DEVELOPMENT AND CHARACTERIZATION OF NEVIRAPINE LOADED AMORPHOUS SOLID DISPERSIONS FOR SOLUBILITY ENHANCEMENT

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ABSTRACT

Objective: The present study entails the development of nevirapine (NVP)-loaded solid dispersions for improvement of solubility and *in vitro* profile.

Methods: Solid dispersions were prepared through blending with a hydrophilic polymer and Vitamin E tocopherol polyethylene glycol succinate (TPGS) using the solvent evaporation method. The optimized formulations were characterized by Fourier transform infrared spectroscopy, differential scanning calorimetry, X-ray diffraction, and morphological investigations by scanning electron microscopy. The optimized formulation was converted into fast dissolving tablets (FDTs) through direct compression technique and was characterized for pre- and post-compression parameters. Both amorphous dispersions and FDTs were evaluated for *in vitro* drug release.

Results: NVP showed pH-dependent solubility in different pH media. Above 0.002% w/v Vitamin E TPGS, a linear relationship was observed between the NVP solubility and Vitamin E TPGS concentration. According to the study, the most suitable formulation was NVP:Vitamin E TPGS (1:0.75) in 30 ml solvent with a drug release of 82.96% in 2 h. The analysis of dissolution data of optimized formulation indicated the best fitting with the Higuchi model. FDTs exhibited faster drug release of about 50% in 5 min indicating desired attributes for the immediate dosage form.

Conclusion: The present study vouches for better *in vitro* profile of NVP from solid dispersion based FDTs.

Keywords: Nevirapine, Vitamin E tocopherol polyethylene glycol succinate, Solid dispersion, Fast dissolving tablets.

INTRODUCTION

A large percentage of potential drug candidates suffer from low aqueous solubility and dissolution rate. This results in low drug concentrations at the absorption sites and hence, low oral bioavailability [1]. Moreover, the poor oral bioavailability arising from poor aqueous solubility makes drug research and development even more difficult. There is a great interest to develop efficient, reliable, economical, and scalable methods to increase the oral bioavailability of poorly water-soluble drugs. Various approaches have been developed with a focus on enhancement of the solubility, dissolution rate, and oral bioavailability of poorly water-soluble drugs such as complex formation, salt formation, solid dispersion, nanosuspensions, cocrystallization, eutectic mixture, solid solutions, particle size reduction (micronization), cosolvancy, supercritical fluid process, and use of solid adjuvant such as surfactants [2-5]. The preparation of solid dispersions in pharmaceutically acceptable water-soluble polymers has been shown to be particularly effective in enhancing the rate of dissolution and oral bioavailability. BCS Class II drugs (high permeability and low solubility) are most likely to benefit from solid dispersion formulation, as once they are solubilized in the gastrointestinal tract, they will achieve an absorption profile similar to that of a Class I drugs (high permeability and high solubility) [5]. In recent years, many water-soluble polymers have been employed for preparing binary and ternary solid dispersions, such as polyethylene glycol (PEG), polyvinylpyrrolidone, HPMC, poloxamer, tocopherol polyethylene glycol succinate (TPGS), Gelucire, and Labrasol [3,4]. Nevirapine (NVP), 2-cyclopropyl-7-methyl-2,4,9,15-tetraazatricyclo [9.4.0.03,8] pentadeca-1(11),3,5,7,12,14 hexaen-10-one (Fig. 1), a reverse transcriptase (RT) inhibitor of human immunodeficiency virus (HIV-1) belongs to BCS-II system. NVP inhibits replication of HIV-1 by interfering with viral RNA-directed DNA polymerase (RT) [6].

Surfactants have historically been used for enhancing solubility and bioavailability of lipophilic compounds. TPGS is a non-ionic surfactant, synthesized from the lipid-soluble antioxidant, α-tocopherol (Vitamin E) by grafting to a PEG oligomer through a succinate di-ester linker and has been reported to increase the bioavailability of poorly water-soluble drugs by enhancing their solubility and permeability [7,8]. Based on all these considerations, the aim of the present study was to prepare a solid dispersion of NVP using Vitamin E TPGS as a drug carrier to enhance the solubility and dissolution profile of the drug.

MATERIALS AND METHODS

Materials

D-α TPGS (Vitamin E TPGS) was purchased from Sigma Laboratories Pvt., Ltd., India; NVP was obtained as a gift sample from Cipla Pharmaceuticals Ltd., India. Triple distilled water (Rions India Lab Water Systems Pvt., Ltd.) was used throughout the study. All other reagents (chemicals and solvents) used were of analytical grade.

