Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 32s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Formulation and Characterization of Efavirenz Nano emulsion Using Grapeseed Oil: A Strategy to Enhance Solubility and Stability

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Cite this paper as: Raushan Kumar, Dr. Nagesh D R, Harish Kumar S, Koustav Dutta, Vasu Choudhary, Dr. Archana Singh, Sachin Kumar, Sonika Prajapati, (2025) Formulation and Characterization of Efavirenz Nano emulsion Using Grapeseed Oil: A Strategy to Enhance Solubility and Stability. *Journal of Neonatal Surgery*, 14 (32s), 1473-1485.

ABSTRACT

The purpose of this research was to create and assess a nanoemulsion of grapeseed oil and Efavirenz to improve the drug's solubility in the formulation and, therefore, its bioavailability.Multiple components were tested in sample formulations to choose the best one based on composition, factorial design, clarity, and simplicity of nanoemulsion generation. Transcutol P was chosen as a co-emulsifying agent, tween 80 as the preferable emulsifying agent, and grapeseed oil as the oil.Factorial design was used to find an optimized formulation using the Design Expert software. To make a clear nanoemulsion, the components were combined, efavirenz was added, and a small amount of water was added to the mixture. Particle-size, Zeta-potential, TEM, DSC, TGA, In-vitro drug release and viscosity tests were all examined for the formulation. The normal droplet size of the formulation were found within the 10nm.The zeta-potential of the preparation was originated to be -20.1mV, representing that the formulation is rather stable. Centrifuge method was used to assess the efficiency of the drug entrapment. The In-vitro release studies of liquid formulation showed an increase in drug release profile of 75.38±1.31% in contrast to the marketed formulation (SUSTIVA600) tablet which showed the maximum release of 44.09±0.45%. The kinetics models were applied to the percentage release profile of the NE and it shows that the optimized formulation follows

the zero order showing constant release pattern. The stability studies for the optimized formulation were performed for in total 90 days in and the shelf life for the formulation was found to be 591 days. Nanoemulsions are the great carrier for improving the bioavailability and solubility of the any lipophilic drug which ultimately helps in increasing the potency of any formulation. Nanoemulsions are great choice for vaccine development and can further used in many other applications like in cosmetics, food and nutrition etc.

1. INTRODUCTION

The administration of pharmaceuticals should aim to maximize therapeutic benefit while limiting undesirable effects, as this is the overall purpose. Historically, administering a dose involved nothing more complicated than mixing the necessary components into a pill and swallowing it. However, thanks to recent developments in science and technology, there are now very complex systems available that are referred to as innovative medication delivery systems. Nanoemulsions are a one-of-a-kind medication delivery method that consists of oil and water droplets that range in size from fifty nanometers to one thousand nanometers. Nanoemulsions are made up of the droplets. In general, the size of droplets may range anywhere from 10 to 500 nm, and they can be classified as either oil-in-water (o/w) or water-in-oil (w/o), depending on the kind of liquid that is contained within the core of the particle. A nanoemulsion is a sort of medication that is produced by making use of pharmaceutical emulsifying chemicals that have been proved to have zero adverse effects. To obtain a high coalescence stability, it is necessary to pick the type of emulsifying agent to use and the concentration of that agent in the aqueous phase with great care. Nanoemulsions may be made from a variety of oils, including natural, semi-synthetic, and synthetic varieties. Nanoemulsions are effective drug delivery vectors due to the fact that they can dissolve large quantities of pharmaceuticals with reduced solubility, that they are typically well-suited to each other, and that they can shield medicines from being broken down by hydrolysis and enzyme activity**. Ravi et al.** the use of nanoemulsions as drug delivery carriers offers a number of advantages, including increased drug loading, improved drug solubility and bioavailability, reduced patient variability, controlled drug release, and protection from enzyme degradation. **Kotta et al.**

The utilization of lipid-based systems is one of several strategies for improving the absorption of unwell water-soluble medications. Thus, improving water solubility is a worthwhile objective with the purpose of construct them into accessible dose forms. For effective delivery of weakly water-soluble pharmaceuticals, a diversity of innovative methods are being discovered, counting formless hard form formulation, nanoparticles, microemulsions, solid dispersions, melt extrusion, salt creation, and production of water-soluble developments. The lipid-based formulation strategy is the most widely recognized of all. **Dixit and Nagarsenker, Shafiq et al.** Lipid-based formulations improve absorption by increasing solubility, extending gastric dwelling time, boosting the duodenal lymphatic transport channel, changing intestinal permeability, lowering efflux transporter activity, and slowing metabolism. Solution, suspension, self-emulsifying system, and nanoemulsion are all available as options in lipid-based formulations.

