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Research Article

ENHANCEMENT OF SOLUBILITY OF NEVIRAPINE BY USING SOLID DISPERSION TECHNIQUE

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Abstract: The present research endeavor was towards the enhancement of solubility of Nevirapine by solid dispersion method. The solid dispersions were prepared by solvent evaporation method using carrier polymers like Polyethylene Glycol 6000 and Poly vinyl pyrrolidone (k 30) in three different ratios like 1:2, 1:4 and 1:6 ratio. The solubility of pure drug and solid dispersion forms of drug were studied in two selected media i.e. pH 1.2 acid buffer and ph 6.8 phosphate buffer. The results have shown that the solid dispersion forms containing PVP- K 30 in 1:4 ratios have shown better drug solubility compared to pure drug and other solid dispersion forms.

Key**words:** Dissolution enhancement; aqueous solubility, water soluble carriers, Nevirapine.

Introduction:

Solid dispersions have attracted considerable interest as an efficient means of improving the dissolution rate and hence the bioavailability of a range of hydrophobic drugs.[1-4] Solid dispersions are the molecular adducts consisting of an insoluble drug and highly water soluble carrier material. Generally the hydrophobic drugs are less water insoluble. In order to increase the aqueous solubility of the drug, it is mixed in molecular level with the hydrophilic carrier materials. The carrier materials are generally polymeric compounds like PVP, Urea.

Nevirapine is an anti-viral drug used in the treatment of HIV infections like AIDS. It is chemically 1,1-cyclopropyl-4-methyl-5,1,1-dihydro-6*H*-dipyrido[3,2-*b*:2′,3′-*e*][1,4]diazepin-6-one. Nevirapine is a non-nucleoside reverse transcriptase inhibitor (NNRTI) of HIV-1. Nevirapine binds directly to reverse transcriptase (RT) and blocks the RNA-dependent and DNA-dependent DNA polymerase activities by causing a disruption of the enzyme's catalytic site. The elimination half life is 45 hours. As it comes under BCS class II, it shows less solubility and high permeability. The present study involves the enhancement of solubility of drug by using solid dispersion technique.

Materials and methods:

Materials:

Nevirapine was gifted from Aurobindo Pharma, Hyderabad and all other chemicals like PEG 6000, PVP (K 30), Potassium Chloride, Hydrochloric Acid, Potassium Di-hydrogen Phosphate, Sodium Hydroxide were purchased from Merck Ltd., Hyderabad.

Methods:

1. Preformulation study

Preformulation studies were conducted to identify the compatibility of drug with polymers. These studies were conducted by using FTIR method. The IR spectra of pure drug and physical mixtures containing drug and polymers were produced and analyzed.

2. Preparation of Solid dispersion of Nevirapine[5-8]

Solid Dispersion of Nevirapine in PEG 6000 containing three different weight ratios(1:2, 1:4, 1:6) were prepared by the solvent evaporation method. An appropriate amount of Nevirapine was added to a solution of PEG 6000 in Methanol. The solution was stirred at 25°c for 2 hours, and the solvent was removed, under vacuum at 40°c in a vacuum tray dryer (VTD) for 12 hours. The solid residue was pulverized and sieved using #40 meshes. The solid dispersions are stored in light resistant container. The same procedure was repeated to prepare the solid dispersion of Nevirapine in PVP - K30.

3. Assay of drug in prepared solid dispersions[9-14]

The individual solid dispersions from each ratio were crushed in mortar and weighed separately. Each weighed SD powders separately added in 100ml of Acid buffer pH 1.2. Then shake for 1 hour and kept for 15 minutes. From that 0.5ml solution from each ratio separately taken and make the volume up to 10ml. Then the samples were analyzed at 314 nm by UV spectrophotometer. Each sample was analyzed in triplicate.

4. Dissolution study

A specified amount of pure drug was dissolved in selected media like pH 1.2 acid buffer and ph 6.8 phosphate buffer. Then the resultant solution was analyzed in UV after proper dilutions. In the same way the prepared solid dispersion forms of all ratios were taken and weighed separately and dissolved in two media individually and analyzed in UV at 314 nm after proper dilution. Then the dissolution results were compared with each other.

