectively. The diffraction spectrum of pure domperidone showed that the drug was of crystalline in nature as demonstrated by numerous, distinct peaks at 2θ. The spectrum of binary solid dispersion prepared with Gelucire 50/13 and ternary solid dispersion prepared with a mixture of gelucire 50/13 and poloxamer 188 showed a reduction in the total number of peaks, base broadening of appeared peak along with a reduction in peak intensity providing convincing evidence for the formation of amorphous form in ternary solid dispersion. The result indicates that the drug in solid dispersion was in amorphous form. Hence, increased dissolution of the drug was observed.

Short-term stability testing of solid dispersion

After stability study, assay of the ternary and binary solid dispersion was found to be within the range of 98.26-99.95. Hence, there was no degradation of domperidone in ternary and binary solid dispersions. Solid dispersion was found satisfactory with respect to physical appearance. It was observed that there was much difference in dissolution of binary solid dispersion before and after stability (similarity factor $f_2 = 66.42$). There was no significant difference found in the dissolution profile of ternary solid dispersion during stability study (similarity factor $f_2 = 85.58$).

After stability conditions, intensity of the endothermic peak of domperidone in binary solid dispersion was changed as shown in Figure 14, but there was no change in ternary solid dispersion as shown in Figure 15. The endothermic peak of pure drug was remained absent in ternary solid dispersion after stability conditions. Hence, ternary solid dispersion was more stable as compared to binary solid dispersion due to the presence of surfactant poloxamer 188 as ternary agent. Studies indicate that the ternary agent prevent the recrystallisation of amorphous drug and improve the stability of solid dispersion.
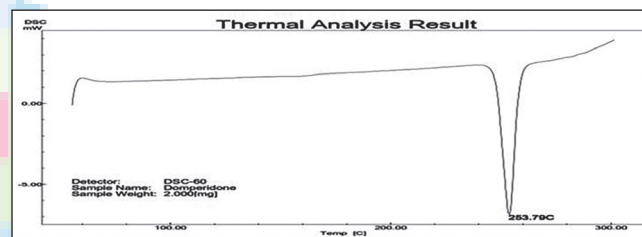

Figure 5: Fourier transform infrared spectroscopy spectrum of the ternary system containing gelucire 50/13 and poloxamer 188

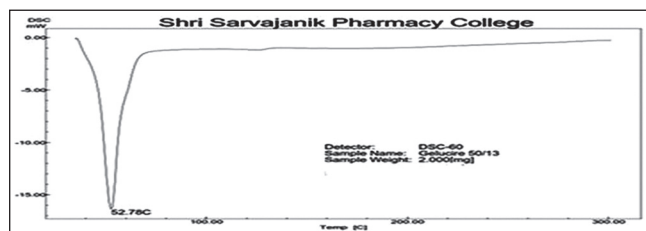**Figure 6:** Differential scanning calorimetry thermogram of pure drug

Figure 7: Differential scanning calorimetry thermogram of gelucire 50/13
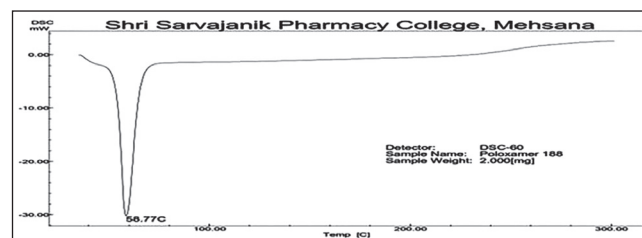

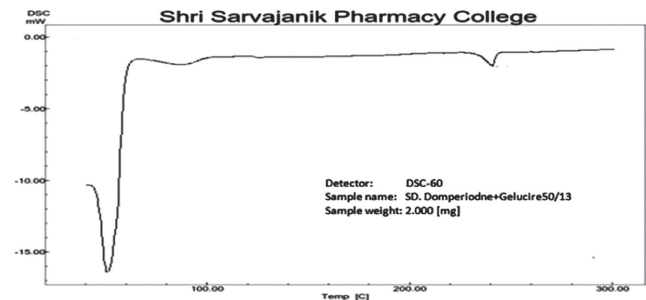**Figure 8:** Differential scanning calorimetry thermogram of poloxamer 188