Efavirenz-loaded nanoemulsions are advanced drug delivery systems designed to enhance the solubility, bioavailability, and therapeutic efficacy of efavirenz, a lipophilic antiretroviral drug used in HIV treatment. These systems address challenges like poor water solubility and variable oral absorption, leveraging nanotechnology to improve pharmacokinetics and reduce dosing frequency. Below is a detailed analysis of their formulation, characterization, and performance:

Formulation and Optimization

Nanoemulsions are typically prepared using low-energy or high-energy methods:

Low-energy techniques (e.g., phase inversion) use flaxseed oil as the lipid phase due to efavirenz's high solubility in it, combined with surfactants like Tween® 80 and Span® 20, and ethanol as a co-solvent3. Pseudo-ternary phase diagrams help identify optimal ratios of oil, surfactant, and water.

High-energy methods (e.g., high-pressure homogenization) produce nanoemulsions with droplet sizes as small as 30–40 nm, using phospholipids and surfactants to stabilize the system4.

Design of Experiments (DoE), such as Box-Behnken designs, optimizes critical parameters like surfactant concentration and oil content to achieve desired droplet sizes and drug-loading capacities.

Key Characterization Parameters

Droplet Size: Ranges from 30–225 nm, depending on formulation methods (3: 156–225 nm;4: 30–40 nm). Smaller sizes enhance permeation and bioavailability.

Polydispersity Index (PDI): ≤0.487, indicating monodisperse distributions3.

Zeta Potential: Negative surface charge (−24 to −41 mV), ensuring stability by preventing droplet aggregation34.

Drug Entrapment Efficiency: Up to 86% in optimized formulations[24].

Pharmacokinetic Advantages

Nanoemulsions significantly improve efavirenz's pharmacokinetic profile:

Enhanced Bioavailability: A 2.2-fold increase in AUC (82.24 ± 18.13 μg·h/mL vs. 37.76 ± 10.37 μg·h/mL for suspensions) and higher C_{max} (2.9 ± 0.18 μg/mL vs. 1.8 ± 0.13 μg/mL)[4].

Controlled Release: Sustained drug release over 24 hours (60.6–98.22%) compared to rapid release from suspensions[24].

Lymphatic Uptake: Smaller droplets (<100 nm) target lymphoid tissues, critical for HIV reservoir reduction[3].

Stability and Safety

Physical Stability: Nanoemulsions remain stable at 40°C and 75% relative humidity for 180 days[28].

Chemical Stability: No degradation observed in differential scanning calorimetry (DSC) or Fourier-transform infrared (FTIR) analyses[5].

Cytotoxicity: Mitochondrial activity tests (MTT assay) confirm minimal cytotoxicity, with cell viability comparable to controls.

Efavirenz-loaded nanoemulsions demonstrate superior stability compared to traditional formulations (e.g., aqueous suspensions) across multiple parameters, as evidenced by these key findings:

Physical Stability

Particle Size Retention: Nanoemulsions maintain droplet sizes of 30–225 nm even after 8 weeks at 25°C/60% RH[13]. Traditional suspensions often exhibit particle aggregation and precipitation under similar conditions.

Example: Nanoemulsions stored at 40°C/75% RH retained 90% encapsulation efficiency for 90 days, while suspensions degraded faster[3].

Zeta Potential: Nanoemulsions show stable zeta potentials (−24 to −41 mV)[13], whereas suspensions lack electrostatic or steric stabilization, leading to instability[1].

Chemical Stability

Drug Integrity: No chemical degradation of efavirenz was observed in nanoemulsions after 90 days at 40°C/75% RH[3]. Traditional formulations are prone to hydrolysis and oxidation due to poor drug solubility[1].

FTIR and DSC analyses confirmed no structural changes in nanoemulsions.

Encapsulation Efficiency: Nanoemulsions achieve >90% drug encapsulation[13], compared to suspensions where drug precipitation reduces effective dosing[3].

Long-Term Stability

Storage Performance: Nanoemulsions remain stable for up to 24 months at 4°C with negligible changes in particle size (e.g., 104.5 nm to 107.7 nm over 2 years)[4]. Suspensions require frequent shaking or reformulation to maintain homogeneity.

Mechanisms Behind Enhanced Stability: Steric Stabilization: Tween® 80 in nanoemulsions prevents droplet aggregation even at lower zeta potentials[1].

Lyophilization Compatibility: Nanoemulsions can be freeze-dried to extend shelf life, whereas suspensions cannot[1].

pH Resistance: Nanoemulsions maintain stability across pH 1.2–7.5, critical for oral delivery.