Methods

High-performance liquid chromatographic (HPLC) analysis of NVP

Reversed-phase column based HPLC method was used. The system consisted of a pump configured to Lab Solutions software with auto-injecting facility. The HPLC was equipped with a column oven and the analytical column used was enable C-18; 4.6 mm×250 mm; 5 μm. The mobile phase used was methanol:water (50:50 v/v) at a flow rate of 0.9 ml/min in an isocratic mode. The prepared mobile phase was sonicated (Ultra cleaner, LABPRO International, India) and filtered with a 0.22 μm filter membrane (Millipore, India) before analysis. The detection was done by the SPD-M 20A photodiode array detector at 284 nm. The data processing and acquisition were done on Lab Solutions System software (version 3.1.05.9) [9].

Solubility determination in different pH solutions

The solubility of the NVP was determined in different media such as distilled water, 0.1N hydrochloric acid (pH 1.2), phosphate buffer of

pH 4.6, pH 6.8, and pH 7.2. Excess amount of drug, i.e., 10 mg of NVP was added to a glass vial containing 5 ml of medium and rotated for 72 h on a water bath shaker (Narang Scientific Works, New Delhi) at room temperature [10]. The content of each conical flask was filtered through 0.22 μm membrane filter and the filtrates were analyzed by optimized HPLC method. The solubility studies were carried out in triplicate to endorse the reproducibility of results.

Phase solubility studies

An excess amount of NVP (10 mg) was added to 5 ml of distilled water containing increasing concentrations of Vitamin E TPGS (0.005-2% w/v). The flasks were sealed and shaken at room temperature for 72 h on a water bath shaker and after attainment of equilibrium; the samples were filtered through a 0.2 μm membrane filter (Millipore, India). The solubilized amount of drug was determined using the optimized HPLC method, and all readings were taken in triplicate [11,12].

Preparation of physical mixtures (PMs) of NVP with Vitamin E TPGS

PMs were prepared by mixing accurate weight of NVP with Vitamin E TPGS in drug to polymer ratio of 1:0.25, 1:0.50, and 1:0.75 (PM1, PM2, and PM3, respectively). The mixture was pulverized and then mixed thoroughly in a mortar with a pestle until homogenous mixture was obtained. The mixture was passed through sieve no. 42 and stored in a closed container till further use.

Preparation of solid dispersions of NVP with Vitamin E TPGS

Solid dispersions of NVP with Vitamin E TPGS were prepared by the solvent evaporation method [13]. Solid dispersions of NVP in Vitamin E TPGS containing three different drugs to polymer ratios (1:0.25, 1:0.5, and 1:0.75) and using three different volumes of solvent (10 ml, 20 ml, and 30 ml) were prepared. Vitamin E TPGS was dissolved in methanol with constant stirring until a clear solution was obtained, NVP was incorporated into the solution, and stirring was continued for 45 min. The solvent was evaporated at 60°C under vacuum in a rotary evaporator (Heidolph 2 Laborota 4001, India). The resultant dispersions were placed in refrigerator for 12 h to obtain solidified dispersions. After solidification, it was pulverized and sieved through sieve no. 42 and stored in a desiccator till further use.

Characterizations of solid dispersions
Fourier transform infrared (FT-IR) spectroscopy

FT-IR spectra of different samples, namely, NVP, Vitamin E TPGS, physical mixture, and solid dispersions were recorded with FT-IR spectrophotometer (PerkinElmer, USA) [14]. The samples were analyzed in a fingerprint range of 4000–450 cm^{-1}.

Differential scanning calorimetry (DSC)

Thermal data analysis of the DSC thermogram was conducted using DSC (Q20 V24.2 Build 107, TA Instruments) software. Approximately 5 mg of NVP, PMs and solid dispersions were placed in a sealed aluminum pan and heated at a scanning rate of 2°C/min from 20°C to 300°C [15].

X-ray diffraction (XRD) study

The powder XRD patterns of NVP, PMs, and solid dispersion systems were recorded using an X-ray diffractometer (Rigaku Analytical XRD, India). XRD studies were performed under the following conditions: CuK$_\alpha$ line (λ=0.154 nm), voltage 40 kV, current 35 mA, and 2θ degrees at ambient temperature [16]. The samples were analyzed over the 2θ range from 5° to 45° at a fixed X-ray source of 100 cm.

