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Research Article

# Formulation and *In Vitro* evaluation of self-nano emulsifying drug delivery system (SNEDDS) containing an anti-HIV drug

**Prakash Ch. Senapati[1], Sunit Kumar Sahoo[2]**
[1]*Sri Jayadev College of Pharmaceutical Sciences, Naharkanta, Bhubaneswar, Odisha, India.*
[2] *UDPS, Utkal University,Vani Vihar, Bhubaneswar, Odisha, India.*

## ABSTRACT
The aim of the research work was to formulate & characterize self-nano emulsifying drug delivery system (SNEDDS) containing an anti-HIV drug for non-invasive delivery. SNEDDS were isotropic mixture of oil, surfactant and cosurfactant. A fixed amount of anti-HIV drug (150mg) was present in each formulation. The solubility studies of the drug were carried out in various vehicles of oils, surfactants and cosurfactants. Pseudoternary phase diagrams were constructed for identifying required self-emulsification region. The optimized formulation containing the fixed amount of drug was assessed by drug content, spectroscopic clarity, emulsification time, phase separation, particle size, FT-IR and dissolution studies. Prepared formulations had good optical clarity, all formulations scare of phase separation and carried good emulsification time with almost 100% drug content. FT-IR analysis study indicates good compatibility of the drug with the excipients. Particle size of maximum formulations was less than 100 nm with better poly dispersivity index (PDI). Comparative dissolution study shows that much better drug release from SNEDDS than a branded tablet and pure drug molecule. These results concluded the potential of SNEDDS as an efficient way of enhancing the dissolution of the anti-HIV drug which may improve the oral absorption.

**Key Words:** SNEDDS, cremophor EL, efavirenz, dissolution

**Address for Correspondence**:
**Sunit Kumar Sahoo**
UDPS,Utkal University,
Vani Vihar,Bhubaneswar,
Odisha,India.
**E mail:** sahoosunitkumar@rediffmail.com
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## INTRODUCTION
SNEDDS consist of an isotropic mixture of oil(s), surfactant(s) and/or cosurfactant(s) with drug and the simple mixing of these ingredients in aqueous media can generate micro/nanoemulsion droplets (with a mean droplet size ≤100 nm) of solubilized drugs (Pouton, 1997).SNEDDS partially avoids the additional drug dissolution step prior to absorption in the GI tract. They increase the amount of solubilised drug in the intestinal fluids resulting in good drug absorption. Maximum recent work on oral dosage forms using self-nanooemulsifying drug delivery systems (SNEDDS) have been designed mainly for the purpose of enhancing the solubility, dissolution, and oral absorption of poorly aqueous-soluble drugs (Itoh *et al.*, 2002; Kim *et al.*, 2000).Available drugs in the market that use this SNEDDS include cyclosporin A, also formulations of ritonavir and saquinavir (HIV protease inhibitors), and the usefulness of this system has also been accessed clinically (Cooney et al., 1998; Porter & Charman, 2001).

Aids is a serious viral disease of the human immune system caused by the human immunodeficiency virus (HIV).During the initial

infection a person may experience a brief period of influenza-like illness. This is typically followed by a prolonged period without symptoms. As the illness progresses it interferes more and more with the immune system, making people much more likely to get infections, including opportunistic infections, and tumours that do not usually affect people with working immune systems. Non nucleoside reverse transcriptase inhibitors efavirenz used either alone or in combination with other drugs for this pandemic curse disease. Which has very poor aqueous solubility hence show dissolution related bioavailability problem. This work aimed to develop a SNEDDS formulation of a poorly aqueous soluble anti HIV drug for improving the dissolution rate and may enhancing the oral bioavailability.

## EXPERIMENTAL

*Materials:*

Efavirenz was obtained as a gift sample from Cipla(Mumbai,India),Cremophor-EL (Cr-EL) and Cremopror RH 40 were gift samples BASF India (BASF, Mumbai, India),.Polyoxyethylene(23) lauryl ether (Brij-35) was obtained from Fluka (a subsidiaries of Sigma-Aldrich, USA), Capmul MCM (Glyceryl Caprylate) were gift samples from Abitec corporation(USA), Transcutol P, Labrafil M 1944 CS were gift samples from Gattefosse India (Mumbai, India),Eucalyptus oil (EO) was purchased from B.D. Pharmaceutical Works (India), Clove oil, Flaxseed oil and Olive oil were purchased from Research Lab Fine Chem(Mumbai, India), Ethanol, 1-Propanol, 1-Butanol, propylene glycol, polyethylene glycol 400 (PEG 400), Tween 20,Tween 40,Tween 60 andTween 80 and Sodium Lauryl Sulphate were purchased from S.D. Fine Chemicals (Mumbai,India). All the excipients and reagents of analytical grade were used as received. Freshly prepared double distilled water was used whenever required.

