Available online at www.ijpsdronline.com

International Journal of Pharmaceutical Sciences and Drug Research
2018; 10(3): 125-130

Research Article

ISSN: 0975-248X
CODEN (USA): IJPSPP

Formulation Development and *in vivo* Evaluation of Nevirapine Solid Dispersions by Solvent Evaporation Technique

Medipalli Viswaja, D.V.R.N Bhikshapathi*

Mewar University, NH-79, Gangrar, Chhitorgarh-312901, Rajasthan, India

ABSTRACT

The objective of the present investigation is focused on the preparation of solid dispersions containing Nevirapine. The effect of various hydrophilic polymers on the aqueous solubility was studied. Kolliphor P188 was selected as carrier and solid dispersions were prepared by solvent evaporation technique. Evaluation of solid dispersion for percentage yield, drug content and solubility were most appropriate. Solid dispersions of drug: Kolliphor P188 and SLS (1:3:1 ratio) (SE9) shown higher dissolution rate i.e. 98.6% compared with and pure drug (37.5%) and other formulations. Powder X-ray diffraction performed on solid dispersion showed that Nevirapine existed in the amorphous form within the solid dispersion formulation fabricated using the solvent evaporation process. Additionally, scanning electron microscopy studies suggested the conversion of crystalline Nevirapine to an amorphous form. Therefore, the solid dispersions prepared by solvent evaporation method using Kolliphor P188 as hydrophilic carrier can be successfully used for improvement of solubility and dissolution of Nevirapine. Both *in vitro* dissolution testing and the *in vivo* studies demonstrated that the solubility and bioavailability of Nevirapine were significantly improved when formulated in a solid dispersion with Kolliphor P188 and SLS. The present study demonstrated that formulation of Nevirapine solid dispersion by solvent evaporation technique is a highly effective strategy for enhancing the bioavailability of poorly water soluble Nevirapine.

Keywords: Nevirapine, Solid dispersions, Kolliphor P188, HIV, Bioavailability studies.

DOI: 10.25004/IJPSDR.2018.100304 **Int. J. Pharm. Sci. Drug Res. 2018; 10(3): 125-130**

***Corresponding author**: Dr. D.V.R.N. Bhikshapathi
Address: Head, Dept. of Pharmaceutics, Vijaya college of Pharmacy, Hayath nagar, Hyderabad-501511, Telangana, India
Tel.: +91-9848514228
E-mail ✉: dbpathi71@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Received: 02 April, 2018; **Revised:** 05 May, 2018; **Accepted**: 10 May, 2018; **Published:** 25 May, 2018

INTRODUCTION

Many potential drug candidates are characterized by a bioavailability , odr ug dissolution/solubility rather than limited permeation through the epithelia of the gastrointestinal tract and responsible for low oral bioavailability. [1] The rate and extent of dissolution of the active ingredient from any dosage form often determines the rate of extent of

absorption of the drug. The oral bioavailability depends on several factors including aqueous solubility, drug permeability, dissolution rate, first pass metabolism, presystemic metabolism and susceptibility to efflux mechanisms. [2] The ability to increase aqueous solubility is thus a valuable aid to increase the efficacy for certain drugs. [3] One of the major challenges of pharmaceutical formulation scientists is to develop the oral dosage forms of poor aqueous solubility drugs, hence, two areas of pharmaceutical research that focus on improving the oral bioavailability of active agents include enhancing solubility and dissolution rate of poorly water-soluble drugs and enhancing permeability of poorly permeable drugs. [4]

There are many methods like salt formation, solubilisation and particle size reduction to enhance oral bioavailability of poorly soluble drugs. However, techniques such as size reduction increases dissolution and bioavailability but, micronization often leads to aggregation and agglomeration, which leads to poor wettability of particles. [5]