5. Characterization of drug in best formulations

The crystalline nature and physical state of drug in selected best formulations was studied by DSC studies. The DSC curves for pure drug, carrier polymer and selected SD form were produced and compared with each other.[15]

Results and Discussion

1. Preformulation study

The peaks observed in FTIR spectrum and DSC curve of pure drug were remained un altered in the in FTIR spectra of physical mixtures (Figure 1).

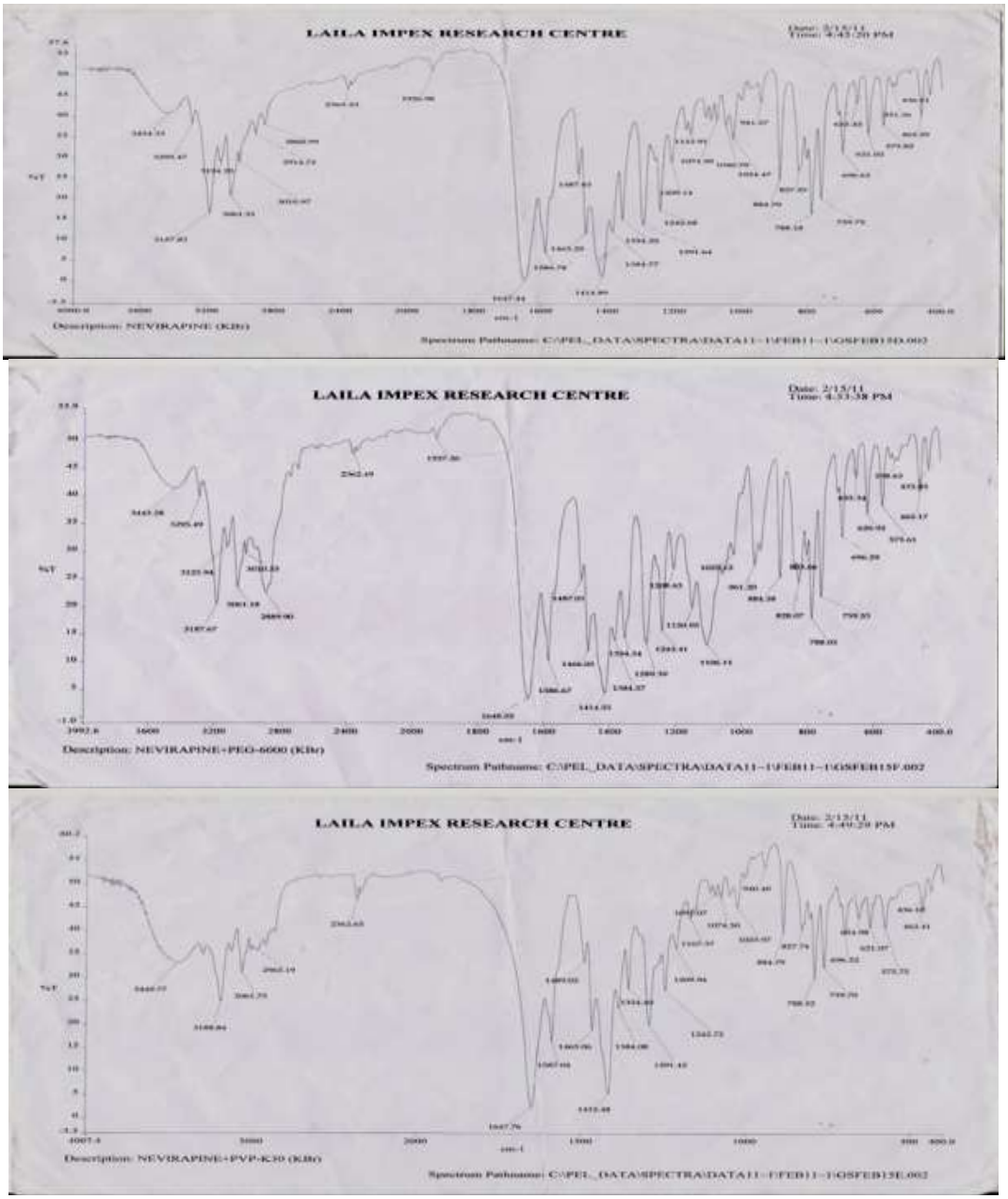

Figure 1: FTIR spectra of Pure Nevirapine, Physical mixture of drug with PEG 6000 and PVP- K30

2. Assay of drug in prepared solid dispersions

The assay for SD of Nevirapine + PEG6000 (1:2 ratio) was found out to be 89.40%, that for SD of Nevirapine + PEG 6000(1:4 ratio) was 91.90% and SD of Nevirapine + PEG 6000(1:6 ratio) was 99.70%.