*Drug solubility:*

Excess amount of Efavirenz was added to 1ml of each excipient (oil, surfactant and cosurfactant) placed in microtubes and the mixture was vortexed, heated to 40°C in a water bath to facilitate drug solubilization. The mixture was finally kept at ambient room temperature (25° C) under continuous shaking for 48 hours to attain equilibrium. The mixtures were then centrifuged at 3000 rpm for 15 min. Aliquots of supernatant were diluted with methanol, and the drug content was quantified using a UV spectroscopic method. The solubility of drug was determined from a calibration curve of drug in methanol. The result of solubility studies was shown in Table 2.

*Pseudoternary phase diagram studies:*

The pseudo-ternary phase diagrams were constructed using the data obtained by titration of homogeneous mixture of oil, surfactants and cosurfactant at varying ratios with water at ambient temperature (Chen *et al.*, 2004). The oil, surfactant and cosurfactant at different ratios(2:1,3:1)were dispersed at weight ratios of 10:0,9:1,8:2,7:3,6:4,5:5,4:6,3:7,2:81:9 and 0:10 into different vials. Each vial containing the liquid mixtures were titrated with water by adding in a drop-by-drop manner from a microsyringe. Following each water addition the mixture was homogenized by vortexing the vial for 2-3 min and sample was monitored visually for any change of optical transparency. The concentration of oil, water, surfactant and cosurfactant in each vial at this stage of critical change in transparency was constituted the points between a clear microemulsion or nanoemulsion phase and a translucent two phase region **(**Fang Zhong *et al*., 2009**)**.The above titrations generate the data to construct the required pseudoternary phase diagram. Formulations were selected with desired component ratios after identification of microemulsion region.

*Preparation of SNEDDS:*

After carefully evaluation of phase diagrams, a series of SNEDDS were formulated using varying ratio of oil, surfactant, co-surfactant, and efavirenz. In all the preparations, the concentration of efavirenz was constant. Accurate quantity of the oil, surfactant and co-surfactant were heated at 40°C for 5 min. The drug was added in the weighed amount of the mixture followed by vortex mixing till drug get solubilized. The formulations were kept in sealed glass container at room temperature until further use. The preparations were presented in Table 1.

| Formulation code | Oil | Surfactant*:cosurfactant* | Drug (mg) |
|---|---|---|---|
| F-1 | 20 | 53.34:26.67 | 150 |
| F-2 | 20 | 60:20 | 150 |
| F-3 | 20 | 53.34:26.67 | 150 |
| F-4 | 20 | 60:20 | 150 |
| F-5 | 20 | 53.34:26.67 | 150 |
| F-6 | 20 | 60:20 | 150 |
| F-7 | 20 | 53.34:26.67 | 150 |
| F-8 | 20 | 60:20 | 150 |
| F-9 | 20 | 53.34:26.67 | 150 |
| F-10 | 20 | 60:20 | 150 |
| F-11 | 20 | 53.34:26.67 | 150 |
| F-12 | 20 | 60:20 | 150 |

**Table 1:** Formulations SNEDDS Composition (% W/W)
*F-1 to F-6 contains Cr El and F-7 to F-12 contains Brij 35 as surfactant respectively.

*F-1, F-2, F-7,F-8 contains transcutol P ,F-3,F-4,F-9,F-10 contains ethanol and F-5,F-6,F-11,F-12 contains n-propanol as cosurfactant respectively.

*Drug content studies:*

Weighed amount of formulations were assayed to determine the drug content. The weighed samples were dissolved in methanol and stirred by vortex mixer. The solutions were diluted to follow Lambert beer law. The solutions filtered, using Whatman filter paper was estimated spectrophotometrically (UV, Shimadzu, Japan) at 247nm using standard curve.

*Percentage Transmittance ($\lambda_{max}$ 500 nm) studies:*

A total of 1 mL of the SNEDDS formulation was diluted 100 ml of distilled water and 2 % w/v SLS solution. Absorbance of the diluted formulation was measured Specrtophotometrically (UV-1800, Shimadzu, Japan) at $\lambda_{max}$ 500 nm at 0,30, 60, 90, 120,180, and 240 minutes post dilutions using water as a blank. This test was performed to access the optical clarity of the formulation after dilution.

*Emulsification time studies:*

The emulsification time of SNEDDS formulation was investigated on USP dissolution apparatus (TDT-08L, Electrolab, Mumbai, India). Each formulation (1ml) containing 150mg of drug was added drop wise to 100 mL of distilled water maintained at 37 ± 0.5° C. Gentle agitation was provided by a standard stainless steel dissolution paddle rotating at 50 rpm. The emulsification time was assessed visually as reported by Khoo *et al*.2008.