This problem is rectified by preparation of solid dispersion of poorly water-soluble drugs by using water soluble carriers. Poorly soluble drugs when formulated as tablet or capsule dosage forms it disintegrate into large solid particles in GI tact, which leads to poor dissolution and less absorbed into the body system. Significantly, solid dispersion disintegrates into colloidal particle of particle size less than 5 microns which enhances the dissolution rate of the drug. Among all the methods, solid dispersion has been widely used to increase oral bioavailability, solubility and dissolution rate of the drug. [6] Tolvaptan is relatively a new chemical and pharmacologic class of drug known as aquaretic sorvaptans. [7]

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-6H- 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. [8] The present study involves the enhancement of solubility of Nevirapine by using solid dispersion technique with solvent evaporation method with different hydrophilic novel carriers.

MATERIALS AND METHODS

Materials

Nevirapine pure drug and Gelucire 44/14 was generous gifts from Aurobindo Pharma Limited, Hyderabad, India. Kolliwax GMS II, Kolliphor P 188, Kolliphor P 407, Kolliphor EL, Kolliphor ELP, Kolliphor HS 15, Soluplus and Kolliphor RH 40 were procured from BASF, Germany. All other chemicals used were of analytical grade.

Preliminary solubility studies of Nevirapine

Solubility measurements of Nevirapine were performed according to a published method. [9] An excess amount of Nevirapine was added to 25ml of aqueous solution of water soluble carriers like Kolliwax GMS II, Kolliphor P 188, Kolliphor P 407, Kolliphor EL, Kolliphor ELP, Kolliphor HS 15, Kolliphor RH 40, PVP K25, Soluplus, PEG 4000, PEG 6000, PEG 400, PEG 600, Tween 20, Tween 80, Gelucire 44/14, Span 80, MCC and DSS 100% in various ratios in Screw capped bottles. Samples were shaken for the 48 hours at room temperature. Subsequently, the suspensions were filtered through Whatman filter paper no 1. Filtered solutions were analyzed for the Nevirapine in UV 264 nm.

Preparation of solid dispersions of Nevirapine by solvent evaporation method

Nevirapine solid dispersions of Eighteen formulations were prepared by using various carriers (shown in Table 1) (Kolliwax GMS 2, Kolliphor P 188, Kolliphor P 407, PVP K25, Soluplus, PEG 4000) in proportions viz. 1:1, 1:2, 1:3 (Drug: Carrier) and SLS was added in all formulations. The drug and carrier was dissolved in ethanol and triturated in dry mortar until the solvent is evaporated and a clear film of drug and carrier was obtained. The resultant solid dispersion was scraped out with spatula. Solid dispersions were pulverized in a mortar and pestle and passed through a 45µm sieve before packing in an airtight container. [10]

Solubility studies of Nevirapine solid dispersion by solvent evaporation method

Solubility measurements of Nevirapine were performed according to a published method. [9] Samples were shaken for the 48 hours at room temperature. Subsequently, the suspensions were filtered through a Whatman filter paper no 1. Filtered solutions were analyzed for the Nevirapine in UV 264 nm.

Evaluation of Nevirapine solid dispersions

Solid dispersions obtained from the above methods were screened for their solubility. The solid dispersion showing good solubility were further studied for the % Practical yield, drug content and in vitro release studies.

% Practical yield

Percentage practical yield was calculated to know about percent yield or efficiency of any method, thus it helps in selection of appropriate method of production. SDs were collected and weighed to determine practical yield (PY) from the following equation.

$$\% \text{ Practical Yield} = \frac{\text{Practical Mass (Solid dispersion)}}{\text{Theoretical Mass (Drug+ Polymer+ Surfactant)}} \times 100$$

Drug content

Solid dispersions equivalent to 200 mg of Nevirapine were weighed accurately and dissolved in 100 ml of 0.1 N HCL.