Practical Implications

Reduced Dosing Frequency: Sustained release in nanoemulsions improves patient compliance. Pediatric Use: Stable nanoemulsions allow dose adjustment without compromising efficacy. In summary, efavirenz-loaded nanoemulsions outperform traditional formulations in stability metrics, enabling reliable long-term storage and controlled therapeutic delivery.

Efavirenz is an effective and safe anti-retroviral (ARV) medicine that, in both pediatric and adult pharmacotherapy, targets exclusively human immunodeficiency virus type 1. According to the biopharmaceutical categorization system, it is classified as a member of class II since it has an oral bioavailability of about 40% and is a highly lipophilic, non-nucleoside reverse-transcriptase inhibitor (NNRTI).

It has a low solubility in water (10 grams per milliliter), which contributes to its restricted bioavailability, and it has a low capacity for absorption in the fluid of the stomach.

Due to low bioavailability the drug has high dosage of about 600mg/day for adults, which can be decreased with

nanoemulsion.

Reason For Selection Of Excipients

Grapeseed-oil is employed as the oil phase for the nanoemulsion. When compared to other selected natural oils, such as sunflower-oil, soybean-oil, olive-oil, and coconut-oil, grapeseed oil showed the best solubility tests for the medicine. Additionally, grapeseed-oil is a natural oil that is non-toxic, does not irritate the skin, and can be consumed, making it an excellent choice for oral dose forms.

Tween 80 (HLB 15) is selected as emulsifying agent for the formulation due to its high HLB value. The emulsifying agent s ranging from HLB of 10-12 are proven suitable for the O/W nanoemulsion as it decreases the droplet size and increases the stability of nanoemulsion. Tween 80 is used to enhance the solubility of different hydrophobic pharmaceuticals as well as to solubilize poorly soluble drugs. This is accomplished by increasing the permeability of the cell membrane.

Diethylene glycol monoethyl ether: Commonly called Transcutol, is selected as co-emulsifying agent due to its high solubility with the drug. The solubility of drug Efavirenz in Transcutol was determined by the solubility studies. Transcutol P helps in solubilizing the hydrophobic drugs and works at a low quantity.

2. METHODS

PRE-FORMULATION STUDIES

Preformulation studies are being performed in-order to know the physiochemical characters of the drug and comparing it with that of standard parameters to establish the characteristics of drug.

Organoleptic Properties

This study is being performed to report the organoleptic properties of the medication such as color, taste, order, etc.

Color- Small amount of API was taken on a butter paper and was detected in a well illuminated place.

Odor- Small amount of API was taken in a butter paper and was smelled to identity it as Efavirenz.

Melting-Point

The melting-point of Efavirenz was found by using capillary-method with the help of melting-point device. The medication was half filled in a capillary and one side of which was sealed to avoid spilling of drug. The capillary was placed on to the apparatus the temperature at which the medication starts melting was recorded as melting point.

UV Spectrophotometric Studies- λ–Max

Ten milligrams of Efavirenz was diluted to one thousand micrograms per milliliter by dissolving it in ten milliliters of water: methanol (55:45) as a solvent system. The absorbance maxima were measured between 200 and 400 nm for aliquots generated at concentrations of 2 g/ml, 4 g/ml, 6 g/ml, 8 g/ml, and 10 g/ml.

Preparation of Calibration-Curve

On basis of different absorbance maxima of different concentration of aliquots through UV spectrophotometry the calibration curve is plotted on MS excel between concentration v/s absorbance.

Partition Coefficient

Partition coefficient is performed to analyze the weather the drug is lipophilic or hydrophilic in nature. In a separation funnel of equal amount of two immiscible liquids that is Octanol and water are used and mixed vigorously for an hour. Specific amount of Efavirenz was then dissolved in the blend and then shaken. The separating funnel was then set aside on stand for overnight. The two liquids were separated in separate beakers and were analyzed through UV spectrophotometry. Succeeding equation was used to determine the quantity of drug in both the liquids-

$$\text{Partition coefficient} = \frac{\text{Conc. of Efavirenz in Octanol phase}}{\text{Conc. of Efavirenz in Aqueous phase}} \qquad (5.1)$$

Solubility-Studies

Solubility-studies of drug in different oils, emulsifying agents and co-emulsifying agents were achieved to find out best excipient among all. Excipients showing higher solubility of drug will be considered for formulation. 10mg of drug was added to 5ml of oils, emulsifying agents and co-emulsifying agents and were diversified with the help of vortex for 2 hours. They each had 1 ml of their sample taken out so that the concentration could be measured by UV spectrophotometry.

