Formulation, optimization, and evaluation of self-emulsifying drug delivery systems of nevirapine

Ramprasad Chintalapudi, T. E. G. K. Murthy, K. Rajya Lakshmi, G. Ganesh Manohar

Department of Pharmaceutical Science, JNTU College of Pharmacy, Guntur, Andhra Pradesh, India

Abstract

Background: The aim of the present study was to formulate and optimize the self-emulsifying drug delivery systems (SEDDS) of nevirapine (NVP) by use of $2^2$ factorial designs to enhance the oral absorption of NVP by improving its solubility, dissolution rate, and diffusion profile. SEDDS are the isotropic mixtures of oil, surfactant, co-surfactant and drug that form oil in water microemulsion when introduced into the aqueous phase under gentle agitation. Materials and Methods: Solubility of NVP in different oils, surfactants, and co-surfactants was determined for the screening of excipients. Pseudo-ternary phase diagrams were constructed by the aqueous titration method, and formulations were developed based on the optimum excipient combinations with the help of data obtained through the maximum micro emulsion region containing combinations of oil, surfactant, and co-surfactant. The formulations of SEDDS were optimized by $2^2$ factorial designs. Results: The optimum formulation of SEDDS contains 32.5% oleic acid, 44.16% tween 20, and 11.9% polyethylene glycol 600 as oil, surfactant, and co-surfactant respectively. The SEDDS was evaluated for the following drug content, self-emulsification time, rheological properties, zeta potential, in vitro diffusion studies, thermodynamic stability studies, and in vitro dissolution studies. An increase in dissolution was achieved by SEDDS compared to pure form of NVP. Conclusion: Overall, this study suggests that the dissolution and oral bioavailability of NVP could be improved by SEDDS technology.

Key words: $2^2$ factorial designs, nevirapine, oleic acid, polyethylene glycol 600, self-emulsifying drug delivery systems, tween 20

INTRODUCTION

Nevirapine (NVP) is a nonnucleotide reverse transcriptase inhibitor for the treatment of HIV infection. NVP is a biopharmaceutical classification system (BCS) class 2 drug, that is, low solubility and high permeability.[1-3] Oral route is the most oldest and convenient route for the administration of therapeutic agents due to low cost of therapy and ease of administration leads to a higher level of patient compliance.[4]

Approximately, 40% of new chemical entities exhibit poor aqueous solubility and present a major challenge to modern drug delivery system. The rate limiting step for the absorption of these drugs is often their solubilization in the gastrointestinal (GI) tract. These drugs are classified as class II drug by BCS, drugs with poor aqueous solubility and high permeability. Lipid-based drug delivery Systems have been demonstrated to be useful in enhancing the bioavailability of highly lipophilic compounds because they can keep the drug in the dissolved state until it is absorbed, thus overcoming the barrier of slow dissolution rates. In practice, lipid formulations range from pure oils to formulations containing some proportions of surfactants, co-surfactants or co-solvents. Recently, a number of studies related to lipid formulations focused attention on microemulsion formulations with particular emphasis on self-emulsifying or self-emulsifying drug delivery systems (SEDDS) to improve oral bioavailability of poorly water soluble drugs.[5]

Therefore, it is necessary to develop alternative oral routes of administration to enhance the bioavailability of poorly water-soluble drugs, and furthermore obtain more successful therapeutic effects. The use of SEDDS is one of the most interesting approaches to improving the solubility, dissolution, and oral absorption for poorly water-soluble drugs.[6-8]

Self-emulsifying drug delivery systems are defined as isotropic mixtures of natural or synthetic oils, solid or liquid surfactants or, alternatively, one or more hydrophilic solvents and co-solvents/surfactants. On mild agitation followed by dilution in aqueous
media such as GI fluids, these systems can form fine oil-in-water (o/w) emulsions or microemulsion. It is thought that the microemulsion is spontaneously formed by the combined action of the specific pharmaceutical excipients with low free energy. The microemulsion droplets dispersed in the GI tract provide large surface area and promote a rapid release of dissolved form of the drug substance and/or mixed micelles containing drug substance, and they may be also responsible for transporting the drug through the unstirred water layer to the GI membrane for absorption. In addition to the enhanced dissolution of drugs by SEDDS, another factor contributing to the increasing bioavailability is that the lymphatic transport is responsible for a portion of the entire drug uptake as well. The lipid composition of SEDDS may be related to facilitate the extent of lymphatic drug transport by stimulating lipoprotein formation and intestinal lymphatic liquid flux.