*Phase Separation Studies:*

As all emulsions prone to phase separation this study is designed at the initial stage of formulation development to access whether the formed nanoemulsion shows any sign of phase separation or not.This test was performed by taking adding 1 mL of SNEDDS to a glass test tube containing 5 mL distilled water at 25° C. After 1 min vortex mixing, mixture was kept for a period of 2 h and any sign of phase separation was observed visually. (Patel D. & Sawant Krutika K.2007)

*Fourier transforms infrared spectroscopic studies:*

FT-IR spectra of pure drug powder, eucalyptus oil cremophor EL, brij 35, transcutol P, ethanol and n-propanol along with some selected SNEDDS were carried out using diffuse reflectance spectroscopy (DRS)–Fourier transform infrared spectroscopy (FTIR) (FTIR-8400S; Shimadzu,Tokyo, Japan). For each spectrum, 32 scans were obtained at a resolution of 4 $cm^{-1}$ from 4000 to 500 $cm^{-1}$.The analysis may be a sign of drug compatibility.

*Droplet Size Analysis:*

SNEDDS containing 150 mg drug (1 mL) was diluted to 100ml with distilled water in a flask and was mixed gently by inverting the flask. The droplet size distributions of resultant nanoemulsion were determined after 1 hr, 2 hr, 3hr and 4hr of post dilution by laser light scattering particle size analyzer (Malvern Instruments). The results are shown in Table 6.

*In vitro release studies:*

The *in vitro* release test was performed in a USP XXIII apparatus I (Dissolution Test Apparatus, USP standard, DA-6D, Bombay, India) at 37 ± 0.5° C with a rotating speed of 50 rpm in 2 % SLS as dissolution media. Each SNEDDS formulation equivalent to 150 mg of drug was freshly filled in hard gelatin capsules (size 0). The same SNEDDS formulation of the same weight but free of drug was placed in hard gelatin capsules and subjected to dissolution to serve as a blank. These capsules were placed in a basket and rotated at 50 rpm using 500 mL 2 % SLS, with a temperature maintained at 37 ± 0.5° C. The samples (1mL each) were removed at specified time intervals, namely, 5, 15, 30, 45, 60, 90 and 120min. The withdrawn samples were filtered using 0.45 µm Millipore filter the drug content was determined spectrophotometrically at the predetermined λmax ie 247 nm against a blank of the same SNEDDS formulation but free of drug. An equal volume of 2 % SLS was added to the release medium to maintain constant dissolution volume. Three such determinations were carried out for each formulation. The calibration curve was made in 2 % SLS and at 247 nm. Release data was statistically analyzed.

**RESULT AND DISCUSSION:**

*Drug Solubility:*

For successful delivery of drugs via SNEDDS, the entire dose of the drug should be soluble in an acceptable volume of oil, surfactant and co-surfactant mixture. If the drug solubility is inadequate there are chances of drug precipitation upon aqueous dilution. Equilibrium solubility measurements of the drug in the selected vehicles were carried out to identify the suitable oil, surfactant/co-surfactant having maximal solubilizing potential for drug under investigation is very important to achieve optimum drug loading (Pouton, 1997, 2000). Thus the solubility of the drug in the excipient is an important criterion for selection apart from the excipient's self-microemulsifying tendency. Equilibrium solubility measurements of the drug were carried out in all available excipients i.e oils and surfactants and co-surfactants and data is

given in Table-1.From the data efavirenz shown good solubility in Eucalyptus oil and among surfactants the solubility is found to be high in Cremophor EL, Brij 35, and labrasol and among the co-surfactants transcutol P ,ethanol and n-Propanol shown considerable solubility. Upon aqueous dilution, the co-surfactants will separate from oil components forming a micellar dispersion producing a reduction in solvent capacity for the drug. Thus it is necessary for the drug to have good solubility in the oil as well as the surfactant. Among the evaluated excipients, Cremophor El, Brij-35, transcutol P ,ethanol and n-propanol demonstrated good solubility for efavirenz suggesting that their use in drug delivery would be appropriate. Upon scanning the $\lambda_{max}$ of the drug in the presence of various vehicles, it was observed that there was no shift in λmax of drug. It can be inferred that selected vehicles will not interfere with the developed analytical method of the drug.