Table: 1 Formulation plan of Nevirapine solid dispersions

Ingredients (g)	SE 1	SE 2	SE 3	SE 4	SE 5	SE 6	SE 7	SE 8	SE 9	SE 10	SE 11	SE 12	SE 13	SE 14	SE 15	SE 16	SE 17	SE 18
Nevirapine	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Kolliwax GMS 2	1	2	3															
Kolliphor P 407				1	2	3												
Kolliphor P 188							1	2	3									
PVP K25										1	2	3						
Soluplus													1	2	3			
PEG 4000																1	2	3
SLS	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Ethanol (ml)	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs

The solution was filtered, diluted suitable and drug content was calculated using the following equation as follows

$$\% \text{ Drug content} = \frac{\text{Actual amount of drug in solid dispersion}}{\text{Theoretical amount of drug in solid dispersion}} \times 100$$

The samples are drawn at specified time intervals and the obtained samples were analyzed by using UV-Visible spectrophotometer at 264 nm. The cumulative percentage release was calculated.

In vitro dissolution studies test parameters

The dissolution test was performed using USP type 2 dissolution apparatus (paddle method) with 900 ml of 0.1N HCl as dissolution medium at temperature of 37±0.5^{0}C with a paddle speed of 50 rpm. The solid dispersion equivalent to 25 mg of Nevirapine was added and the sample of 10ml were withdrawn and replaced with the same volume of the dissolution medium at 5, 10, 20, 30, 40, 50 and 60 minutes time intervals. The obtained samples were analyzed by using UV-Visible spectrophotometer at 264 nm. The cumulative percentage drug release was calculated.

Characterization

Powder X-ray diffraction

A Bruker D8 diffractometer was used to perform powder X-ray diffraction (PXRD) of all samples. A Cu K-α 1 tube was the source, set at 40 KV and 50 mA. A scan from 2 to 60° 2 θ was carried out at a rate of 0.01220° 2θ/s. The diffractometer was calibrated using powdered α-alumina. Hot-melt extruded samples were ground before analysis.

Scanning electron microscopy

The shape and surface morphology of the Nevirapine and optimized formulation of solid dispersion prepared by solvent evaporation was examined using XL 30 model JEOL 6800 scanning electron microscope (Japan).

Stability studies

Prepared solid dispersions were placed inside sealed 40cc HDPE container with child resistant cap under controlled temperature environment inside stability chamber (Thermo Lab, India) with relative humidity of 75% ± 5% RH and temperature of 40°C ± 2°C for stability studies. Samples were removed after 1, 2, 4 and 6 months, evaluated for % drug content and in vitro dissolution study and compared with those SD tested immediately after preparation.

In vivo bioavailability studies

Animal preparation

Healthy male Wistar rats were (weighing approximately 250 ± 25 g) selected for this study, all the animals were healthy during the period of the experiment. The study protocol was approved by the Institutional Animal Ethics Committee (**IAEC NO: P43/VCP/IAEC/2015/10/DBP/AE12**).

All efforts were made to maintain the animals under controlled environmental conditions (Temperature 25°C ± 2°C, Relative Humidity 45% ± 5% RH and 12 h alternate light and dark cycle) with 100% fresh air exchange in animal rooms, uninterrupted power and water supply. Rats were fed with standard diet and water *ad libitum*.

The pharmacokinetic characteristics for Nevirapine pure drug suspension 1gm and optimized preparation of solid dispersion (SE9) 1 g was evaluated using twelve healthy Male Wister rats weighing 250 ± 25 g. Rats were divided in to two groups at random, each group containing six animals. First group was administered Nevirapine (as such) suspension was prepared in 0.5% w/w of HPMC 2.5cPs, second group was administered optimized preparation of solid dispersion suspension (SE9) was prepared in 0.5% w/w of HPMC 2.5cPs by oral route at an equivalent dose of 25 mg/kg body weight. About 500µl of blood was withdrawn from retro orbital plexus at different time intervals such as 0.25, 0.50, 1.00, 1.50, 2.00, 2.50, 3.00, 4.00, 5.00, 6.00, 8.00, 12.00, 16.00, 18.00, 24.00 h. Blood samples were transferred into eppendorf tubes containing heparin in order to prevent blood clotting. The samples were centrifuged immediately at 4000 rpm and the plasma was stored in light-protected container at -20°C till analysis. [11]