The main objective of the present study is to develop and evaluate an optimal SEDDS formulation containing NVP.

MATERIALS AND METHODS

Materials
Nevirapine was obtained from Cipla Ltd., Pune. Oleic acid was obtained from LOBA Chemie Pvt. Ltd., Mumbai. Tween 20 was obtained from S D Fine Chemicals Ltd., Mumbai. Polyethylene glycol (PEG) 600 was obtained from S D Fine Chemicals Ltd., Mumbai.

Methods

Solubility studies
The most important criterion for the screening of components for micro emulsion is the solubility of poorly soluble drug in oils, surfactants, and co-surfactants. The solubility of NVP in various oils was determined by adding an excess amount of drug in 2 ml of selected oils and surfactants and co-surfactants in 5 ml capacity stopper vials, and mixed using a vortex mixer. The vials containing samples were then kept at 25°C ± 10°C in an ultra-sonicator for 48 h to reach equilibrium. The equilibrated samples were removed from the shaker and centrifuged at 5000 rpm for 15 min. The supernatant was taken and filtered through a 0.45 μm membrane filter. The concentration of NVP in the samples was determined using ultraviolet (UV) spectrophotometer by measuring the absorbance of samples at 313 nm.

Construction of pseudo-ternary phase diagrams
In order to find out the concentration range of components for the existing range of microemulsions, pseudo-ternary phase diagram was constructed using the water titration method. Ternary plots were constructed using oil, surfactant and co-surfactant containing different proportion of surfactant: Co-surfactant, that is, S/Co (1:1, 1:3, 1:2 1:1 and 4:1 w/w). In brief S and oil were mixed at ratio of 1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2 and 9:1 in preweighed test tube. The mixtures of oil and surfactant and co-surfactant at certain weight ratios were diluted with water, under moderate stirring. After being equilibrated, the mixtures were assessed visually and determined as being microemulsions or coarse emulsions. The data obtained was used for the construction of ternary plots with the help of Triplot V4.1 software (Todd Thompson).

Formulation and optimization of nevirapine self-emulsifying drug delivery system by using 2^3 full factorial designs
It is desirable to develop an acceptable pharmaceutical formulation in shortest possible time using a minimum number of man-hours and raw materials. Traditionally pharmaceutical formulations after developed by changing one variable at a time approach. The method is time-consuming in nature and requires a lot of imaginative efforts. Moreover, it may be difficult to develop an ideal formulation using this classical technique since the joint effects of independent variables are not considered. It is, therefore, very essential to understand the complexity of pharmaceutical formulations by using established statistical tools such as factorial design. In addition to the art of formulation, the technique of factorial design is an effective method of indicating the relative significance of a number of variables and their interactions.

Self-emulsifying drug delivery systems formulations were developed based on the microemulsion regions and maximum amount of drug that can be solubilized in a particular ratio of surfactant and co-surfactant with oil meeting the desired criteria for formation of microemulsion after dispersing in aqueous media. The developed formulation consisted of NVP and the selected excipients obtained through screening of solubility studies and by plotting pseudo ternary phase diagrams. Optimum ratios of oil and S/CoS were selected from the phase diagrams. SEDDS formulations were prepared by dissolving NVP in S/CoS mixtures along with gentle vortexing and heating at ≤90°C, and then by adding Oil. To study the effects of the formulation variables, different batches were prepared using 2^3 factorial designs, with each batch containing NVP and varying amounts of oil and S/CoS. Formulations were stored in a desiccator at ambient conditions for further study.