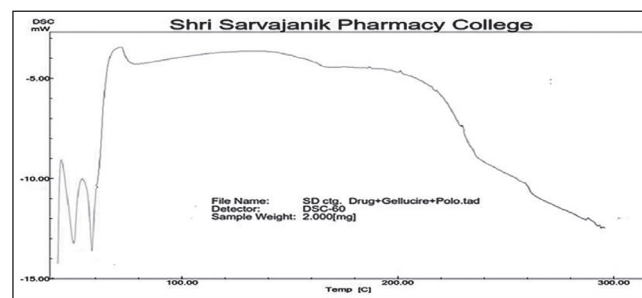**Figure 9:** Differential scanning calorimetry thermogram of binary solid dispersion

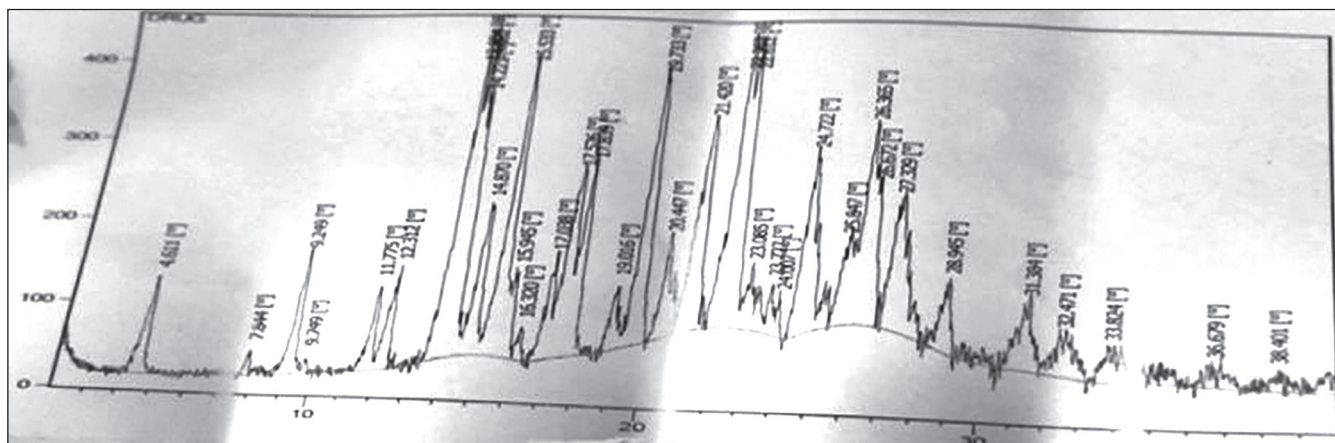**Figure 10:** Differential scanning calorimetry thermogram of optimized ternary solid dispersion

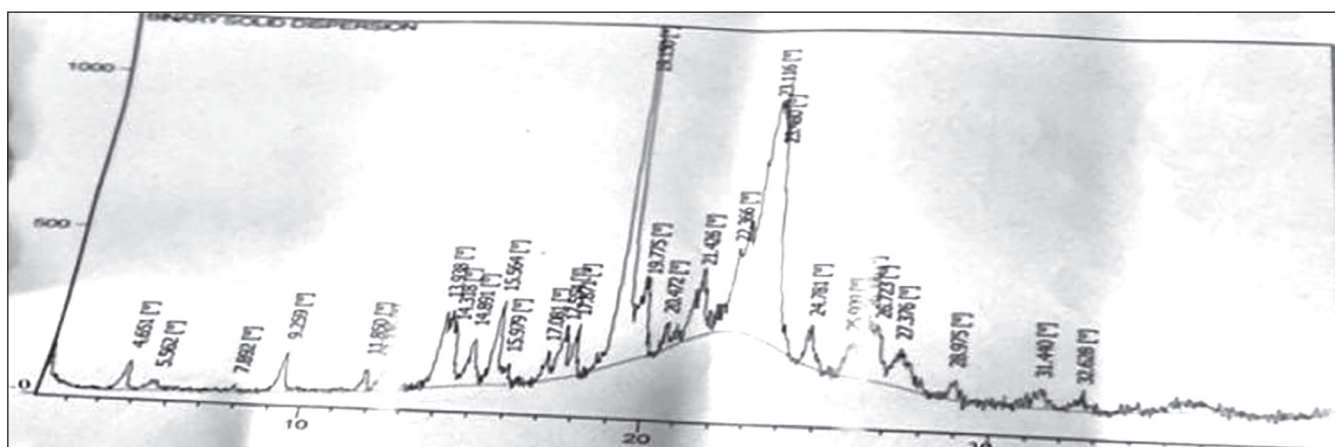**Figure 11:** X-ray diffractogram of pure drug