Determination of Nevirapine in Rat plasma by HPLC method [12]

Determination of Nevirapine by high performance liquid chromatography using a RP-C18 chromatographic column, Phenomenex Kinetex (150 mm × 4.6 mm with i.d of 0.5 mm.) and mobile phase consisting of a mixture of ammonium acetate buffer (pH 4.0 ± 0.05) and acetonitrile (85:15 v/v) as the mobile phase. The eluents were monitored for the drug by UV detection at 254 nm. Oxcarbazepine was used as an internal standard for this study. The retention times for nevirapine and oxcarbazepine were found to be 7.2 and 14.7 min respectively.

Pharmacokinetic data analysis for optimized formulation of solid dispersions and pure drug suspension

The area under the drug concentration-time curve from zero to 24 h (AUC) was calculated using the trapezoidal rule. The maximum plasma concentration of the drug (C_{max} and the time to reach C_{max} (T_{max}) was obtained directly from the plasma profiles. The pharmacokinetic parameters were performed by a non compartmental analysis using Win Nonlin 3.3® pharmacokinetic software (Pharsight Mountain View, CA USA). All values are expressed as the mean±SD. Statistical analysis was performed with Graph Pad InStat software (version 3.00, Graph Pad Software, San Diego, CA, USA) using one-way analysis of variance (ANOVA) followed by Tukey–Kramer multiple comparison test. Difference with $p<0.05$ was considered statistically significant.

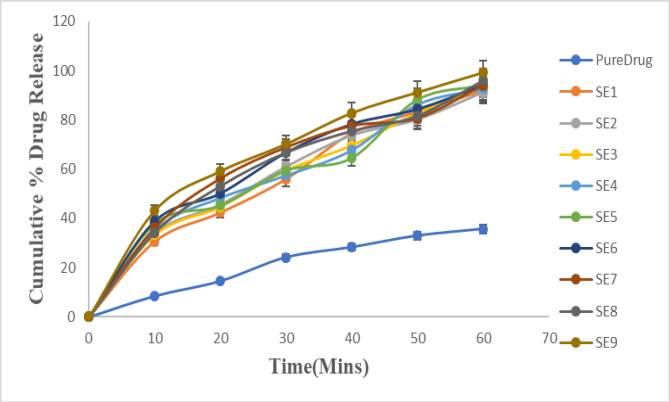


Fig. 1: Cumulative % drug release of Nevirapine solid dispersions (SE1-SE9) with pure drug

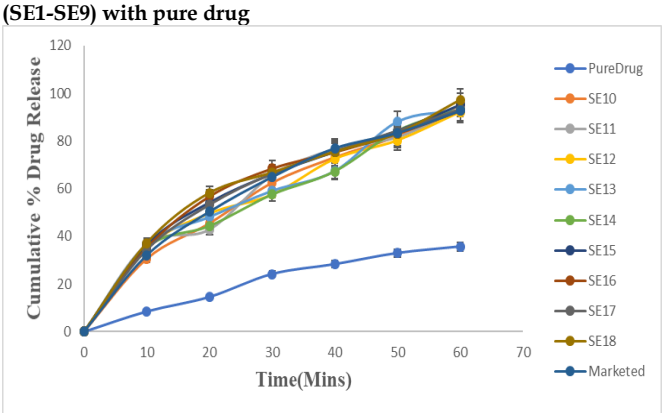


Fig. 2: Cumulative % drug release of Nevirapine solid dispersions (SE10-SE18) along with pure drug and marketed formulation

RESULTS AND DISCUSSION

Preliminary solubility studies of Nevirapine

In case of Solid dispersions initially preliminary solubility analysis were carried out to select the appropriate water soluble carriers for the preparation of solid dispersions in which pure drug solubility was found to be 0.10 mg/ml.