| Excipients | | Solubility (mg/ml) ± S.D. |
|---|---|---|
| OILS | 1.Eucalyptus oil | 900±.054 |
| | 2.Clove oil | 477±.012 |
| | 3.Olive oil | 25±.028 |
| | 4.Castor oil | 64±.014 |
| | 5.Linseed oil | 30±.029 |
| | 6.Capmul MCM | 169±.034 |
| SURFACTANTS | 1.Cremophor EL | 500±.034 |
| | 2.Cremopror RH 40 | 400±.027 |
| | 3.Tween 20 | 156±.023 |
| | 4.Tween 40 | 167±.027 |
| | 5.Tween 60 | 189±.032 |
| | 6.Tween 80 | 220±.042 |
| | 7.Brij 35 | 480±.041 |
| | 8.Labrafil M 1944 CS | 450±.046 |
| COSURFACTANTS/ CO-SOLVENTS | 1.Ethanol | 612±.045 |
| | 2.n-Propanol | 713±.023 |
| | 3.n-Butanol | 812±.045 |
| | 4.Transcutol P | 1600±.056 |
| | 5.Propylene Glycol | 368±.062 |
| | 6.PEG 400 | 420±.042 |

**Table 2:** Solubility Studies of Various Excipients

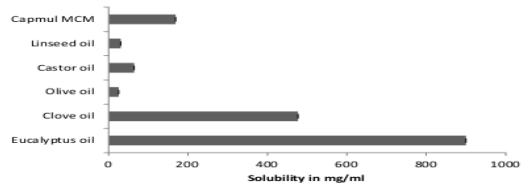


**Figure 1:** Comparative histogram of drug solubility in different oils.

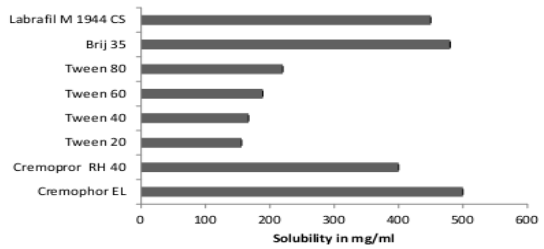


**Figure 2:** Comparative histogram of drug solubility in different surfactants.

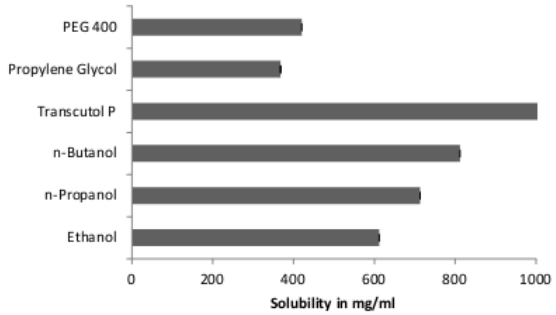


**Figure 3:** Comparative histogram of drug solubility in different cosurfactants.

*Pseudoternary phase diagram studies:*

SNEDDS forms thermodynamically stable, isotropic, fine oil in water dispersion upon its introduction to aqueous media with only gentle agitation, since very low free energy required to form emulsion (Craig, Barker, Banning, Booth, 1995). Pseudo ternary Phase diagrams constructed to identify self-nanoemulsifying region and to obtain the optimum concentration of the oil, surfactant and co-surfactant for the formulation of SNEDDS. Surfactant covers the emulsion droplets and reduces the interfacial energy as well as prevents coalescence by providing a mechanical barrier to it. The spontaneity of emulsion formation simply measured by visual assessment. The series of SNEDDS were prepared and their self-emulsifying properties were observed visually. The Fig. 4 shows the pseudoternary pahse diagrams of systems containing Brij 35 and different cosurfactants. Here increasing the ratio of surfactant to cosurfactant from 2:1 to 3:1 has not significantly affect the monophasic zone. Fig.5 shows the pseudoternary pahse diagrams containing Cremophor El as surfactant the increase in ratio increases the monophasic zone . The reason may be due to the availability of more amount of surfacatant at oil water interface to reduce the surface free energy and enabling a stable emulsion formation. Moreover in both cases the cosurfactant n-Propanol shows maximum monophasic area because of has the ability to provide additional support to the surfactant made interfacial film at the oil water interface. Tweleve formulations were selected

for further evaluations on the basis of solubility and pseudoternary phase diagram studies (Table 1).

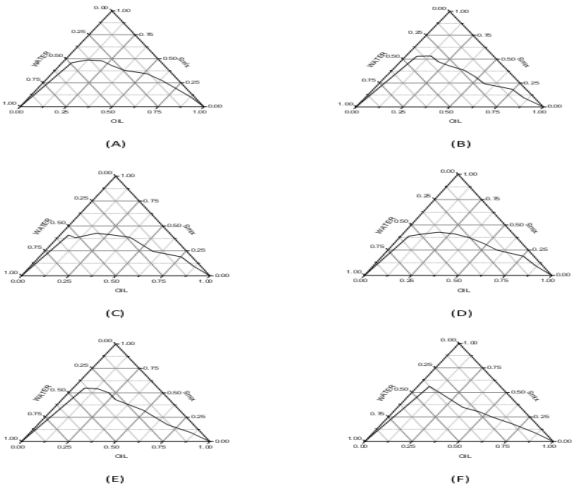


**Figure 4:** Pseudoternary phase diagrams of the systems of (A)oil/Brij 35:ethanol(2:1)/water; (B)oil/Brij35:ethanol(3:1)/water(C)oil/Brij35:propanol(2:1)/ water,(D)oil/Brij35:propanol(3:1)/water,(E) oil/Brij 35:transcutol(2:1)/water,(F) oil/Brij 35:transcutol(3:1)/water. The area outside the curve represents monophasic zone.