The assay for SD of Nevirapine + PVP-K 30 (1:2 ratios) was found out to be 88. 00%, that for SD of Nevirapine + PVP-K 30 (1:4 ratio) was 91.7% and SD of Nevirapine + PVP-K 30 (1:6 ratio) was 89.50%.

3. Dissolution study

There was significant increase of dissolution rate of Nevirapine, in SD of Nevirapine + PEG 6000(1:6) than Nevirapine + PEG 6000 (1:2) and Nevirapine + PEG 6000(1:4) in pH1.2 Acid buffer pH 6.8 Phosphate buffer as a dissolution Medium (Figure 2).

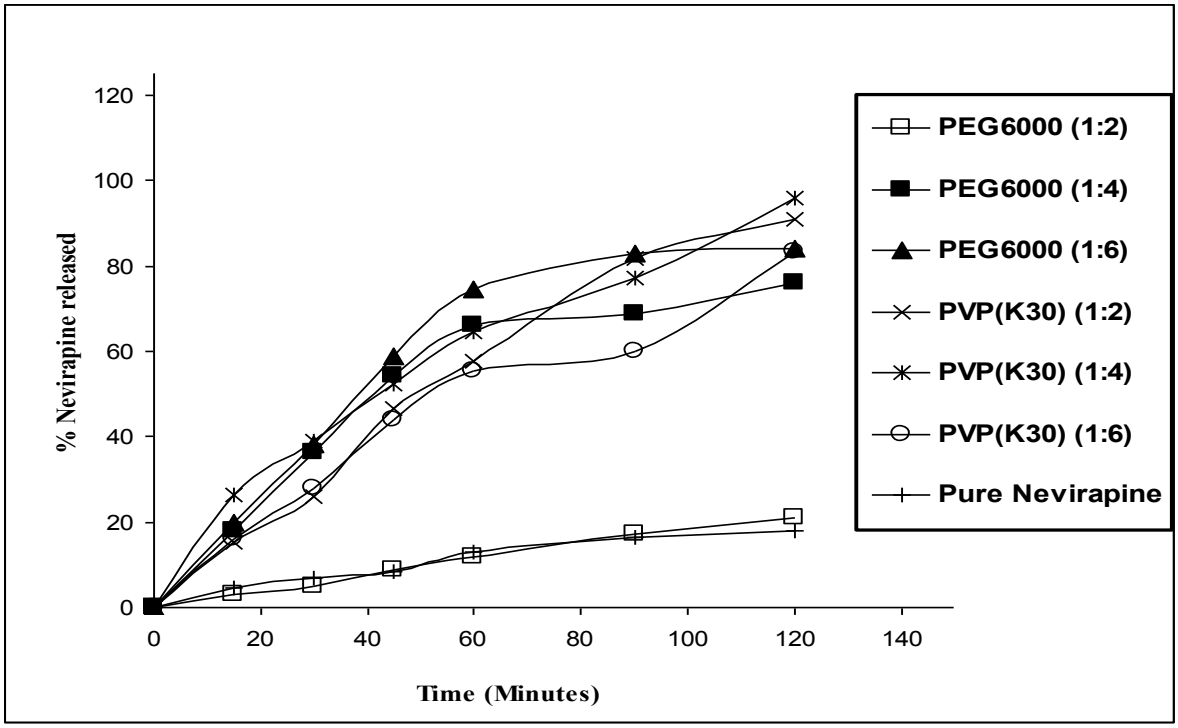

Figure 2: Comparative dissolution study of pure drug and its SD forms

There was significant increase of dissolution rate of Nevirapine, in SD of Nevirapine + PVP (k 30) (1:4) than Nevirapine + PVP (k 30) (1:2) and Nevirapine + PVP (k 30) (1:6) in Acid buffer pH 1.2 as a Dissolution Medium and there was no significant increase in drug release in pH 6.8 phosphate buffer as medium.