From this physical mixture of drug and Kolliphor P188 in the ratio of 1:1 shown highest drug solubility i.e. 0.42 mg/ml. For all the water-soluble carriers used in preliminary solubility studies, except Kolliphor P188, Kolliwax GMS2, Kolliphor P407, PVP K25, Soluplus and PEG-4000 gave turbid solutions.

Preparation of Nevirapine solid dispersions

Solid dispersions of Nevirapine were prepared by using Kolliphor P188, Kolliphor P407, Kolliwax GMS2, PVP K25, Soluplus and PEG-4000. In the present investigation eighteen formulations were prepared and their complete composition is shown in Table. All the Solid dispersions were found to be fine and free flowing powders.

Evaluation Parameters

Solubility studies of Nevirapine solid dispersions

Eighteen formulations of solid dispersions were prepared by solvent evaporation method with their respective carriers. After preparation of solid dispersion solubility analysis was carried out, this is compared with physical mixtures of the same drug to carrier ratio. The formulation with Drug: Kolliphor P188: SLS in the ratio of 1:3:1 respectively, which had increased the solubility almost 12.3 fold compared to that of the pure drug (Pure drug solubility is 0.10 & Drug with carrier SE9 is 1.23 mg/ml).

% Practical yield

The results of % Practical yield for all formulations of solid dispersions found to be 92%-98.2%. Maximum % practical yield was found in SE9 i.e. 98.2% when compared with other formulations. The drug content of the prepared solid dispersions was found to be in the range of 86%-96.15% and highest % drug content i.e. 96.15% was found in the formulation SE9.

In vitro dissolution studies

In Vitro studies of Nevirapine different formulations reveal that there is marked increase in the dissolution rate of Nevirapine from all the solid dispersions when compared to pure Nevirapine itself. From the in vitro drug release profile, formulation SE9 containing Kolliphor P188 (1:3 ratio of drug: Kolliphor P188) shows higher dissolution rate i.e. 98.2% compared with other formulations. This may be attributed to the increase in drug wettability, conversion to amorphous form and solubilization of the drug due to hydrophilic carrier. The increase in dissolution rate is in the order of Kolliphor P188> Kolliwax GMS2> PVP K25> Kolliphor P407> Soluplus> PEG 4000. The graphical representation of solid dispersions of SE1-SE9, SE10-SE18 with marketed formulation was depicted in Figures 1 & 2 respectively.

X-Ray Diffraction patterns

The presence of numerous distinct peaks in the XRD spectrum of pure Nevirapine indicates that it was present as a crystalline material. The XRD pattern depicted by physical mixture reveals a decrease in the number of peaks which probably represents decrease in crystallinity. On the other hand, the spectrum of optimized formulation SE9 of solid dispersion was characterized by the complete absence of any diffraction peak, which is characteristic of an amorphous compound (Figure 3). The enhancement in the dissolution rate of the drug from the drug-Kolliphor P188 and SLS solid dispersion is ascribed to the marked reduction in the crystallinity of the drug.