Figure 12: X-ray diffractogram of binary solid dispersion

Evaluation of tablet properties

The hardness, thickness, friability, uniformity of weight, disintegration time, wetting time, and percentage of drug content formulations F1, F2, and F3 are shown in Table 6. From the evaluation parameters, it has been shown that F1 batch showed good disintegration and wetting time. Hence, crospovidone was selected for further study in different concentrations (2-4%). The hardness, thickness, friability, uniformity of weight, disintegration time, wetting time, and percentage of drug content P1, P2, and P3 are shown in Table 7. The hardness values of formulations were within the range of 3-5 kg/cm². Friability values of all formulations were <1% was an indication of good mechanical resistance of the tablets. All formulations were found to be within IP limits as per weight variation test. The uniformity of content was found within Pharmacopoeial limits of 98-102%. Wetting time and disintegration time result shows that as the amount of crospovidone increase, it leads to decrease the disintegration time and wetting time [Table 7]. Among all batches, P3 batch having 4% of crospovidone gave best release. Hence, P3 batch was selected as optimized formulation. The *in vitro* drug release of optimized formulation was found to be near to 100% at 30 min.

Table 6: Evaluation parameters of F1, F2 and F3 batches

Parameters	F1	F2	F3
Hardness (kg/cm²) (*n*=6)	3.986±0.503	3.921±0.465	4.311±0.473
Thickness (mm) (*n*=6)	2.27±0.012	2.29±0.099	2.26±0.029
Friability (%) (*n*=6)	0.681±0.068	0.704±0.079	0.694±0.065
Weight variation (mg) (*n*=20)	151.1±0.185	150.9±0.243	151.3±0.379
Disintegration time (s) (*n*=6)	25±0.44	38±0.37	45±0.12
Wetting time (s)	28±1.06	42±0.94	58±1.13
Percentage of drug content (*n*=6)	99.71±1.20	98.47±1.48	101.51±1.70

n: Number of tablets

Table 7: Evaluation parameters of P1, P2, and P3 batches

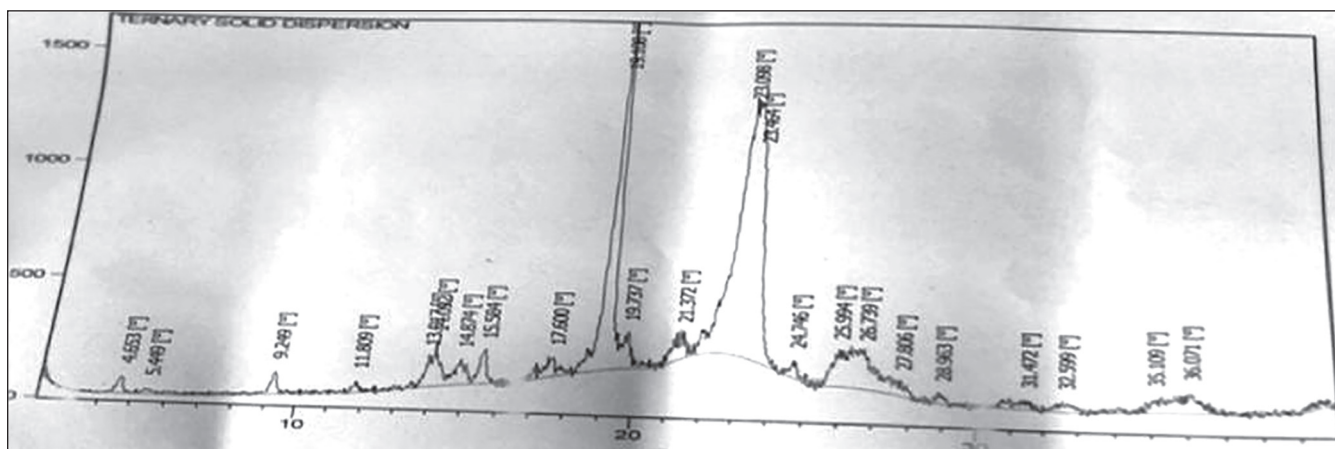| Parameters	P1	P2	P3
Hardness (kg/cm²) (*n*=6)	4.125±0.643	3.986±0.503	4.268±0.348
Thickness (mm) (*n*=6)	2.33±0.11	2.27±0.012	2.34±0.12
Friability (%) (*n*=6)	0.711±0.031	0.681±0.068	0.512±0.055
Weight variation (mg) (*n*=20)	149.98±0.134	151.1±0.185	150.7±0.178
Disintegration time (s) (*n*=6)	35±0.37	25±0.44	19±0.58
Wetting time (s)	39±1.16	28±1.06	20±0.94
Percentage of drug content (*n*=6)	98.76±1.45	99.71±1.20	100.58±1.12