Scanning electron microscopy (SEM)

The surface topography was analyzed with a scanning electron microscope (Carl Zeiss SUPRA 55) operated at an acceleration voltage of 5 kV. The SEM analysis was carried out to study the surface morphology of NVP, its PMs, and the solid dispersions.

In vitro dissolution studies

NVP, PMs, and solid dispersions equivalent to 50 mg of the drug were used for studying the rate and extent of drug dissolution. The study was performed using USP Type II (paddle type) dissolution apparatus (Lab India Dissolution Test Apparatus, DISSO 2000, India) maintained at 37±0.5°C at 75 rpm, using 900 ml of distilled water as dissolution medium. The test samples were filtered through 0.2 μm membrane filter and analyzed using HPLC method. Percent dissolution efficiency (DE) for each formulation was computed as the percent ratio of area under the dissolution curve up to the time *t*, to that of the area of the rectangle described by 100% dissolution at the same time (Equation 1) [17].

$$DE = \left(\frac{\int_0^t y.dt}{y100.t} \right) 100 \tag{1}$$

Other dissolution parameters such as dissolution rate DP_5, DP_{30}, and DP_{120} were also calculated.

Mathematical modeling of release kinetics

The *in vitro* drug release data of the optimized solid dispersion were fitted to various release kinetic models, namely, zero-order, first-order, Higuchi, and Korsmeyer-Peppas model employing the following set of equation [18].

Zero-order kinetic model
$$M_0 - M_t = K_0 t \tag{2}$$

First-order model
$$\ln(M_0/M_t) = K_1 t/2.303 \tag{3}$$

Higuchi model
$$M_t = K_H \sqrt{t} \tag{4}$$

Korsmeyer-Peppas model
$$M_t/M_\infty = Kt^n \tag{5}$$

Where, M_0, M_t and M_∞ correspond to the drug amount at zero, dissolved at a particular time, t, and at infinite time, respectively. Various other terms, namely, K_0, K_1, K_H, and K refer to the release kinetic constants obtained from the linear curves of zero-order, first-order, Higuchi model, and Korsmeyer-Peppas, respectively.
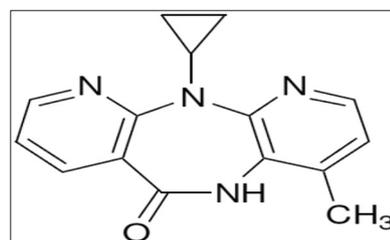

Fig. 1: Structure of nevirapine

Table 1: Composition of various ingredients used to prepare FDTs

S. No.	Ingredients (mg)	F1 (%)	F2 (%)	F3 (%)
1.	Solid dispersion	350 (70)	350 (70)	350 (70)
2.	Sodium starch glycolate	50 (10)	60 (12)	70 (14)
3.	Microcrystalline cellulose	10 (2)	20 (4)	30 (6)
4.	Mannitol	30 (6)	20 (4)	15 (3)
5.	Talc	30 (6)	20 (4)	15 (3)
6.	Magnesium stearate	30 (6)	30 (6)	20 (4)
	Total weight of tablet (mg)	500	500	500

FDTs: Fast dissolving tablets

Preparation of fast dissolving tablets (FDTs) of NVP solid dispersion

FDTs of NVP were prepared using different excipients, i.e., super disintegrants, binders, lubricants, and then evaluated for various parameters to select the best combination to prepare NVP tablets [19]. A series of trials were taken to formulate an optimized formulation with sufficient mechanical strength, disintegration time, and dissolution profiles (Table 1). The batches F1, F2, and F3 were prepared, and the uniform mass was sieved through mesh #42. The powder mass was also characterized by flow properties by different techniques. However, after the characterization of powder, tablets were prepared using direct compression method and evaluated by various evaluation tests for tablets.

Evaluation of FDTs

Pre-compression evaluation for the powder blend

Various micro metrics parameters such as angle of repose by static funnel method, bulk, and tapped density by tapping method were determined. The values so obtained were put into standard equations (Equations 6 and 7) to determine the compressibility index and Hausner's ratio for determination of the optimum flowability of the solid dispersion powders [19-21].

$$\text{Carr's compressibility Index} = \frac{\text{Tapped density - Bulk density}}{\text{Tapped density}} \times 100 \quad (6)$$

$$\text{Hausner's Ratio} = \frac{\text{Tapped density - Bulk density}}{\text{Bulk density}} \quad (7)$$

Post-compression evaluations

Various post-compression parameters of tablets such as hardness, thickness, weight variation, drug content, friability, wetting time, water absorption ratio, and disintegration test were determined as per the standard USP monographs [22-26].