3. DRUG-EXCIPIENT COMPATIBILITY STUDIES

Before formulation, one of the most important steps in the process of developing a new drug is evaluating whether or not the active component in question is compatible with the excipient. This stage takes place before formulation. The medicine and the excipients were mixed together and then weighed one last time before being placed on an F.T.I.R plate to make sure that their concentrations were the same. After conducting an F.T.I.R analysis of the mixtures in question in order to determine the drug-excipient interactions, the results of which were then compared to a reference standard and noted, the existence of a singular peak was investigated further.

Drug excipient compatibility testing were performed by using F.T.I.R.

4. PREPARATION OF NANOEMULSION

Selection of Components

The solubility of the medicine in the excipients played a role in the selection of the components of the formulation. An aqueous phase, emulsifying agents, and oil are the main building pieces that go into the creation of a nanoemulsion. Oils can originate from a broad range of plants and animals and are sold under a dizzying array of brand names, including sunflower-oil, olive-oil, castor-oil, peanut-oil, and many more. A combination of oil and water can give rise to an emulsion that is only temporary, but when some time has passed, the dispersed globules will come together and the two substances will become distinct. Examples of emulsifying agents are spans and tweens, while examples of emulgents that function on a molecular level include hydrophilic colloids and acacia. The patient must not be in any risk from any of the excipients, and they must all be safe to use individually and in combination.

In order to get to the formula, we need to: In this particular instance, we utilized a method known as spontaneous emulsification. In order to get a uniform mixture, (emulsifying agent) and (co emulsifying agent) were combined in a glass vial of 20 milliliters using magnetic stirring at a speed of 1200 revolutions per minute for a period of 45 minutes. After that, the oil phase was added, and the resultant emulsion was mixed for thirty minutes at a speed of six hundred revolutions per minute (rpm). The process of progressively putting the mixture into deionized water and then gently vortexing it resulted in the production of a transparent nanoemulsion.

Preparation of Efavirenz (EFV) Loaded NE

By adding 10 mg of EFV to 2 g of mix, stirring magnetically at 1200 rpm for six hours at 30°C, and letting the resulting formulation cool to room temperature, an EFV integrated formulation was created. Then, 0.6 mL of the oil-emulsifying agent combination containing the drug was added to 5 mL of deionized water. A clear, EFV nanoemulsion was successfully produced in a short amount of time.

Design And Optimization Of Nanoemulsion As Per Box-Behnken Design

Box-Behnken designs are one type of research strategy used with response surface methods in the discipline of statistics. George E. P. Box and Donald Behnken aimed to achieve the following with their designs: Each component, also recognized as a self-determining variable, is assigned to one of 3 values that are evenly spaced apart and are often represented by the codes -1, 0, and +1. (In order to accomplish the next aim, you will need at least three levels.) The design need to be adequate to accommodate a quadratic model, which is well-defined as one that incorporates squared terms, the products of 2 components, linear terms, and an intercept. It is crucial that the number of trial points be sufficient in relation to the total number of quantities in the quadratic model (in fact, their designs kept in the range of 1.5 to 2.6). Within the smallest (hyper) cube containing the experimental sites, the estimate variance should be independent of any other factors other than distance from the center (this is achieved exactly for the designs with 4 - 7 elements). All expectations are met for 4- and 7-factor systems. Design and optimization of preparation was done using Design Expert 13 software. The preparation was optimized on 3 levels and with 2 parameters which created the Box Behnken design. The Box-Behnken design is a popular experimental layout for response surface methods in statistical analysis. A consensus persists that the Box-Behnken layout is the most reliable and powerful choice.

Characterization Of The Optimized Formulation

Visual Assessment

The prepared NE formulations are evaluated visually by observing the transparency of the samples.

Entrapment-Efficiency

To assess the percentage of the medication that was kept in the formulation, a predetermined amount of the formulation was added to a mixture consisting of water and methanol, and the resulting mixture was centrifuged for 15 minutes at a speed of 4000 revolutions per minute. Following the removal of the supernatant layer, ultraviolet spectrophotometry at 246 nm was carried out. Use the following formula to get the value of E.E.

$$\text{Entrapment-efficiency(E.E)-} \frac{Total amount of medicine - Amount of medicine in supernatent}{Tolal amount of drug} \text{ x100}$$

Determination of Particle-size and Zeta-potential

After diluting the NE samples with filtered water at a ratio of 1:100, droplet size and Zeta-potential were restrained with a Litesizer 500 using omega cuvette Mat.No.155755 cell from ONIOSOME HEALTHCARE PRIVATE LIMITED, Mohali, and Punjab.

