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Formulation And Evaluation Of Self Emulsifying Drug Delivery System Of Nevirapine

Divya Palaparthi, S.Jeganath*
Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Pallavaram, Chennai - 600117, Tamil Nadu, India.
*Corresponding author: S.Jeganath; Email Id: jeganaths@gmail.com

ABSTRACT:
A common non-nucleoside reverse transcriptase inhibitor in HIV treatment is nevirapine (NVP). NVP's oral bioavailability is limited by its poor water solubility and high permeability, which classify it as a Class II medication under the Biopharmaceutical Classification System (BCS). Self-emulsifying drug delivery systems, or SEDDS, have drawn interest as a useful strategy for improving the solubility and dissolving of medications that are not highly soluble in water. When gastrointestinal fluids are gently shaken, SEDDS isotropic combinations of oils, surfactants, and co-surfactants form fine oil-in-water emulsions, boosting surface area and promoting absorption. In this study, oleic acid was used as the oil phase, Tween 20 as the surfactant, and PEG600astheco-surfactant in different ratios to create NVP-loaded SEDDS. Solubility assessment, drug content analysis, Fourier-transform infrared spectroscopy (FT-IR) compatible excipient evaluation, measurement of droplet size and zeta potential, rheological analysis, and in vitro diffusion tests were all part of the pre formulation investigations. In comparison to pure NVP, the improved formulation, which included 32.5% oleic acid, 44.16% Tween 20 and 11.9%PEG 600, demonstrated high drug loading, enhanced solubility, nano sized droplets, and quick self-emulsification. Significantly enhanced release was validated by in vitro diffusion, and formulation robustness was shown by thermodynamic stability testing. Compatibility for encapsulation in firm gelatin capsules was demonstrated by viscosity tests. Overall, NVP's solubility and dissolution were significantly increased by the created SEDDS, which may have improved the drug's oral bioavailability and therapeutic efficacy. For the administration of NVP and other poorly soluble medications, the se results show that SEDDS technology can be a viable substitute, deserving of more research before being used in clinical settings.

Keywords: *Nevirapine, Self-emulsifying drug delivery system (SEDDS), Oral bioavailability, Solubility enhancement, Lipid-based formulation, In vitro drug release*

INTRODUCTION:

A non nucleotide reverse transcriptase inhibitor called nevirapine (NVP) is used to treat HIV infection. NVP is classified as a class 2 drug under the Biopharmaceutical Classification System (BCS), meaning it has high permeability and low solubility. Given the low cost of therapy and the convenience of administration, which increases patient compliance, the oral route is the most traditional and practical way to provide therapeutic substances.

A significant obstacle to contemporary drug delivery systems is the poor aqueous solubility of about 40% of novel chemical entities. The solubilization of these medications in the gastrointestinal (GI) tract is frequently the rate-limiting step for their absorption. According to BCS, these medications are categorized as class II medicines because of their high permeability and poor aqueous solubility. The bioavailability of highly lipophilic substances has been shown to be improved by lipid-based drug delivery systems, which can overcome the obstacle of slow dissolution rates by maintaining the medication in the dissolved state until it is absorbed. In actual use, lipid formulations can be anything from pure oils to formulations with varying amount sofco-solvents, surfactants, orco-surfactants. Recently, number of lipid formulation studies have concentrated on micro emulsion formulations, specifically on self-emulsifying or self-emulsifying drug delivery systems (SEDDS), to increase the oral bioavailability of medications that are not very water soluble.

Therefore, in order to improve the bioavailability of weakly water-soluble medications and achieve more effective therapeutic effects, alternate oral routes of delivery must be developed. One of the more intriguing methods for enhancing the solubility, dissolution, and oral absorption of medications that are

not very water soluble is the use of SEDDS.

One or more hydrophilic solvents and co-solvents/surfactants, oriso tropic mixes of natural or synthetic oils and liquid or solid surfactants, are examples of self-emulsifying drug delivery systems. These systems can create fine oil-in-water(o/w) emulsions or microemulsions upon gentle agitation and dilution in aqueous media, such as GI fluids.' The selected pharmaceutical excipients with low free energy are believed to work together to spontaneously generate the microemulsion. The GI tract's micro emulsion droplets offer a lot of surface area, facilitatethequickreleaseofthedrug'sdissolvedformand/ormixedmicelles containing it, and may also be in charge of moving the drug across the undisturbed water layer to the GI membrane for absorption. SEDDS's improved drug solubility is one factor that contributes to the increased bioavailability; another is that part of the total drug uptake is caused by lymphatic transport. Through the stimulation of intestinal lymphatic liquid flux and lipoprotein production, the lipid content of SEDDS may contribute to the extent of lymphatic drug transport.

The primary goal of this study is to create and assess the best SEDDS formulation with NVP.

Formulation of Nevirapine SEDDS:

Oleic acid was used as the oil, Tween20 as Surfactants, PEG600 were used as co-surfactants in the formulation of SEDDS Nevirapine.