RESULTS AND DISCUSSION

Solubility studies in different pH solutions

The solubility of NVP was determined at 25±0.5°C, in distilled water and wide range of pH solutions of 0.1 N HCl (pH 1.2), phosphate buffer of pH 4.6, pH 6.8, and pH 7.2. As NVP is a weekly basic drug (pK$_a$ 2.8), an increase in solubility was anticipated with a decrease in pH as shown in Fig. 2. The pH solubility profile indicated a gradual decline in solubility with an increase in pH from 1.2 (1.35 mg/ml) to 4.6 (0.229 mg/ml) and remained steady at pH 7 and 7.2 (0.1 mg/ml). These results revealed that the solubility of NVP is pH dependent, which is in accordance with the reported literature [27-30].

Phase solubility studies

The appropriate amount of Vitamin E TPGS was dissolved in water and various concentrations in the range of 0.002–2% w/v were prepared. Phase solubility studies indicated that solubility of NVP increased with increase in the concentration of Vitamin E TPGS. The critical micelle concentration of Vitamin E TPGS was found to be 0.2 mg (0.002% w/v) [31]. At about 0.002% w/v Vitamin E TPGS concentration, the micellization occurs, leading to increased accommodation of NVP molecules in the micelles with enhancement in solubility as depicted in Fig. 3.

In vitro dissolution studies

In vitro drug release studies are important assessment tools to determine systemic drug availability in biological media. The *in vitro* release profile of NVP, PMs, and the optimized solid dispersions are depicted in Figs. 4 and 5, respectively. The incomplete release profile of pure drug (20.43%) in 2 h could be attributed to the pH-dependent solubility of NVP, suggesting a strong need to enhance its dissolution. Moreover, the rate of dissolution from PMs PM1, PM2, and PM3 was found to be 36.58%, 37.90%, and 44.96%, in 2 h, respectively. The dry mixing in PMs has been reported to bring drug in close contact with the hydrophilic polymers, and the increased dissolution rate can thus be explained as a result of increased wettability and dispersibility of drug [32].
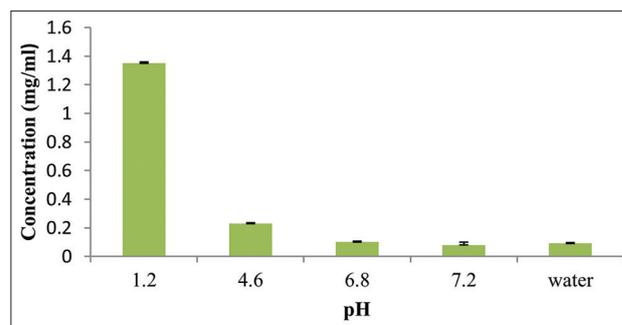

Fig. 2: Solubility studies of nevirapine in different pH solutions (mean ± standard deviation n=3)
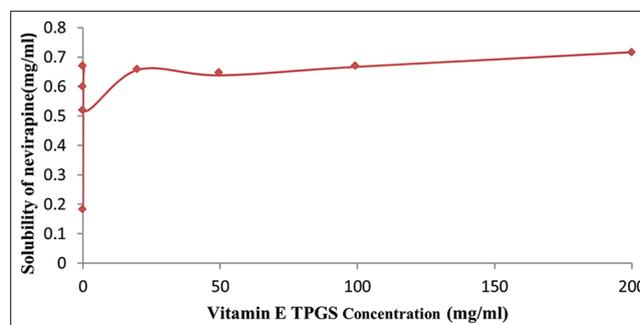

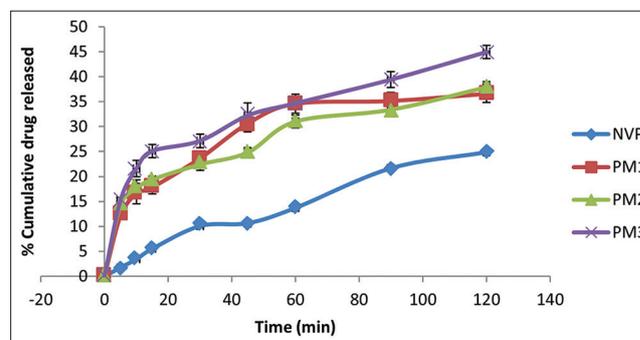**Fig. 3: Phase solubility analysis of nevirapine with Vitamin E tocopherol polyethylene glycol succinate**