F.T.I.R Analysis

F.T.I.R examination of formulation was accomplished using Perkin Elmer instrument for observing any interaction in the prepared NE.

Transmission-Electron-Microscopy

The transmission electron microscope (TEM) imaging carried out by a Hitachi, Japan-based H-7500 was utilized in order to investigate the final formulation's surface morphology. ONIOSOME HEALTHCARE PRIVATE LIMITED, based in Mohali, Punjab, was the organization that carried out the readings.

Differential-Scanning-Calorimetry (D.S.C)

Differential scanning calorimetry, often known as DSC, is a technique for doing thermal analysis that entails measuring the amount of heat that is added to or removed from a sample over the course of a predetermined amount of time and/or temperature. This method may be used to analyse a wide variety of characteristics, including but not limited to glass transition temperature, melting point, crystallization, specific heat capacity, cure time, purity, oxidation behaviour, and thermal stability. IIT Kanpur was the location where the DSC investigations were conducted utilizing the SDT Q600 V20.9 Build 20 equipment.

Thermo-Gravimetric-Analysis (T.G.A)

When conducting T.G.A, a thermogravimetric analyser is used. A thermogravimetric analyser continuously measures mass even when sample temperature varies. Mass, temperature, and time are the fundamental quantities used as the starting points for a wide variety of calculations in thermogravimetric analysis. IIT Kanpur conducted the T.G.A tests using the SDT Q600 V20.9 Build 20 instrument.

Viscosity Studies

A viscometer was utilised in order to get readings on the nanoemulsion samples' levels of viscosity (Brookfield DV-II+ pro Apparatus). The spindle with the number 2 was utilised in a viscometer, and after being dipped in nanoemulsion, it was revolved at 5, 10, 20, and 50 revolutions per minute at a temperature of 25 degrees Celsius. Readings were taken from the viscometer at each and every speed. After doing three separate rounds of sampling, mean values were evaluated for each set of replicated data.

In-Vitro. Studies

The in vitro study measures the percentage of drug released from the formulation at various times.

In vitro studies of release were performed in nine hundered millilitre of 0.1M HCl with 2 percent sodium lauryl sulphate (SLS) at 50 rpm and 37C. We injected 1 mL of the nanoemulsion formulation into the 2.4nm dialysis bag. The 5 ml samples were taken at 30 min intervals. An aliquot of the dissolving medium was added to the original supply. A UV/VIS spectrophotometer, with the wavelength set to 245nm, was used to analyse the samples for the presence of the drug.

Drug Release Kinetics

Drug release kinetics is the kind of application of mathematical model of drug release. It is the overall release pattern of drug from the formulation. Values are put in different models such as zero-order, first-order, Higuchi, Korsmeyer-Peppas.

Results

Drug Identification Test

Organoleptic Properties

Color- The color of the medication was observed to be white which matches to that of standard which can be considered that the drug is EVF.

Odor- EFV does not tend to have any specific odor and observed medication was concluded to be odorless.

Melting-Point

In its purest form, Efavirenz melts at around 137 degrees Celsius, which is consistent with the melting point range mentioned

in the literature.