FORMULATION	**NEVIRAPINE**	**OLEIC ACID**	**TWEEN60**	**PEG600 {%w/w}**
F1	75mg	75	30	27
F2	75mg	75	20.6	35.5
F3	75mg	75	15.6	40.7
F4	75mg	75	12	43
F5	75mg	75	45	13

PRE-FORMULATION:

Studies on solubility :

The solubility of poorly soluble drugs in oils, surfactants, and co-surfactants is the most significant factor for selecting components for microemulsion. The solubility of NVP in various oils was evaluated by dissolving an excess quantity of medication in 2 ml of selected oils, surfactants, and co-surfactants in 5 ml stopper vials and mixing with a vortex mixer. To achieve equilibrium, sample vials were maintained at 25°C ± 10°C in an ultrasonicator for 48 hours. The equilibrated samples were removed from the shaker and centrifuged at 5000 RPM for 15 minutes. After that, a 0.45 µm membrane filter was used to filter the supernatant. The absorbance of the samples at 313 nm was measured using an ultraviolet (UV) spectrophotometer to determine the concentration of NVP in the samples.

Drug content:

A formulation of a self-emulsifying drug delivery system containing 75mg of NVP was taken and dissolved in a tiny amount of methanol.0.1N HCl (1mg/ml)was used to get the volume up to 100 ml.0.2 ml (200 µg/ml) of the stock solution mentioned above was taken out and diluted with 20 µg/ml of methanol to make 10 ml. A UV-visible spectrophotometer was used to measure the absorbance at 313 nm after the samples were prepared in triplicate.0.1N HCl served as the standard solution.

Study compatibility of drug excipients :

The physical, chemical, and biological properties of the medicine and the excipients used in its manufacture must be taken in to account when designing and formulating the dosage form. For a product to be stable, effective, aesthetically pleasing, and safe, compatibility between the active component and

other excipients must be established. Compatibility studies are crucial if the excipient or excipients are novel and there is no prior research on their use with an active ingredient. Covalent bonds are linked to infrared (IR), and the spectra provide precise details about the molecular structure. Therefore, the Fourier transform infrared (FT-IR) spectroscopy technique was used to verify NVP's compatibility with various polymers and other excipients prior to creating the real formulation.
Fourier transform infrared spectroscopy is a practical analytical method that is used to examine the chemical interactions between the drug and other formulation excipients . With FT-IR, the interaction between the drug and the anticipated excipients was examined. Dry potassium bromide powder was combined with the intended samples, which were pulverized. After taking the powdered combination in a diffuse reflectance sampler, the FT-IR spectrophotometer was used to capture the spectra by scanning in the wavelength range of 4000-400 cm−1.

Zeta potential and droplet size determination :
Zeta potential measurement was used to determine the droplets' charge. Zeta potential aids in forecasting stability and the flocculation impact in emulsion systems. When the zeta potential drops below a particular threshold, colloid will assemble because of attraction forces. With a ZetasizerZS90 (Malvern Instruments, UK), the droplet size and zeta potential of the resulting emulsion were measured. At 25°C and a 90° angle, light scattering was seen.

FORMULATION CODE	DROPLET SIZE (nm)	POLYDISPERSIBILITY INDEX	ZETA POTENTIAL (mV)
F1	1768	1.00	-39.9
F2	929.8	1.00	-40.5
F3	706.1	0.595	-71.5
F4	319.2	0.478	-68.9

Study of in vitro diffusion :
The NVP SEDDS was the subject of an in vitro diffusion research using the dialysis procedure. A dialysis medium of 0.1N HCl was employed. After clamping one end of the dialysis tube (Dialysis membrane 70, HIMEDIA; MWCO 12,000-14,000 daltons; pore size: 2.4 nm), the experimental formulation sample was put within one end. After securing the opposite end of the tubing with dialysis closure clips (HIMEDIA, Mumbai), it was submerged in 900millilitersofdialyzingmediaandagitatedat50revolutionsper minute using a magnetic stirrer (Remi Instrument Ltd., Mumbai, India) at 37 degrees Celsius.At30-minuteintervals,5-mlaliquotsweretakenoutandappropriatelydiluted. The new dialyzing medium was used each time the aliquot volume was changed. These samples were examined using a UV-visible spectrophotometer set to 313 nm to determine whether NVP was present in the dialyzing liquid at the relevant period.
The determination of rheological properties:

In the current investigation, the SEDDS devices were placed within hard gelatin capsules. It can thus be easily poured into capsules, and systems of this kind shouldn't be overly thick. For SEDDS to manage the system's stability and provide a physical description of it, viscosity studies are required. Utilizing a spindle RV-6 at 100rpmand 25°C ± 0.5°C, the Brookfield viscometer (Japan) DV-E is used to assess the microemulsion's rheological characteristics (viscosity, flow). Whether the system is w/o oro/w, this viscosity determination is consistent. A low viscosity indicates an o/w kind of system, while a high viscosity indicates a w/o type of system.

TABLE:2

FORMULATION CODE	TYPES OF FLOW	TYPES OF FLOW
F1	Plastic flow	1113
F2	Plastic flow	829
F3	Plastic flow	1775
F4	Plastic flow	476.3

The ideal SEDDS formulation has 32.5% oleic acid, 44.16% tween 20, and 11.9% polyethylene glycol 600 as oil, surfactant, and co-surfactant, respectively. The SEDDS was assessed for drug content, self-emulsification time, rheological characteristics, zeta potential, in vitro diffusion, thermodynamic stability, and in vitro dissolution. SEDDS increased dissolution when compared to the pure form of NVP.

CONCLUSION:

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 oral 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, Tween20 (surfactant) and11.2% w/wPEG600 (co-surfactant) was successfully developed with a 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.

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