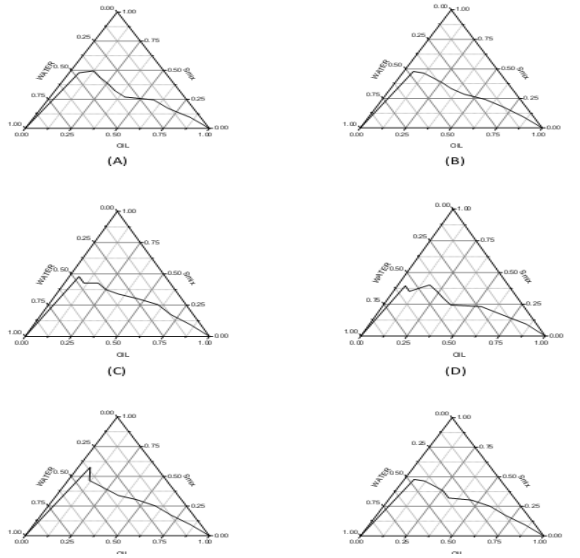


**Figure 5:** Pseudoternary phase diagrams of the systems of (A) oil/Cr El:ethanol (2:1)/water; (B) oil/CrEl:Ethanol (3:1)/water(C)oil/CrEl:propanol (2:1)/water,(D) oil/CrEl:propanol (3:1)/water,(E) oil/ Cr El:transcutol(2:1)/water,(F) oil/ Cr El:transcutol(3:1)/water. The area outside the curve represents monophasic zone.

*Determination of Drug Content:*

Drug content of the twelve SNEDDS formulation was obtained in the limit of 99.47-101.81 with low standard deviations (±1.91) showing uniform dispersion of drug in formulations, which was in the limit (Patil, Praveen, Shobha Rani, &Paradkar, 2004). This test eliminates the effect of overloading the capsule with more than 150 mg of drug, which would give false results later in the *in vitro* dissolution studies. The result was shown in Table 3.

| Formulation code | Amount of Drug(Mean±SD) | % Drug Entrapment |
|---|---|---|
| F-1 | 151.97±0.112 | 101.31 |
| F-2 | 152.79±0.213 | 101.81 |
| F-3 | 151.34±0.142 | 100.89 |
| F-4 | 150.56±0.182 | 100.373 |
| F-5 | 151.52±0.156 | 101.11 |
| F-6 | 149.31±0.310 | 99.54 |
| F-7 | 150.56±0.225 | 100.37 |
| F-8 | 151.24±0.234 | 100.82 |
| F-9 | 149.37±0.126 | 99.58 |
| F-10 | 151.35±0.126 | 100.90 |
| F-11 | 149.21±0.145 | 99.47 |
| F-12 | 148.45±0.152 | 98.96 |

**Table 3:** Drug Content in Different Formulations

*Percentage Transmittance ($\lambda_{max}$ 500 nm):*

Optical clarity study show how much clear the micro emulsion for how much time. The more clarity for maximum time show there is no sedimentation of drug particle or no aggregation of globule phase or any precipitation in the Emulsion. Increase in clarity show decreases in droplet size of the emulsion cause more stable of the formulation. To measure the optical clarity quantitatively, UV-VIS spectrophotometer was used to determine the amount of light of a given wavelength transmitted by the solution. Percentage transmittance of microemulsion after 100 times dilution was shown in Table 4 .Which indicates clear microemulsion was formed from formulations containing transcutol as cosurfactant.This fine microemulsion also shown no remarkable change in transmittance within 4 hrs of study which is an indication of stability in terms of particle size of the formulation.