Fig. 4: *In vitro* dissolution profile of nevirapine and its corresponding physical mixtures with Vitamin E tocopherol polyethylene glycol succinate
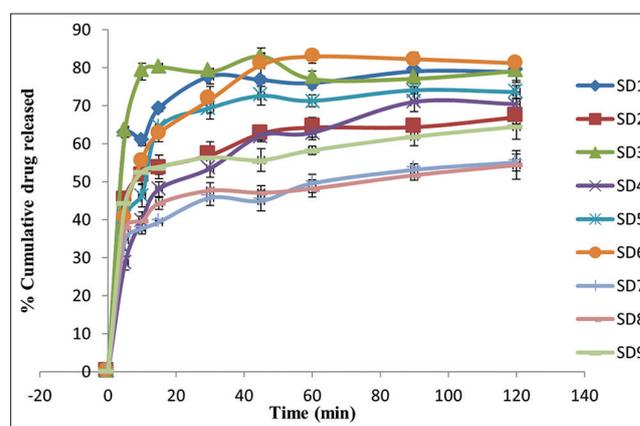

Fig. 5: *In vitro* dissolution profile of prepared solid dispersions in optimized media at 37±0.5°C

Solid dispersions of NVP in Vitamin E TPGS containing three different ratios of drug and polymer (1:0.25, 1:0.50, and 1:0.75) and also using

Table 2: Dissolution parameters of solid dispersions of NVP and Vitamin E TPGS

Solid dispersion batches	$DE_{30\ (min)}$	$DE_{60\ (min)}$	$DP_{5\ (min)}$	$DP_{30\ (min)}$	$DP_{120\ (min)}$
SD1	63.09	69.94	62.58	77.71	78.86
SD2	46.95	53.62	45.40	56.90	66.88
SD3	70.11	75.25	63.24	78.90	79.08
SD4	41.30	50.97	28.53	55.46	70.40
SD5	53.19	62.31	40.47	69.37	73.56
SD6	54.92	66.93	41.01	71.53	81.15
SD7	36.57	41.41	34.63	45.71	55.04
SD8	39.53	43.52	37.82	47.62	54.35
SD9	48.18	52.32	44.14	56.35	64.44

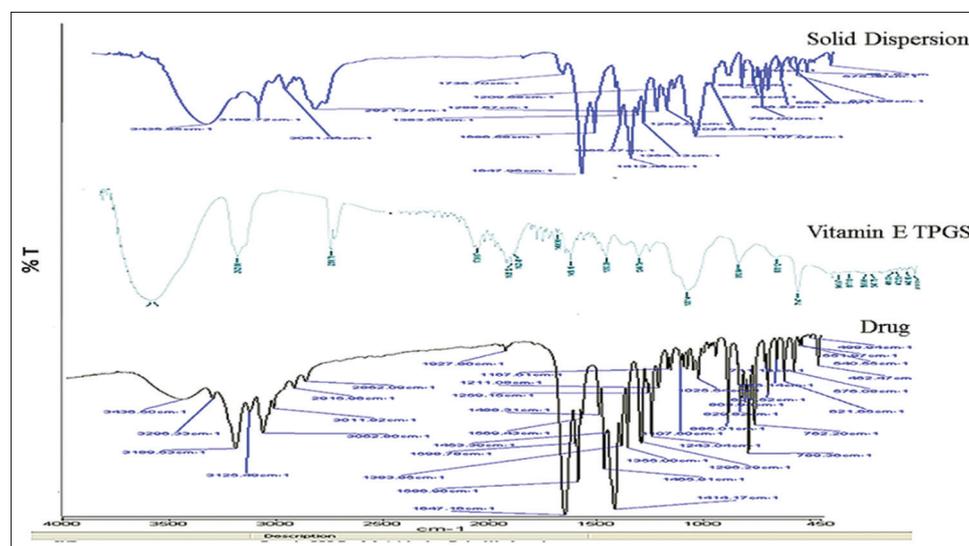TPGS: Tocopherol polyethylene glycol succinate, NVP: Nevirapine