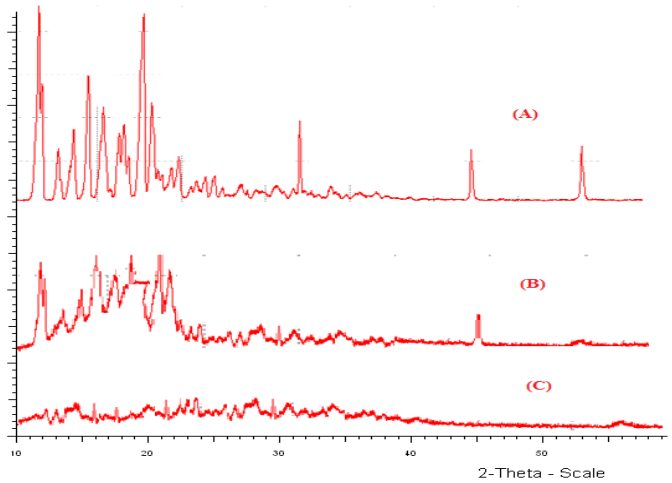
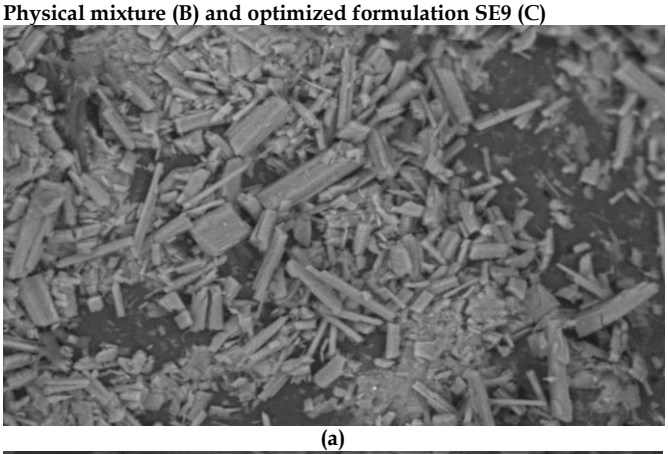
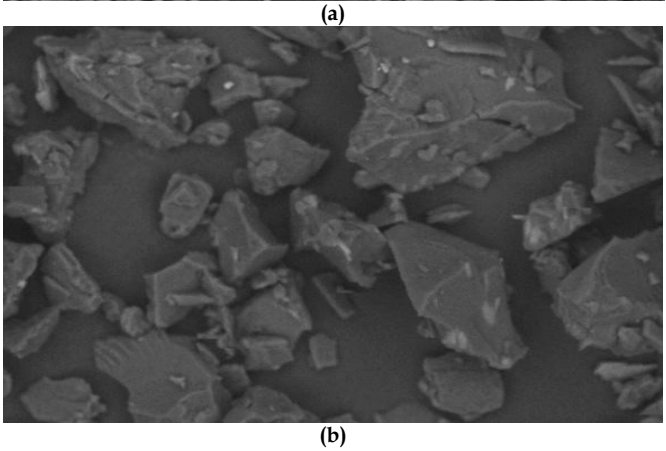


Fig. 3: X-Ray powder diffractograms of Nevirapine pure drug (A), Physical mixture (B) and optimized formulation SE9 (C)



(a)



(b)

Fig. 4: SEM photographs of Nevirapine pure drug (a) and optimized formulation SE 9 (b.)

SEM Studies

SEM photographs for Nevirapine pure drug (a) and optimized formulation SE 9(b) are shown in **Figure 4.** The drug crystals seemed to be smooth-surfaced, irregular in shape and size. In case of Solid dispersions, it was difficult to distinguish the presence of drug crystals. The drug surface in solid dispersion seems to be more porous in nature. Solid dispersions appeared as uniform and homogeneously mixed mass with wrinkled surface. Drug crystals appeared to be incorporated into the particles of the polymers. The solid dispersion looked like a matrix particle. The results could be attributed to dispersion of the drug in the molten mass of the polymer.

Stability studies

Optimized formulation (SE9) was selected for stability studies based on high cumulative % drug release. Stability studies were conducted for 6 months at Accelerated stability conditions according to ICH guidelines. To evaluate the physical state of the drug, the systems were evaluated for drug content, In vitro drug release profile and characterized by XRD after storage for 6 months. The systems were stable during a 6-month period. From these results it was concluded that, optimized formulation is stable and retained their original properties with minor differences.