| Formulation code | % Transmittance at time interval (min) | | | | | | |
|---|---|---|---|---|---|---|---|
| | 0 | 30 | 60 | 90 | 120 | 180 | 240 |
| F-1 | 93.1 | 92.7 | 92.9 | 93.2 | 93.3 | 93.0 | 93.3 |
| F-2 | 97.0 | 96.5 | 96.3 | 96.8 | 97.0 | 96.9 | 96.3 |
| F-3 | 80.3 | 76.7 | 77.0 | 78.0 | 78.3 | 77.7 | 70.0 |
| F-4 | 72.4 | 70.0 | 70.3 | 71.1 | 71.2 | 71.3 | 71.4 |
| F-5 | 85.5 | 85.1 | 85.9 | 86.2 | 85.8 | 86.4 | 86.6 |
| F-6 | 80.7 | 80.1 | 80.7 | 80.5 | 80.9 | 81.4 | 81.6 |
| F-7 | 80.5 | 80.2 | 80.1 | 79.8 | 80.1 | 79.5 | 78.9 |
| F-8 | 84.5 | 84.0 | 82.9 | 84.1 | 85.3 | 82.4 | 88.2 |
| F-9 | 50.7 | 17.2 | 14.0 | 12.9 | 12.4 | 11.3 | 11.9 |
| F-10 | 52.2 | 19.0 | 15.5 | 13.8 | 12.9 | 11.9 | 12.7 |
| F-11 | 59.3 | 24.3 | 20.3 | 18.3 | 17.2 | 15.6 | 15.7 |
| F-12 | 63.5 | 27.3 | 22.5 | 19.8 | 18.8 | 17.7 | 20.9 |

**Table 4:** Percentage Transmittance of Different Formulations

*Emulsification study:*

The efficiency of emulsification was evaluated

by assessing the rate of emulsification when SNEDDS dispersed in an aqueous media with mild agitation. The result was shown in Table 5. The tendency to form emulsions appeared to be highly dependent on composition. The samples containing Cremophor El show rapid formation Crystal clear transparent blue or bluish white microemulsion/nanoemulsion which are in absolute molecular range. Also co-surfactant takes role in formation of micro emulsion. SNEDDS containing transcutol P and n-propanol show a better emulsion. There is no sedimentation for 4 h of study but formulation containing Brij-35 with ethanol and n-propanol show milky white translucent which is gradually changes from transparent bluish colour. It was found that diluting the self-nanoemulsified system by the aqueous phase various liquid crystalline phases are observed between the formulation and water (Iranloye TA, Pilpel N, Groves MJ. 1983).A delay in the emulsification time with increasing *S*mix content may be because of the time required for the transformation from one liquid crystalline structure to another during the emulsification process. However, these systems produced very fine dispersions within 1 minute under mild agitation (Singh, S.K., Verma, P. R. P., & Razdan, B. 2010).

| Formulation code | Ease of Emulsification | Time of Emulsification In second |
|---|---|---|
| 1 | Very good | 20 |
| 2 | Very good | 14 |
| 3 | Very good | 23 |
| 4 | Very good | 17 |
| 5 | Very good | 19 |
| 6 | Very good | 12 |
| 7 | Very good | 26 |
| 8 | Very good | 17 |
| 9 | Very good | 23 |
| 10 | Very good | 18 |
| 11 | Very good | 29 |
| 12 | Very good | 21 |

**Table 5:** Emulsification Time of Different Formulations

*Phase Separation Studies:*

Phase separation study indicates that formulations bearing the code F-1,F-2,F-7 and F-8 exhibited a very negligible phase separation during the 2 hr period were used for subsequent study (Shengmiao, Chunshun, Dawei, & Zhongui,2005).

*Fourier transforms infrared spectroscopic studies:*

FTIR study carried out for knows there is any structural interaction of drug polymer in the formulation. So drug oil and surfactant & co-surfactant in specific ratio intended for drug excipinent compatibility were subjected to IR analysis in order to evaluate for possible interaction and changes in drug properties. Any interaction between drug and surfactant or co surfactant may change in properties of drug in formulation which may cause change in actual pharmacological action of the drug may be fatal. The IR absorption spectra of the pure drug and its mixture with each of the excipients used individually was taken in the range of 4000-500cm$^{-1}$. The major Peaks were reported for evaluation of purity. Comparing the spectra of drug, excipients and formulations it was found that there was no difference in the position of the absorption bonds, hence providing an evidence for the absences of any chemical incompatibility between pure drugs with the excipients.