Fig. 6: Fourier transform infrared spectrograms overlay of nevirapine, Vitamin E tocopherol polyethylene glycol succinate, and optimized solid dispersion (SD3)
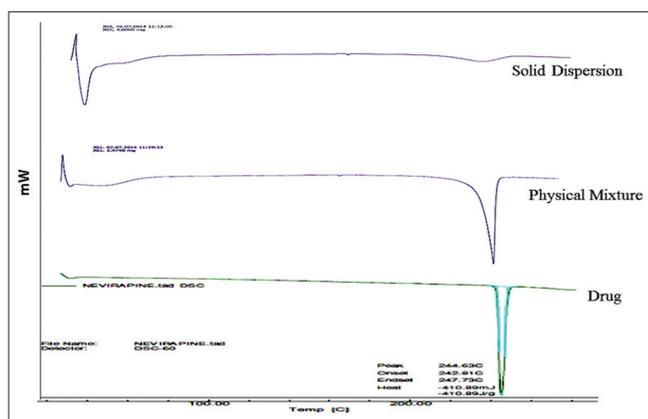

Fig. 7: Differential scanning calorimetry overlay of nevirapine, physical mixture, and optimized solid dispersion (SD3)
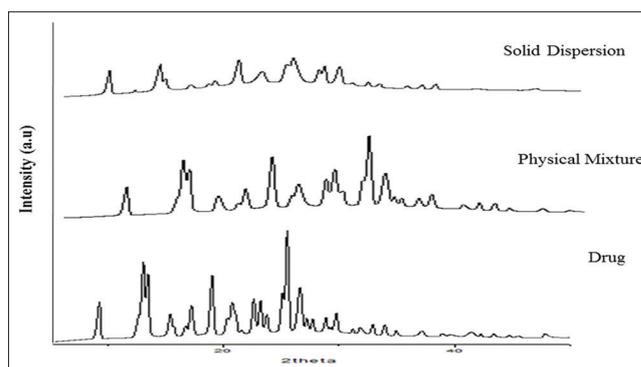

Fig. 8: X-ray diffraction overlay of nevirapine, physical mixture, and optimized solid dispersion

three different amounts of solvent (10 ml, 20 ml, and 30 ml) were fabricated. The solid dispersions SD1, SD2, and SD3 (having drug to polymer ratios 1:0.25–1:0.75 and solvent 10 ml) showed the maximum release of 66.93%, 78.85%, and 82.96% in 2 h, respectively. In solid dispersions SD4, SD5, and SD6, the drug to polymer ratios vary from 1:0.25 to 1:0.75, while the solvent amount of 20 ml was used. The solid dispersions SD4, SD5, and SD6 showed the maximum release of 70.40%, 73.56%, and 81.15%, respectively, in 2 h, i.e., DP_{120}. The solid dispersions SD7, SD8, and SD9 (having drug to polymer ratios 1:0.25–1:0.75 and solvent used 30 ml) showed the maximum release of 55.04%, 54.35%, and 64.44%, respectively, in 2 h, i.e., DP_{120}. Moreover, the enhancement

of dissolution of NVP from drug carrier systems can be described by several factors like lack of crystallinity, i.e., amorphization, increased wettability, and dispersibility and micellization of Vitamin E TPGS [31].

Furthermore, from the DE, it was observed that SD3 showed DE_{30} of 70.11%, while SD6 shows DE_{30} of 54.96% (Table 2). Thus, SD3 ratio was selected to carry out for further formulation development studies.

Characterization of NVP, Vitamin E TPGS, PMs, and optimized solid dispersion
FT-IR spectroscopy
Results of spectroscopic investigations revealed no inherent physical interactions as no major shifting of peaks were observed in the physical

Table 3: Pre-compression parameters of prepared formulations

Batch code	Angle of repose (θ)	Bulk density (g/cm³)	Tapped density (g/cm³)	Hausner's ratio	Compressibility index (%)
F1	31.38±1.67	0.3846±0.07	0.4545±0.083	1.181±0.038	15.37±1.34
F2	32.41±1.98	0.3807±0.05	0.4500±0.032	1.182±0.046	15.40±2.34
F3	31.79±1.56	0.3830±0.45	0.4527±0.034	1.181±0.036	15.39±2.49

Table 4: Post-compression parameters of prepared formulations

Batch code	Disintegration time (seconds)	Hardness (kg/cm³)	Friability (%w/w)	Wetting time (seconds)	Water absorption ratio (% w/w)	Drug content (%)
F1	120±5.5	3.2±1.2	0.82±0.6	46±2	41.44±2.50	93.05±5.65
F2	90±4.54	3.3±1.6	0.86±0.3	48±3	41.20±2.30	95.74±7.39
F3	40±2.65	3.5±1.3	0.70±0.4	44±2	45.45±1.50	97.16±6.29

mixture of drug with Vitamin E TPGS (Fig. 6). Furthermore, the major stretching and bending peaks were observed in the prepared formulation indicating the physical compatibility of the drug with the polymer [33,34].