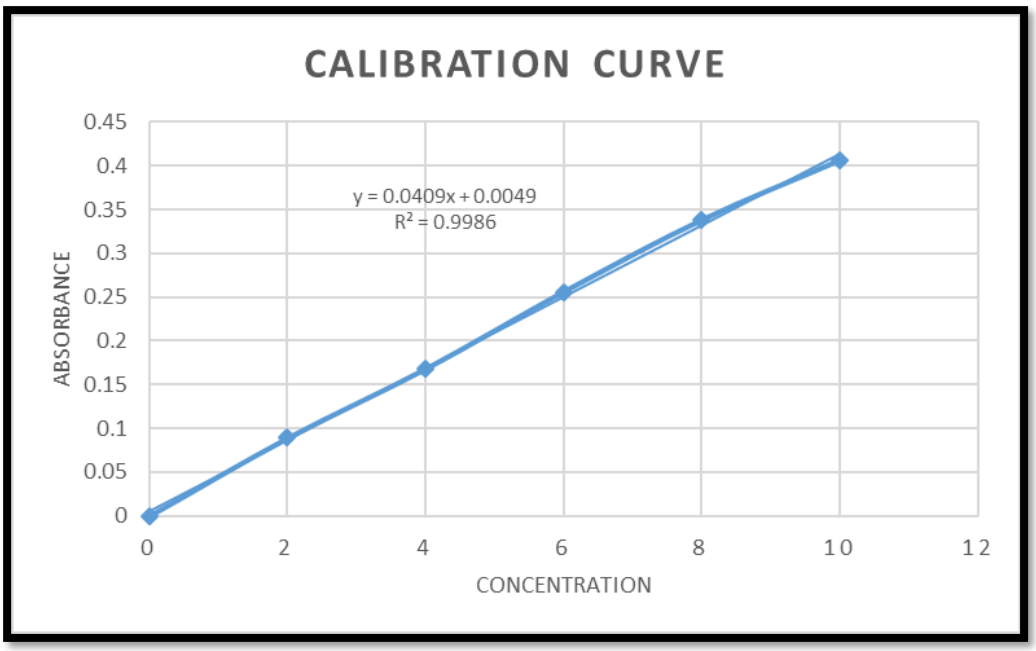
U.V Spectrophotometric Studies- λ–max

U.V Spectrophotometric analysis was performed in a water: methanol (55:45) combination because of the improved solubility, scanning from 200 to 400 nm with a -max of 204 nm.

Preparation of Calibration-Curve

Preparation of Calibration-Curve

S. no.	Concentration (µg/ml)	Absorbance (n.m) ±SD
1	0	0
2	2	0.089±0.25
3	4	0.168±1.17
4	6	0.256±1.31
5	8	0.338±0.12
6	10	0.406±0.24



Preparation of calibration curve

Partition Coefficient

The partition coefficient of Efavirenz was calculated using two immiscible phases of Octanol and water mixture, and it was estimated to be 4.6, showing that the drug is lipophilic.

Solubility

Solubility of EFV was determined in various oils and emulsifying agent s to choose the excipients with highest solubility.

Solubility in oils

Oils	Solubility (mg/ml) ±SD
Grapeseed oil	85.56±1.85
Olive oil	74.65±1.34
Soybean oil	56.44±0.88
Coconut oil	52.68±0.58
Sunflower oil	36.56±0.32

Solubility in emulsifying agent s

Emulsifying agent s	Solubility (mg/ml)±SD
Tween 80	78.32±1.33
Tween 20	55.12±0.86
Span 20	45.55±0.44
Tween 40	30.78±0.23

Solubility in Co-Emulsifying agent s

Co-emulsifying agent s	Solubility (mg/ml) ±SD
Transcutol P	527.07±0.30
Ethanol	42.61±1.28
Propylene glycol	37.15±1.17

Grapeseed oil, Tween 80 and Transcutol P are chosen as they exhibit higher solubility for the drug EFV. Maximum solubility for Transcutol P was calculated to be 527.070.38mg/ml. Because of their great solubility and their capacity to generate a clear transparent nanoemulsion, the aforementioned excipients were selected.The excipients are also nontoxic and comes under the generally regarded as safe (GRAS) materials.

Compatibility Studies Among Drug And Excipients

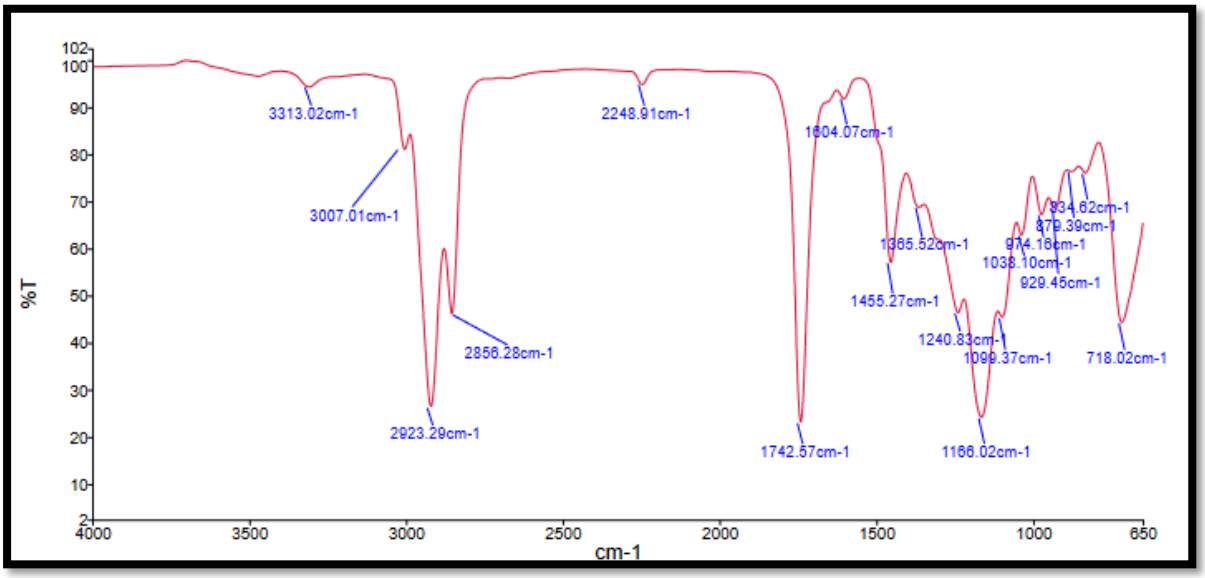
The knowledge gained here will be put to use in the next step of the drug development process, formulation, where it will be used to evaluate drug-excipient compatibility. In this experiment, the drug and excipients were weighed and mixed at the same time before being transported to the F.T.I.R plate. The mixes were analyzed using F.T.I.R to look for drug-excipient interactions; readings were recorded, compared to a reference, and any novel peaks were studied. The excipients included in the medication formulation are evaluated for their compatibility with the active pharmaceutical ingredient through a drug compatibility study. The F.T.I.R spectra of efavirenz with the various excipients studied here are shown. The peaks did not appear or depart. The discovered peaks fall within the bounds of typical spectra.