In vivo bioavailability studies

The Nevirapine plasma concentrations in rats treated with optimized preparation of solid dispersion was significantly higher than those treated with pure drug suspension. Plasma pharmacokinetic parameters of Nevirapine after oral administration of the formulation to Wister rats are shown in Table 2 & Figure 5.

Table 2: Pharmacokinetic Parameters of Nevirapine Optimized Solid dispersion formulation, Nevirapine (API)

Pharmacokinetic Parameters	Nevirapine Pure drug	Nevirapine solid dispersion optimized formulation
C_{max} (µg/ml)	407 ± 1.32	644 ± 0.56
AUC_{0-t} (µg h/ml)	2720 ± 1.55	7504 ± 1.74
AUC_{0-inf} (µg h/ml)	4085 ± 0.24	9805 ± 0.45
T_{max} (h)	2.00 ± 0.05	1.00 ± 0.04
$t_{1/2}$ (h)	3.52 ± 0.01	4.02 ± 0.04
K el (h^{-1})	0.194 ± 1.22	0.151 ± 1.42

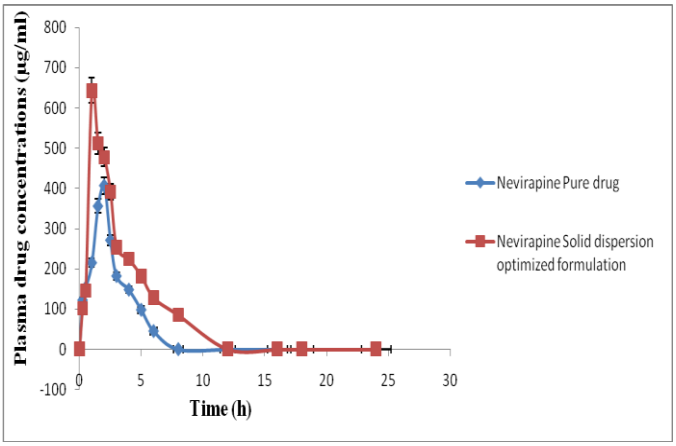


Fig. 5: shows the plasma profiles of Nevirapine in rats after the oral administration of the reference (pure drug suspension), optimized preparation of solid dispersion containing Nevirapine

Based on the results, it was clearly evident that Nevirapine from a solid dispersion was significantly increased in comparison with that of the pure drug (Rilpivirine suspension). C_{max} of the optimized preparation of solid dispersion was 644 ± 0.56µg/ml, was significantly higher as compared to C_{max} of the pure drug suspension, i.e., 407 ± 1.32µg/ml. T_{max} of optimized preparation of solid dispersion, and pure drug suspension was 1.00 ± 0.04 h, 2.00 ± 0.05 h respectively. AUC is an important parameter in evaluating bioavailability of drug from dosage form, as it represents the total integrated area under the blood

concentration time profile and represents the total amount of drug reaching the systemic circulation after oral administration. $AUC_{0\text{-}inf}$ for optimized solid dispersion formulation was much higher (9805 ± 0.45µg h/ml) than $AUC_{0\text{-}inf}$ of the pure drug suspension 4085 ± 0.24µg h/ml. Statistically, $AUC_{0\text{-}t}$ of the optimized preparation of solid dispersion was significantly higher (p<0.05) as compared to pure drug suspension. Higher amount of drug concentration in blood indicated better systemic absorption of Nevirapine from optimized solid dispersion formulation as compared to the pure drug suspension.