DSC

The DSC endotherms of NVP, physical mixture, and the optimized solid dispersion are shown in Fig. 7. NVP shows an endothermic peak at 247.43°C while the physical mixture showed endothermic peaks of drug and TPGS at 246°C and 39°C, respectively [35]. The intensity of endothermic peak corresponding to the melting point of drug was decreased in the optimized solid dispersion formulation, suggesting the molecularly dispersed state of NVP in the solid dispersions. This observation confirms the amorphous nature of NVP after encapsulating in the Vitamin E TPGS [36].

XRD studies

XRD of NVP showed characteristic peaks at various diffraction angles (2θ) of 9.2°, 13.1°, 19.04°, and 25.54°, which confirmed its crystalline nature (Fig. 8). The XRD pattern of the physical mixture showed characteristics diffraction peaks of 14°, 24°, and 35°, but with lesser intensity. However, the absence of sharp diffraction peaks was noticeable in optimized solid dispersions, which indicate the amorphous embedding or molecular dispersibility of drug within polymer matrix [37].

SEM

NVP existed as partial crystalline material with soft edges (Fig. 9a) while Vitamin E TPGS existed as waxy solid which may melt at 37°C; hence, it was quite difficult to obtain the SEM images. In the physical mixture, the characteristic NVP crystals which were mixed with Vitamin E TPGS particles or adhered to their surface were clearly detectable (Fig. 9b). In the solid dispersion, the surface is slightly rougher compared with NVP and the particle size is much bigger than NVP, suggesting that the surface morphology of solid dispersion got changed, i.e., particle size decreases (Fig. 9c). Therefore, the increased surface area and the close contact between the hydrophilic polymer and the drug might be responsible for the enhanced dissolution of the solid dispersion [38].

Evaluation of FDTs

Pre-compression evaluation of the powder blend

Pre-compression evaluation studies were carried out to ensure the flow properties of the powder blend as shown in Table 3 experimental findings revealed that the powder blends of all formulations (F1, F2, and F3) possess good flow properties and hence, formulated into FDTs.

Post-compression evaluation of the powder blend

The tablets obtained after compression were evaluated on various parameters to determine their quality and to ensure that the resultant product meets all necessary criteria required for the FDTs (Table 4).

The wetting time and water absorption ratio indicate the capacity of the super disintegrants to absorb water and completely wet the tablet at the earliest time possible, which are the significant characteristics of

Table 5: Post-compression parameters of formulation F3

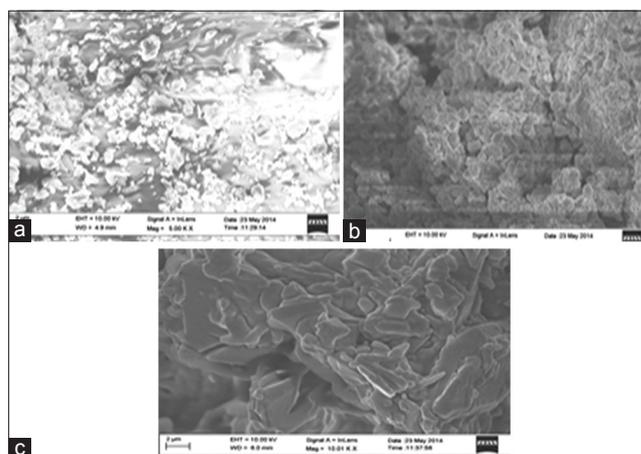| Evaluation parameters	Results
Hardness	3.5±1.3 kg/cm³
Diameter	12±2.53 mm
Thickness	7±1.97 mm
Weight variation test	Complies (±5%)
Drug content	Complies (97.16%)
Friability	0.702±0.4%
Wetting time	44±2.56 s
Water absorption ratio	45.45±1.23%
Disintegration time	40±2 s

Fig. 9: Scanning electron micrographs of (a) nevirapine, (b) physical mixtures, and (c) optimized solid dispersion

FDTs. The minimum wetting time and maximum water absorption ratio enable faster disintegration of the tablets, which is the prime criterion for the FDTs (Fig. 10). The wetting time of formulations, i.e., F1, F2, and F3 was found to be 46, 48, and 44 s and water absorption ratios were found to be 41.44%, 41.20%, and 45.45%, respectively.