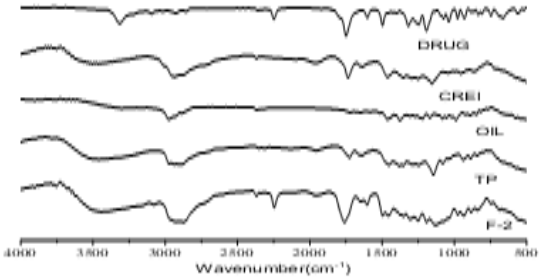


**Fig. 6** FT-IR spectra of drug, excipients and formulation F-2

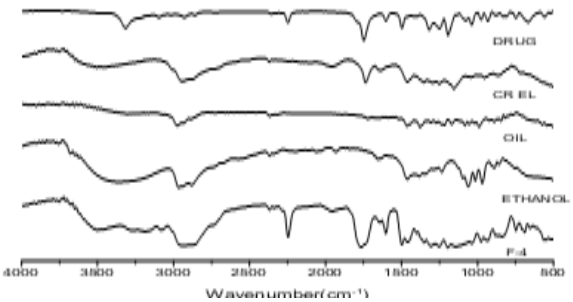


**Fig. 7** FT-IR spectra of drug, excipients and formulation F-4

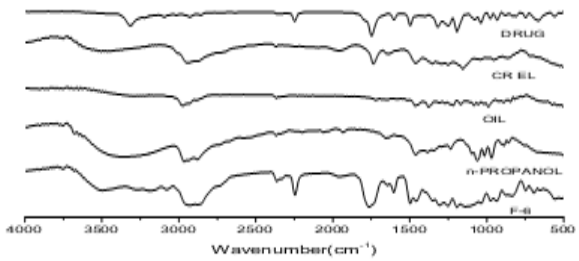


**Fig. 8** FT-IR spectra of drug, excipients and formulation F-6

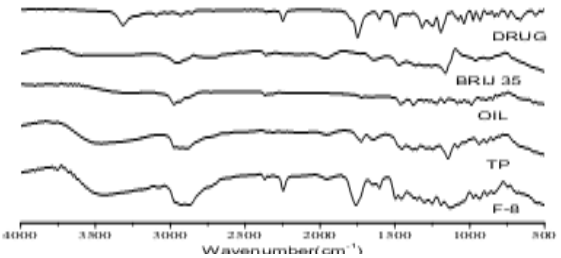


**Fig. 9** FT-IR spectra of drug, excipients and formulation F-8

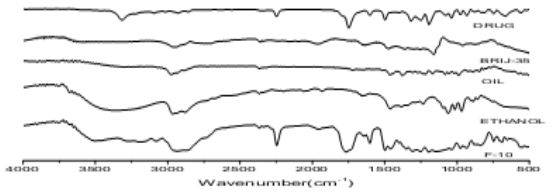


**Fig. 10** FT-IR spectra of drug, excipients and formulation F-10

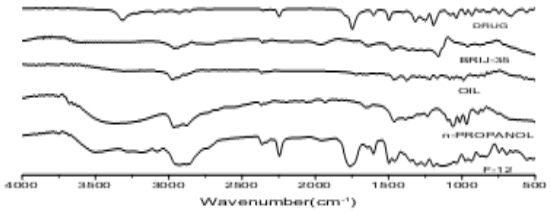


**Fig. 11** FT-IR spectra of drug, excipients and formulation F-12

*Droplet Size Analysis:*

The droplet size of the nanoemulsion is important since it determines the rate and extent of drug release and absorption. The drug can diffuse faster from smaller droplets into the aqueous phase, thereby increasing the drug dissolution. Smaller droplet size presents large surface area for drug absorption. Reduction in droplet size improved bioavailability of drug in nanoemulsion when compared to a coarse emulsion. Increase in surfactant concentration decreases the droplet size up to a certain size but thereafter anymore increase in surfactant concentration results in an increase in droplet size. The reduction in droplet size can be attributed to the stabilization of oil droplets due to localization of surfactant mono layers at the oil-water interface.

Increase in surfactant concentration causes enhanced water penetration into oil droplets leading to breakdown of larger oil droplets into very smaller ones. Visual observations clarified that at increasing levels of surfactant, the process of self-micro/nanoemulsification was more spontaneous. This is because of excess penetration of water into the bulk oil causing massive interfacial disruption and ejection of droplets into the bulk aqueous phase (Pouton, 1997). Presence of cosurfactant remarkably influence the particle size of the droplets formed from a SNEDDS because when a cosurfactant was added (in addition to surfactant) to the system, it lowered the interfacial tension, fluidized the hydrocarbon region of the interfacial film, and decreased the bending stress of the interface (Eccleston, 1992). The results are shown in Table 6.