The formulation was prepared by dissolving the NVP in the mixture of Surfactant and Co-surfactant at 50°C in a water bath. Oil was then added. This mixture was mixed by cyclomixer until a transparent preparation obtained. The prepared NVP SEDDS were loaded in hard gelatin capsule.
at 313 nm using UV-visible spectrophotometer. 0.1N HCl was used as a reference solution. [14]

**Drug excipient compatibility studies**

A proper design and formulation of the dosage form requires considerations of the physical, chemical and biological characteristics of both drug and excipients used in the fabrication of the product. Compatibility must be established between the active ingredient and other excipients to produce a stable, efficacious, attractive and safe product. If the excipients(s) are new and if no previous literature regarding the use of those particular excipients with an active ingredient is available, then compatibility studies are of paramount importance. Infrared (IR) is related to covalent bonds, the spectra provided detailed information about molecular structure. Hence, before producing the actual formulation, compatibility of NVP with different polymers and other excipients were tested using the Fourier transform infrared (FT-IR) spectroscopy technique. Fourier transforms infrared spectroscopy is a useful analytical technique utilized to check the chemical interaction between drug and other excipients used in the formulations. Drug and the intended excipients interaction were studied by FT-IR. The intended samples were powdered and intimately mixed with dry powdered potassium bromide. The powdered mixture was taken in a diffuse reflectance sampler, and the spectrum was recorded by scanning in the wavelength region of 4000-400 cm$^{-1}$ in FT-IR spectrophotometer.

**Determination of droplet size and zeta potential**

The charge of the droplets was determined by zeta potential measurement. Zeta potential helps in predicting the flocculation effect and stability in emulsion systems. Colloid will aggregate due to attractive forces if the zeta potential falls below a certain level. Droplet size and the zeta potential of the formed emulsion were determined using a Zetasizer ZS 90 (Malvern Instruments, UK). Light scattering was monitored at 25°C at a 90° C angle. [15]

**In vitro diffusion study**

**In vitro** diffusion study of the NVP SEDDS was performed by use of dialysis technique. 0.1N HCl was used as a dialysis medium. One end of dialysis tubing (Dialysis membrane 70, HIMEDIA; MWCO 12,000-14,000 daltons; pore size: 2.4 nm) was clamped and then the experimental formulation sample, was placed in it. The other end of the tubing was also secured with dialysis closure clips (HIMEDIA, Mumbai) and was placed in 900 ml of dialyzing medium and stirred at 50 rpm over a magnetic stirrer (Remi Instrument Ltd., Mumbai, India) at 37°C. Aliquots of 5 ml were removed at 30 min time intervals and suitably diluted further. Each time the volume of aliquots was replaced with the fresh dialyzing medium. [16] These samples were analyzed for NVP present in the dialyzing medium at corresponding time by UV-visible spectrophotometer at 313 nm.

**In vitro dissolution technique**

The quantitative in vitro dissolution studies are carried out to assess drug release from oil phase into aqueous phase by USP type II dissolution apparatus use of 900 ml of pH 1.2 phosphate buffer solution at 100 rpm and maintain the temperature at 37°C ± 0.5°C. Aliquots of 5 ml samples were withdrawn at regular intervals of time and volume withdrawn was replaced with fresh medium. [20] Samples taken were then analyzed by use of UV spectrophotometer at 313 nm.
RESULTS AND DISCUSSION

Screening of oils and surfactants
The results of the solubility of NVP in appropriate vehicles were showed in the Tables 1-3. From the solubility data; the oleic acid, tween 20, and PEG 600 were selected as oil, surfactant, and co-surfactant respectively.

Plot of pseudo ternary phase diagrams
Phase diagrams of the systems containing Oleic acid as an oil phase, Tween 20 as a surfactant and PEG 600 as a co-surfactant were constructed at the surfactant/co-surfactant (S/CoS) ratio of 1:4, 1:3, 1:2, 1:1 and 4:1 (w/w) to determine the existence of microemulsion region as showed in Figures 1-5, respectively.