Above results for pre- and post-compression parameters of tablets reveal that formulation F3 exhibited better flow properties, quick disintegration time, maximum water absorption, and minimum wetting time along with optimum hardness and lower friability as compared to other batches (Table 5). The probable reason for the better results with F3 batch might be due to the optimum amount of superdisintegrant used in the formulations [39].

Dissolution studies for optimized FDTs

The dissolution studies were performed to evaluate the release profile of the drug, which relates the percentage of drug release from its dosage form with the function of time. The desired quality of FDTs was to have

Table 6: Fitting of drug release from prepared FDTs (F3) to various release kinetic models

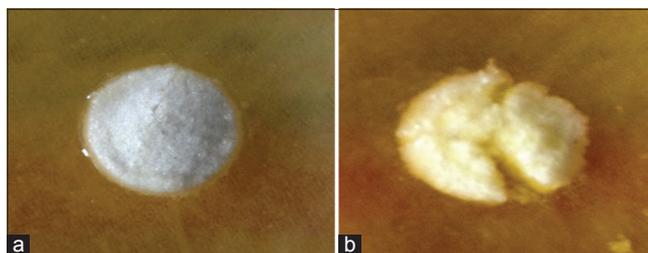| Mechanism	Zero-order		First-order		Higuchi		Korsmeyer-Peppas	
	Slope	r^2	Slope	r^2	Slope	r^2	Slope	r^2
F3	0.135	0.972	0.001	0.957	1.808	0.983	11.20	0.922

FDTs: Fast dissolving tablets

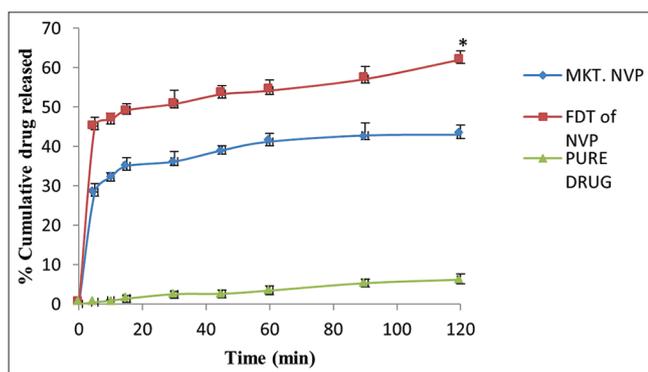**Fig. 10: Wetting time of fast dissolving tablets of batch F3 (a) initial and (b) after 44 s**

Fig. 11: Dissolution profile of the fast dissolving tablets of nevirapine (NVP) (F3) and marketed formulation of NVP. *p<0.01 compared with pure drug and marketed product, respectively

a maximum release of therapeutic dose at a very minimal time period (Fig. 11). The percentage cumulative release of FDTs and marketed tablets of NVP was compared and revealed that the dissolution rate of the drug of the marketed tablets was low as compared to the FDTs of the NVP (p<0.01) prepared by direct compression method after the formulation of solid dispersions (F3).

However, the use of superdisintegrant and microcrystalline cellulose in the FDTs of NVP would enhance the drug release from the tablets. Hence, it can be concluded that solid dispersion technology improves the dissolution profile of drug from the prepared FDTs [40].

Mathematical modeling of release kinetics of the prepared FDTs
Table 6 lists the regression parameters obtained after fitting various release kinetic model so the *in vitro* dissolution data. The R^2 value was found to be highest for the Higuchi model, i.e., 0.983 which indicates that the polymer formed a hydrophilic matrix in which drug gets entrapped in an amorphous form. As the matrix depletes, the drug in the amorphous form is available for dissolution.

CONCLUSION

We focused on solid dispersion as a novel drug delivery carrier for the enhancement of solubility and dissolution rate of NVP. The solid dispersion of drug:polymer ratio, i.e., 1:0.75 showed maximum DE (75.25%) and maximum dissolution rate (79.02%) in 2 h. Furthermore, FDTs of optimized solid dispersion showed a cumulative drug release of 45.18% in 5 min and 62.06% in 2 h, which is higher than that of marketed tablets of NVP. Therefore, the results from our study suggest

that solid dispersion technology can be used as a better alternative to produce FDTs, especially for drugs having poor water solubility.

AUTHORS' CONTRIBUTIONS

All the authors have contributed equally.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest to disclose. Moreover, this research did not receive any specific grant from funding agencies in the public, commercial, or not for profit sectors.

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