n: Number of tablets

Figure 13: X-ray diffractogram of optimized ternary solid dispersion
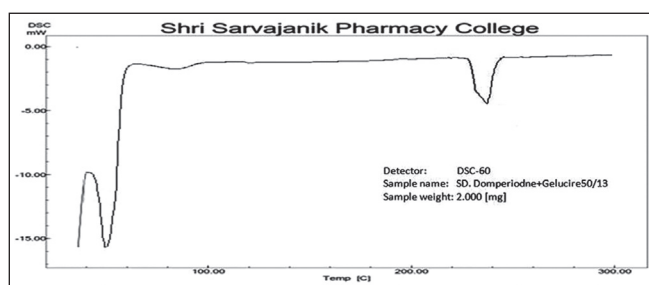

Figure 14: Differential scanning calorimetry thermogram of binary solid dispersion after stability period
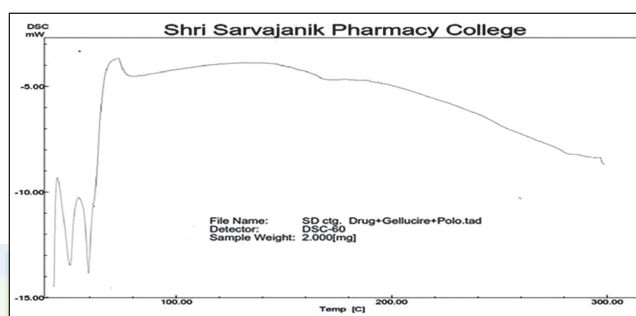

Figure 15: Differential scanning calorimetry thermogram of ternary solid dispersion after stability period
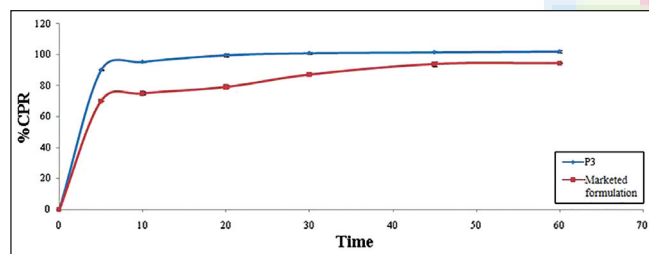

Figure 16: Comparison of dissolution between optimized batch P3 and marketed formulation

Comparison of optimized formulation with marketed formulation

The *in vitro* drug release of optimized formulation was found to be 100% at 30 min and *in vitro* drug release of marketed formulation was found to be near to 85% as shown in Figure 16. Hence, studies indicate that optimized formulation shows better dissolution as compared to marketed formulation.

Stability testing of optimized fast dissolving tablet

The result of stability testing indicates that there was no significant change in hardness, percentage of drug content, Disintegration time, and in wetting time at 40°C ± 2°C/75 ± 5% RH for 1 month. There was no significant difference found in the dissolution profile during stability study in comparison to the initial formulation. Similarity factor f_2 for before and after the stability of optimized fast dissolving tablet was found to0 be in 89.01, which indicates there was no significant difference in the dissolution profile of optimized formulation before and after stability.

CONCLUSION

The binary dispersions of domperidone with the Gelucire 50/13 and its ternary dispersion with gelucire 50/13 and poloxamer 188 were successfully prepared by the fusion method. This study demonstrated that the ternary dispersion system of the domperidone with gelucire 50/13 and poloxamer 188 possessed dramatically higher dissolution rates as compared to pure drug and also their binary dispersion. The FTIR study indicated no chemical interaction between drug and excipients. Due to the presence of surfactant in the ternary system, there was more amorphizing effect as compared to binary solid dispersion as confirmed by the DSC and XRD study. The intermolecular interactions between drug and carriers leading to better dispersion of drug in the polymer matrix, reduction in size of drug particles, increase in the amorphous nature, increase in wettability, and decrease in surface tension resulted in enhanced dissolution of the drug from the ternary dispersion systems. The ternary dispersion with poloxamer 188 presented better dissolution than those with poloxamer 407. The stability study demonstrated that

ternary drug dispersion was physically more stable than the binary dispersion as confirmed by DSC study. Fast dissolving tablet containing superdisintegrant crospovidone (4%) having disintegration time of 19 s and at 30 min was near to 100% in 0.1N HCL. Stability studies indicate that fast dissolving tablet containing ternary solid dispersion was stable at accelerated environmental conditions for 1 month.

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