The phase study revealed that the obtained microemulsion regions at S/CoS ratios of 1:1 [Figure 1] was low, when compared with all other ternary plots. At S/CoS ratios of 1:2 [Figure 2], 1:3 [Figure 3], and 1:4 [Figure 4], an increase in the microemulsion regions gradually as concentration of co-surfactant increases, it indicates that the co-surfactant has some effect on the capability of forming micro emulsion. The ratio 4:1 [Figure 5] of S/CoS showed maximum microemulsion region when compared to all other ternary plots, which points that an increase in the concentration of surfactant gives the highest microemulsion regions among all other ternary plots. It indicates that the concentration of surfactant has a major effect on the microemulsion region forming capability of SEDDS.

From the observed experimental results, it was observed that the surfactant: co-surfactant ratios of 4:1 showed maximum microemulsion region when compared with all other ratios. Hence, S/Co-S ratio of 4:1 was selected for the formulation of SEDDS based on microemulsion region forming capability, and it was subjected to further studies.
Formulation and optimization of nevirapine self-emulsifying drug delivery system by using $2^2$ full factorial design

From the studies of pseudo ternary phase diagrams, it was found that the Surfactant: Co-surfactant ratio of 4:1 was showing large micro emulsion regions. And it was selected for formulation of SEDDS. In the 4:1 (S:Cs), we have 9 different ratios of $S_{mix}$: Oil, that is, 9:1, 8:2, 7:3, 6:4, 5:5, 4:6, 3:7, 2:8, and 1:9. In the listed ratios, the first two highest water consuming ratios are selected and are used for the formulation and optimization of NVP SEDDS by using $2^2$ factorial design.\cite{21} The results of Formulation and Optimization of NVP SEDDS by using $2^2$ full factorial design were showed in Table 4.

Characterization of self-emulsifying drug delivery systems

Drug content

Assay of prepared NVP SEDDS was carried out by UV-visible spectrophotometer. A linear calibration curve was obtained at 313 nm in the range of (2-10 $\mu$g/ml) with a correlation coefficient ($R^2$) of 0.999. The Assay results are shown in Table 5.

The % drug content of all SEDDS formulations was found to be within the acceptable limits of drug content test.

Fourier transform infrared studies

The FT-IR studies were done to characterize the drug. Here, we are performing the FT-IR studies of the pure drug and best formulation (F4) to elicit interactions of drug with other excipients present in the formulation. The IR spectrum for the pure drug and SEDDS best formulation (F4) were given in Figures 6 and 7. The peak observed at 758.787 cm$^{-1}$ is characteristic of the C-H bending of the aromatic group. The peak produced at 1289 cm$^{-1}$ is characteristic of C=O stretching seen in alcohols. The peak observed at 1461 cm$^{-1}$ is typical of C=C stretching of the aromatic group. The peaks observed at 1585 cm$^{-1}$ and at 1643 cm$^{-1}$ are characteristic of N=N and C=N stretching. The peak observed at 3184 cm$^{-1}$ is characteristic of C-H alkene group present in the molecule. No interactions were detected between excipients and the NVP after observation of the spectrum of SEDDS best formulation, when compared with the pure drug spectrum.

Determination of droplet size and zeta potential

The charge of the droplets was determined by zeta potential measurement. Droplet size and the zeta potential of the formed emulsion were determined use of Zetasizer ZS 90 (Malvern Instruments, UK). Light scattering was monitored at 25°C at a 90° angle. The results of SEDDS formulations were listed in Table 6. From the data obtained through Figures 8 and 9, Table 6, it was found that the F4 formulation was best when compared with all other formulations and showed droplet size of 319.2 nm and zeta potential of $-68.9$ mV.