Efavirenz with Grapeseed Oil

The spectra of EFV and GSO was collected between 4000cm^{-1} to 450cm^{-1}.

The F.T.I.R of both the excipients does not tends to show any interaction, however careful examination of both the excipients shows some minor differences in peak region 1750-1700cm^{-1} (1742cm^{-1}), 3500-3300cm^{-1} (3313cm^{-1}), 1190-1000cm^{-1} (1651cm^{-1}) which indicate presence of carbonyl, -OH, -NH and CF group respectively.

However presence of all the functional groups of EFV reveals that the drug is present with the mixture of GSO and difference in peak lengths may be because of the existence of other groups of GSO such as carbonyl group at 1750-1700cm^{-1} region.



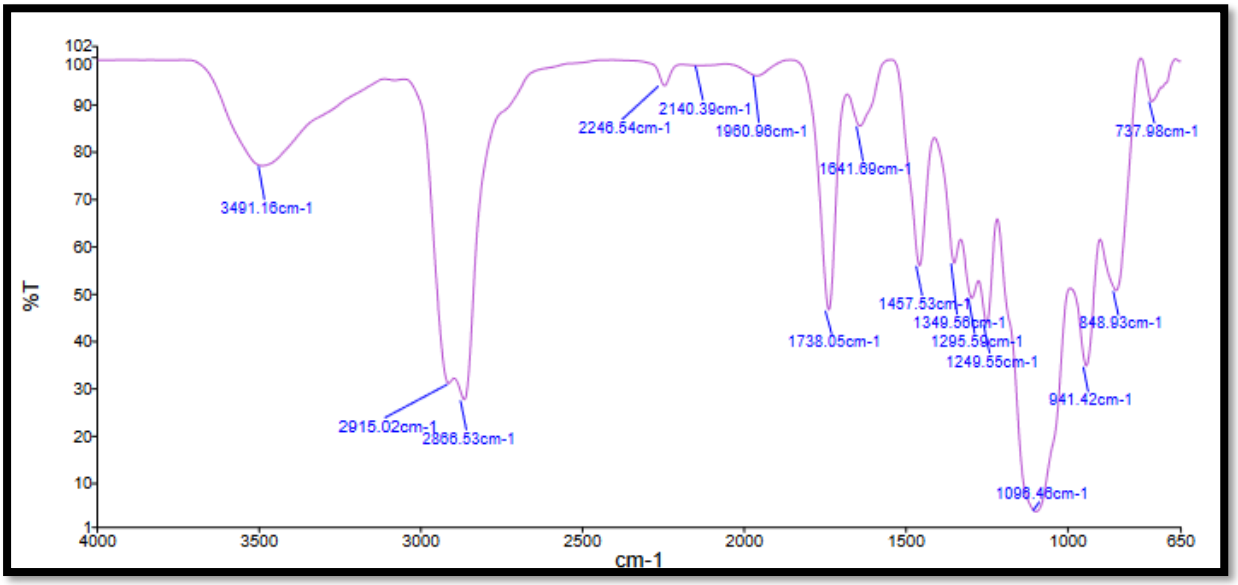
F.T.I.R spectra of EFV with Grapeseed oil

Efavirenz with Tween 80

The spectra of EFV and Tween 80 was collected between 4000cm^{-1} to 450cm^{-1}.