The dissolution rate of Nevirapine was increased with solid dispersions prepared by solvent evaporation technique without any physical and chemical interaction. Solid dispersions of drug: Kolliphor P188 and SLS (1:3:1 ratio) (SE9) shown higher dissolution rate i.e. 98.6% compared with and pure drug (37.5%) and other formulations. Analysis by powder X-ray diffraction showed that Nevirapine existed in the amorphous form within the solid dispersion formulation fabricated using the solvent evaporation process. Additionally, scanning electron microscopy studies suggested the conversion of crystalline Nevirapine to an amorphous form. A marked increase in solubility and dissolution was exhibited by optimized Nevirapine solid dispersion (SE9). Thus, the study has illustrated the potential use of a solid dispersion system for the delivery of a very poorly soluble drug Nevirapine with a better solubility and dissolution rate. Both *in vitro* dissolution testing and the *in vivo* studies demonstrated that the solubility and bioavailability of Nevirapine were significantly improved when formulated in a solid dispersion with Kolliphor P188 and SLS. The present study demonstrated that formulation of Nevirapine solid dispersion by solvent evaporation technique is a highly effective strategy for enhancing the bioavailability of poorly water soluble Nevirapine.

REFERENCES

1. Verheyen S, Blaton N, Kinget R. Mechanism of increased dissolution of diazepam and temazepam from polyethylene glycol 6000 solid dispersions. Int J Pharm. 2003; 249: 45:58.
2. Sakaeda T, Okamura N, Nagata S. Molecular and pharmacokinetic properties of commercially available oral drugs in humans. Bio Pharm Bull. 2001; 24: 935-940.
3. Wagh VT, Jagtap VA, Shaikh TJ, Nandedkar SY. Formulation and Evaluation of Glimepiride Solid Dispersion Tablets for Their Solubility Enhancement. J. Adv Sci Res. 2012; 3(4): 36-41.
4. Bhaskar D, Rama Rao T. Formulation and in vitro evaluation of flurbiprofen-polyethylene glycol 20000 solid dispersions. J. Applied Pharm Sci. 2014; 4(7): 76-81.
5. Singh S, Singh R, Yadav L. A review on solid dispersion. Int. J. pharm. & Life sci. 2011; 2(9): 1078-1095.
6. Deepthi Naidu K, Prasanna Lakshmi A, Ajay Kumar B, Narendra Reddy J. Formulation and *In-vitro* evaluation of conventional tablets of Ezetimibe by using Solid Dispersion. Int J Pharm Sci. 2013; 5(2): 331-335.
7. Sree Giri Prasad B, Gupta VRM, Vijaya K, Tamils Elvan A, Siva Subramanian N. Formulation and evaluation of fast dissolving tablet of Tolvaptan. JGTPS. 2015; 6(1): 2403 – 2410.
8. Venkatchalam Raju P, Goverdhan Reddy P. Enhancement of solubility of Nevirapine by using solid dispersion technique. Int. Res J Pharm. App Sci. 2013; 3(1): 169-172.
9. Appa Rao B, Shiva lingam M R, Kishore Reddy Y V, Soma Sekhara Rao, Rajesh K, Sunitha N. Formulation and Evaluation of Aceclofenac Solid Dispersions for Dissolution Rate Enhancement. Int J Pharma Sci and Drug Res. 2010; 2(2): 146-150.
10. Higuchi T, Connors KA. Phase solubility techniques. Adv. Anal. Chem. Instrum. 1965; 4: 117–122.
11. Ramesh K, Chandra Shekar B, Khadgapathi P, Bhikshapathi DVRN, Gourav N. Enhancement of Solubility and Bioavailability of Etravirine Solid Dispersions by Solvent Evaporation Technique with Novel Carriers, Journal of Pharmacy and Biological Sciences. 2015; 10(4):30-41.
12. Venkata kumar Ch, Ananth kumar D, Seshagiri rao JVLN. A New Validated RP- HPLC Method for the Determination of Nevirapine in Human Plasma. E-Journal of Chemistry. 2010; 7(3): 821-826.

HOW TO CITE THIS ARTICLE: Viswaja M, Bhikshapathi DVRN. Formulation Development and *in vivo* Evaluation of Nevirapine Solid Dispersions by Solvent Evaporation Technique. Int. J. Pharm. Sci. Drug Res. 2018; 10(3): 125-130. **DOI: 10.25004/IJPSDR.2018.100304**