| Formulation code | Zeta Average(nm) | | Pdl | |
|---|---|---|---|---|
| | Instant | 4th hr | Instant | 4th hr |
| F-1 | 61.85±1.3 | 58.56±1.1 | 0.375±0.023 | 0.387±0.098 |
| F-2 | 65.08±2.3 | 63.52±0.78 | 0.232±0.045 | 0.313±0.075 |
| F-3 | 84.82±2.1 | 83.32±0.29 | 0.383±0.043 | 0.513±0.095 |
| F-4 | 80.19±2.8 | 75.48±1.2 | 0.362±0.063 | 0.367±0.021 |
| F-5 | 88.25±2.7 | 89.48±1.8 | 0.279±0.012 | 0.265±0.023 |
| F-6 | 93.0.7±1.9 | 98.50±1.7 | 0.328±0.023 | 0.348±0.098 |
| F-7 | 63.86±1.8 | 62.22±1.6 | 0.372±0.045 | 0.229±0.065 |
| F-8 | 66.6±1.6 | 65.56±1.4 | 0.211±0.025 | 0.429±0.053 |
| F-9 | 124.0±1.11 | 128.6±19 | 0.286±0.043 | 0.272±0.045 |
| F-10 | 128.7±1.7 | 116.5±2.3 | 0.310±0.075 | 0.462±0.067 |
| F-11 | 119.2±0.98 | 112.3±3.7 | 0.408±0.071 | 0.425±0.087 |
| F-12 | 117.5±0.81 | 110.2±2.8 | 0.362±0.091 | 0.234±0.098 |

**Table 6:** Droplet Size of Different Formulations

*In Vitro release studies:*

The release of the drug from the SNEDDS (all twelve formulations), from a pure drug in a capsule and branded tablet was evaluated in 2% SLS as dissolution media, the percentage of the drug released from the SNEDDS was significantly higher than that from branded tablet and also from the pure drug(Fig. 12-15).The percentage release of drug from formulations F-1 &F-2 was more than 90% within 30 min .From the results, it can be concluded that the performance of SNEDDS depends on two important factors: 1) the ability of the self-microemulsifying mixture to form a nanoemulsion with uniform fine particle size droplets and 2) the ability of SNEDDS to present the drug in a solubilised and highly dispersed form, thereby overcoming the dissolution rate-limited step(Shengmiao C., Chunshun, Z., Dawei, C., & Zhonggui, H. 2005).

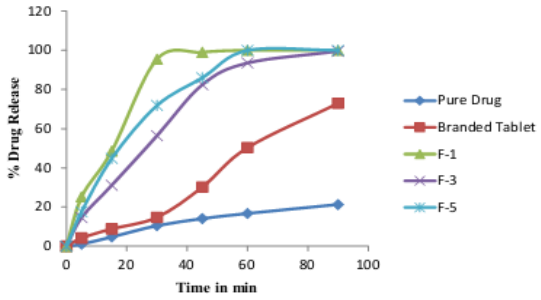


**Figure 12:** Comparative dissolution profile

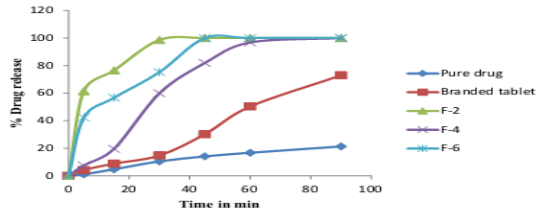


**Figure 13:** Comparative dissolution profile

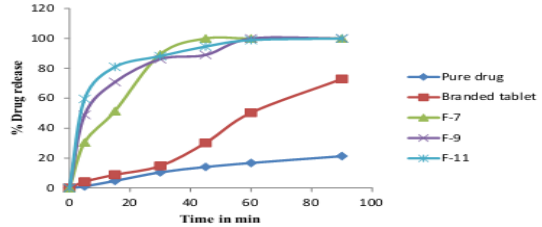


**Figure 14:** Comparative dissolution profile

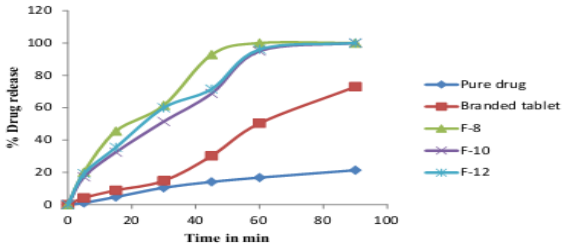


**Figure 15:** Comparative dissolution profile

## CONCLUSION

In the above research work, potential of SNEDDS formulation for oral delivery of a poorly aqueous soluble anti-HIV drug was investigated. Among the twelve preparations (F-1–F-12) formulated and evaluated, F-1 and F-2 are better for drug-loaded SNEDDS. FTIR studies indicated no interaction between drug, oil, and surfactants. Formulations containing CrEl as surfactant showed mean particle size less than 100nm after 4 hours post dilution in aqueous media. All formulation devoid of phase separation and F-1 and F-2 showed near 100% optical clarity.The results of the *in-Vitro* dissolution study indicate that the SNEDD formulations of drug owing to nanosize have much better percent drug release charcterstics than the pure drug and a branded formulation. Furthermore, the selected formulations (F-1 and F-2) that have been duly screened may be evaluated for their pharmacokinetic and pharmacodynamic profile in humans to the best of their advantage.

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