In vitro diffusion study

In vitro diffusion study was performed to compare the drug release from the developed NVP SEDDS. In vitro diffusion study of the NVP SEDDS (F1, F2, F3, and F4) was performed by using a dialysis technique. The drug release results of In vitro diffusion study were listed in Table 7 and Figure 10. After observation of the results, it was found that, nearly 55.634% ± 0.661% of drug was released from NVP SEDDS F4 formulation within 1 h compared with the other formulations, that is, F1, F2, and F3, which released 36.999% ± 0.012%, 49.422% ± 0.475%, and 43.211% ± 0.312%, of

---

**Table 4: Composition of formulation**

| Component | F1 | F2 | F3 | F4 |
|-----------|----|----|----|----|
| Nevirapine (mg) | 100 | 100 | 100 | 100 |
| $S_{mix}$ (%) | Low (48.3) | High (56) | Low (48.3) | High (56) |
| Oil (%) | Low (24) | High (32.2) | High (32.2) | Low (24) |

**Table 5: Drug content results**

| Formulation | Percentage of drug content ($\bar{x} \pm SD$) |
|-------------|-------------------------------------------|
| F1          | 97.4±1.9                                  |
| F2          | 98.2±0.8                                  |
| F3          | 97.9±0.98                                 |
| F4          | 98.9±0.7                                  |

SD: Standard deviation
the drug respectively. At the end of 5 h period, almost all the drug (98.245% ± 0.03%) diffused from the SEDDS F4 formulation compared with drug released from the other formulations, that is, F1, F2, and F3, which released 82.817% ± 0.56%, 94.685% ± 0.09%, and 88.751% ± 0.302% of the drug respectively [Figure 10].

It was found that, all the formulations followed first order kinetics as correlation ($R^2$) values of first order release kinetics were higher than that of zero order release kinetics showed in Table 8. The first order rate constant (K) was calculated from the slope of first order linear plot showed in Figure 11.

Thus, the drug release from the NVP SEDDS F4 formulation was found to be significantly rapid and higher as compared to that of the remaining SEDDS formulations. It could be suggested that the SEDDS F4 formulation resulted in a spontaneous formation of a microemulsion with a small droplet size, which permitted a faster rate of drug release into the aqueous phase. Thus, this greater availability of dissolved NVP from the SEDDS F4 formulation could lead to higher and rapid absorption and oral bioavailability.

### Determination of self-emulsification time

Emulsification time is an important index for the assessment of the efficiency of emulsion formation. SEDDS should disperse
completely and rapidly when subjected to aqueous dilution under mild agitation. The emulsification time of all formulations was reported in Table 9.

After observation of Table 9, it was found that the F4 formulation forms microemulsion in a short time relatively among all other formulations which indicate that the F4 was best of all prepared formulations.

**Rheological properties determination**

The SEDDS systems were loaded in hard gelatin capsules. So SEDDS were easily pourable into capsules and such systems should not be too thick. The rheological properties (viscosity, flow) of the microemulsion are reported in Table 10.

From Table 10, it was found that F4 formulation was showing low viscosity and plastic flow, which indicates stability and pourability of formulation F4 was best among all other formulations.

**Thermodynamic stability studies**

The physical stability of the formulation is very important for its performance as it can be adversely affected by precipitation of the drug in an excipient matrix. Poor physical stability of the formulation can lead to phase separation of excipients that affects bioavailability, as well as therapeutic efficacy. Furthermore, the incompatibility between formulation and gelatin shell caused brittleness, softness and delayed the disintegration or incomplete release of drug. The following cycles were carried out for these studies, and the results were reported in the Table 11.

From Table 11, it was observed that, there were no appreciable changes in the formulations during stability studies, and hence it was concluded that the formulations are thermodynamically stable.