From the above comparison study, the SD of Nevirapine + PVP (K30) (1:4 ratio) is selected as best one showing good dissolution properties.

5. Characterization of drug in best formulations

DSC study revealed that the endothermic peak of pure drug was remained unaltered in selected best formulations (Figure 3).

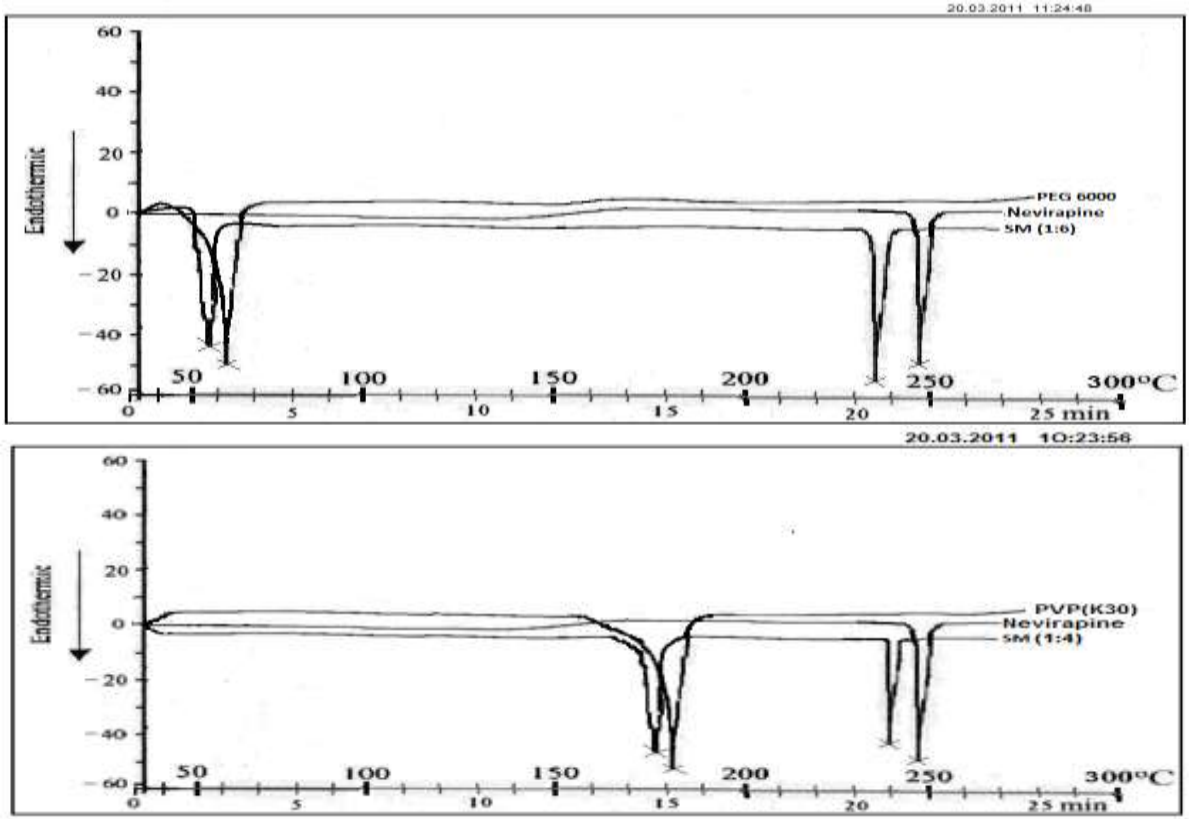

Figure 3: DSC curves of drug, carrier and SD forms

Conclusion:

From this research study it can be concluded that the solubility of Nevirapine drug is better enhanced in solid dispersion forms. The solvent evaporation method has given good solid dispersions. The carrier materials like PEG 6000 and PVP-K30 have successfully enhanced the solubility of poorly soluble drug Nevirapine.

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