**In vitro dissolution study**

**In vitro** dissolution study was performed to compare the drug release from the developed NVP SEDDS formulations and pure drug. The quantitative in vitro dissolution studies is carried out to assess drug-release from the oil phase into the aqueous phase by USP type II dissolution apparatus. The results of

| Dissolution medium | Formulation code | Correlation co-efficient | $K$ (min$^{-1}$) | $T_{50}$ (min) | $T_{90}$ (min) |
|--------------------|------------------|--------------------------|----------------|--------------|--------------|
| 0.1N HCl           | F1               | 0.8918                   | 0.9251         | 0.0414       | 16.8         | 55.7         |
|                    | F2               | 0.7539                   | 0.9122         | 0.0574       | 12.1         | 40.1         |
|                    | F3               | 0.8353                   | 0.9478         | 0.0475       | 14.6         | 48.5         |
|                    | F4               | 0.6693                   | 0.9603         | 0.0705       | 9.8          | 32.6         |

In vitro dissolution studies were listed in Table 12 and Figures 12 and 13 (first order plot). After observing the results, it was found
that, nearly 95.23% ± 0.13% of drug was released from NVP SEDDS F4 formulation within 45 min compared to the other formulations, that is, F1, F2, F3, and pure drug which released 77.332% ± 0.674%, 89.27% ± 0.268%, 84.137% ± 0.446% and 28.032% ± 0.395% of the drug respectively. At the end of 50 min period, almost all the drug (99.432% ± 0.03%) released from the SEDDS F4 formulation compared to the other formulations, that is, F1, F2, and F3, and pure drug which released 82.817% ± 0.124%, 94.685% ± 0.122%, and 89.7% ± 0.398% and 29.886% ± 0.639% of the drug respectively. Thus, the drug release from the NVP SEDDS F4 formulation was found to be significantly higher as compared to that of the remaining SEDDS formulations and pure drug. It could be suggested that the SEDDS F4 formulation resulted in a spontaneous formation of a microemulsion with a small droplet size, which permitted a faster rate of drug release into the aqueous phase. Thus, this greater availability of dissolved NVP from the SEDDS F4 formulation could lead to higher absorption and higher oral bioavailability.

It was found that, all the formulations followed first order kinetics as correlation ($R^2$) values of first order release kinetics were higher than that of zero order release kinetics. The first order rate constant ($K$) was calculated from the slope of first order linear plot showed in Figure 13. In vitro dissolution parameters such as, $T_{50}$ (time required for dissolution of 50% of drug), $T_{90}$ (time required for dissolution of 90% of drug), DE45 (Dissolution Efficiency), and correlation co-efficient values (first order) of all SEDDS formulations and pure drug are presented in Table 13.

By observing all the results, it implies that all the formulations of SEDDS were showing more drug release than pure drug. It indicates that the SEDDS formulations were helpful for the enhancement of solubility of NVP.

Among the four formulations of SEDDS and pure drug, F4 formulation offered the rapid release rate of NVP. The formulation F4 prepared with 56% of Smixture (surfactant [Tween 80] 44.8% + co-surfactant [PEG 600] 11.2%) and 24% of oil (oleic acid) was selected for further studies as it offered relatively rapid release of NVP when compared with other formulations used in this investigation.

![Figure 12: Comparative in vitro dissolution profile plot of different formulations of self-emulsifying drug delivery system and pure drug in 0.1N HCl](image)

### Table 12: Comparison of dissolution studies of SEDDS formulations with pure drug

| Time (min) | Pure drug | F1 | F2 | F3 | F4 |
|------------|-----------|----|----|----|----|
| 0          | 0.000     | 0.000 | 0.000 | 0.000 | 0.000 |
| 5          | 6.974±0.8 | 30.959±0.77 | 30.959±0.73 | 35.956±1.79 | 49.698±0.98 |
| 10         | 9.011±0.67 | 36.999±1.98 | 37.378±0.56 | 42.962±1.08 | 56.634±0.234 |
| 15         | 11.185±1.11 | 42.969±0.987 | 43.831±0.33 | 49.022±1.876 | 61.500±0.543 |
| 20         | 12.121±1.5 | 48.870±0.909 | 50.318±0.454 | 55.135±1.43 | 67.296±0.786 |
| 25         | 13.562±0.99 | 54.701±1.27 | 56.841±1.78 | 61.175±3.445 | 73.023±0.547 |
| 30         | 16.134±1.22 | 60.463±2.08 | 63.398±0.49 | 67.022±1.908 | 78.681±0.448 |
| 35         | 19.595±1.38 | 66.156±1.43 | 69.998±0.779 | 72.797±2.08 | 84.270±0.879 |
| 40         | 21.576±0.87 | 71.779±1.49 | 76.162±1.33 | 78.502±2.21 | 89.798±0.359 |
| 45         | 25.191±0.53 | 77.332±1.98 | 83.277±2.09 | 84.137±1.23 | 95.238±0.857 |
| 50         | 29.90±1.71 | 82.817±2.01 | 89.973±1.99 | 89.700±0.999 | 99.432±0.143 |
| 55         | 35.01±0.972 | 88.232±1.45 | 96.703±0.943 | 94.249±1.767 |
| 60         | 39.87±0.47 | 93.577±0.92 | 98.503±1.879 |
| 65         | 43.33±0.59 | 97.687±0.77 |

SEDSS: Self emulsifying drug delivery systems

### Table 13: In vitro dissolution kinetics of nevirapine SEDDS formulations and pure drug in 0.1N HCl

| Dissolution medium | Formulation code | Correlation co-efficient | $K$ (min$^{-1}$) | $T_{50}$ (min) | $T_{90}$ (min) | % DE$_{45}$ (%) |
|--------------------|------------------|--------------------------|-----------------|---------------|---------------|----------------|
| 0.1N HCl           | Pure drug        | 0.9114                   | 0.9545          | 0.0075        | 92.8          | 308.2          | 18.03          |
|                   | F1               | 0.8918                   | 0.9251          | 0.0414        | 16.8          | 55.7           | 50.17          |
|                   | F2               | 0.7539                   | 0.9122          | 0.0574        | 12.1          | 40.1           | 61.73          |
|                   | F3               | 0.8353                   | 0.9478          | 0.0475        | 14.6          | 48.5           | 56.07          |
|                   | F4               | 0.6693                   | 0.9603          | 0.0705        | 9.8           | 32.6           | 67.5           |

SEDSS: Self emulsifying drug delivery systems, DE: Dissolution efficiency
The new emulsion formulations, that is, SEDDS are a promising approach for the formulation of NVP. The oral delivery of water-insoluble drugs like NVP can be made possible by SEDDS, which have been showed to be substantially improve bioavailability with future development of this technology. These current results demonstrated that SEDDS containing 24% w/w oleic acid oil (oil), 44.8% w/w, Tween 20 (surfactant) and 11.2% w/w PEG 600 (co-surfactant) was successfully developed with an increased solubility, increased dissolution rate of a poorly water-soluble drug, NVP when compared to all other formulations of SEDDS and pure form of the drug. The result from the thermodynamic stability studies confirms the stability of the developed formulation. Thus, the study confirms that the SEDDS of NVP can be used as a possible alternative drug delivery to traditional oral formulations of NVP with improved solubility and drug release.

ACKNOWLEDGMENTS

The authors thank full to Bapatla College of Pharmacy, T.E.G.K. Murthy (principal), and K. Rajya Lakshmi (guide) for their valuable support and providing facilities to carry out this research work.

REFERENCES

1. Lamson MJ, Sabo JP, MacGregor TR, Pav JW, Rowland L, Hawi A, et al. Single dose pharmacokinetics and bioavailability of nevirapine in healthy volunteers. Biopharm Drug Dispos 1999;20:285-91.
2. Macha S, Yong CL, Darrington T, Davis MS, MacGregor TR, Castles M, et al. In vitro-in vivo correlation for nevirapine extended release tablets. Biopharm Drug Dispos 2009;30:542-50.
3. Macha S, Yong CL, MacGregor TR, Castles M, Quinson AM, Rouyre N, et al. Assessment of nevirapine bioavailability from targeted sites in the human gastrointestinal tract. J Clin Pharmacol 2009;49:1417-25.
4. Gedar S, Kataria MK, Bilandi A. An overview on techniques implemented for sustained release matrix tablet of glipizide. Int J of advanced Pharm. 2014;4: 93-98.
5. Pallavi M, Swapnil L. Self-emulsifying drug delivery system (SEDDS). Indian J Pharm Biol Sci 2012;2:42-52.
6. Constantinides PP. Lipid microemulsions for improving drug dissolution and oral absorption: Physical and biopharmaceutical aspects. Pharm Res 1995;12:1561-72.
7. Constantinides PP, Scalart JP. Formulation and physical characterization of water-in-oil micro emulsion containing long-versus medium-chain glycerides. Int J Pharm 1997;158: 57-68.
8. Kommuru TR, Gurley B, Khan MA, Reddy IK. Self-emulsifying drug delivery systems (SEDDS) of coenzyme Q10: Formulation development and bioavailability assessment. Int J Pharm 2001;212:233-46.
9. Bajaj H. Self-emulsifying delivery system: An approach to enhance bioavailability. Int J Pharm Res Dev 2008;3:59-75.
10. Khoo SM, Humberstone AJ, Porter CJ, Edwards GA, Charman WN. Formulation design and bioavailability assessment of lipidic self-emulsifying formulations of halofantrine. Int J Pharm 1998;167:155-64.
11. Iwanaga K, Kushibiki T, Miyazaki M, Kakemi M. Disposition of lipid-based formulation in the intestinal tract affects the absorption of poorly water-soluble drugs. Biol Pharm Bull 2006;29:508-12.
12. Wu W, Wang Y, Que L. Enhanced bioavailability of silymarin by self-microemulsifying drug delivery system. Eur J Pharm Biopharm 2006;63:288-94.
13. Gupta AK, Mishra DK. Preparation and evaluation of self-emulsifying drug delivery system of anti-hypersensitive drug valsartan. Int J Pharm Life Sci 2011;2: 633-639.
14. Chopade VV, Chaudhari PD. Development and evaluation of self-emulsifying drug delivery system for lornoxicam. Int J Res Dev Pharm Life Sci 2013;2:531-7.
15. Patel PA, Chaulang GM, Akolkotkar A, Mutha SS, Hardikar SR, Bhosale AV. Self-emulsifying drug delivery system: A review research. J Pharm Technol 2008;1:54-68.
16. DeshmukhA, Nakhat P, Yeole P. Formulation and in-vitro evaluation of self microemulsifying drug delivery system (SMEDDS) of furosemide. Sch Res Lit Der Pharm Let 2010;2:94-106.
17. Patel MJ, Patel NM, Patel RB, Patel RP. Formulation and evaluation of self-micro-emulsifying drug delivery system of lovastatin. Asian J Pharm Sci 2010;5:266-75.
18. Patil P, Patil V, Paradkar A. Formulation of a self-emulsifying system for oral delivery of simvastatin: In vitro and in vivo evaluation. Acta Pharm 2007;57:111-22.
19. Sapraa K, Saprab A, Singha SK, Kakkarb S. Self-emulsifying drug delivery system: A tool in solubility enhancement of poorly soluble drugs. Indo Glob J Pharm Sci 2012;2:313-32.
20. Harshal DM, Shaikh T, Baviskar D, Rajendra DW. Design and development of solid self-micro-emulsifying drug delivery system (smeds) of fenofibrate. Int J Pharm Sci 2011;3 Suppl 4: 163-166.
21. Pandya D, Patel P, Patel S. Formulation & development of self-micro emulsifying drug delivery systems of amiodarone HCl for dissolution enhancement. Discov Pharm 2013;5:6-12.

How to cite this article: Chintalapudi R, Murthy T, Lakshmi KR, Manohar GG. Formulation, optimization, and evaluation of self-emulsifying drug delivery systems of nevirapine. Int J Pharma Invest 2015;5:205-13.

Source of Support: Nil. Conflicts of Interest: None declared.