Two broad bands at 2915cm-1 and 2866cm-1 shows the C-H-stretching, band of methylene-group of Tween-80. The existence of –NH2 group of EFV can be understood at 3491cm-1 and peak at 1738cm-1 confirms the presence of carbonyl group of both EFV and Tween 80. CF group can also be seen at 1641cm-1.

Bands at 1095cm-1 and 737cm-1 refer to C-O-C stretching of Tween 80. Presence of all the functional groups of EFV shows that there's no interaction between the two excipients.

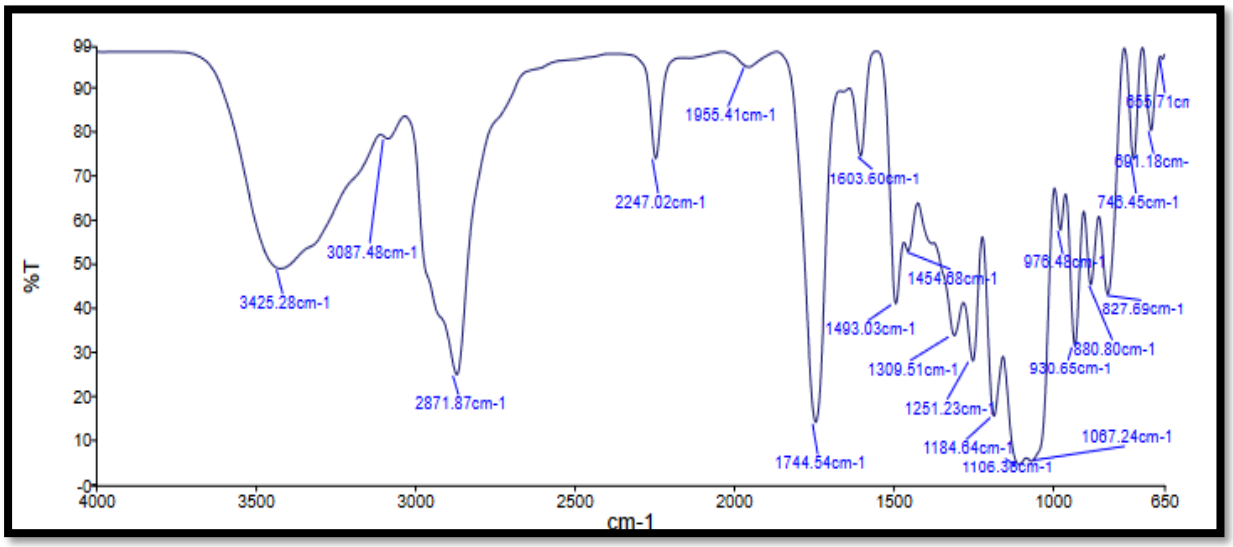


F.T.I.R spectra of EFV with Tween 80

Efavirenz with Transcutol P

The spectra of EFV and Tween 80 was collected between 4000cm^{-1} to 450cm^{-1}.

The broad band at 3426cm-1 is because of presence of great number of –OH groups in Transcutol P, peak at 2871cm-1 reveals the presence of –CH aliphatic group of Transcutol P. Triple bond of EFV can be confirmed at 2247cm-1 with carbonyl group at 1744cm-1. There's no prominent interaction between the excipients and presence of EFV can be confirmed



F.T.I.R spectra of EFV with Transcutol P

Characterization Of Formulation

Visual assessment

The prepared nanoemulsion was detected to be clear and transparent**.**

Percentage Entrapment-Efficiency

Only optimized preparations were employed in the entrapment efficiency research that was performed in order to calculate the amount of medication encapsulated within the preparation. The calculated percentages for each dish are as follows:

The entrapment efficiency of the preparation was evaluated to be 86.15±1.33%.

Particle-size and Zeta-potential

The droplet size distribution of a nanoemulsion is a crucial characteristic for evaluating the formulation's stability and biopharmaceutical properties. The lesser the particle-size, the bigger the interfacial-surface area available for drug preoccupation or penetration through biological membranes, and the greater the drug's bioavailability from the formulation.The formulation showed maximum distribution of droplets in the range of 10.00nm

When the Zeta-potential is greater than 30 mV, a stable dispersion may emerge. This is owing to the occurrence of repulsion-forces that prevent particles from aggregating.Low Zeta-potential levels might create inter-particulate contact between particles, jeopardizing the formulation's stability. The Zeta-potential for the preparation was found to be **-20.1mV** which shows that are formulation is fairly stable.

F.T.I.R Analysis

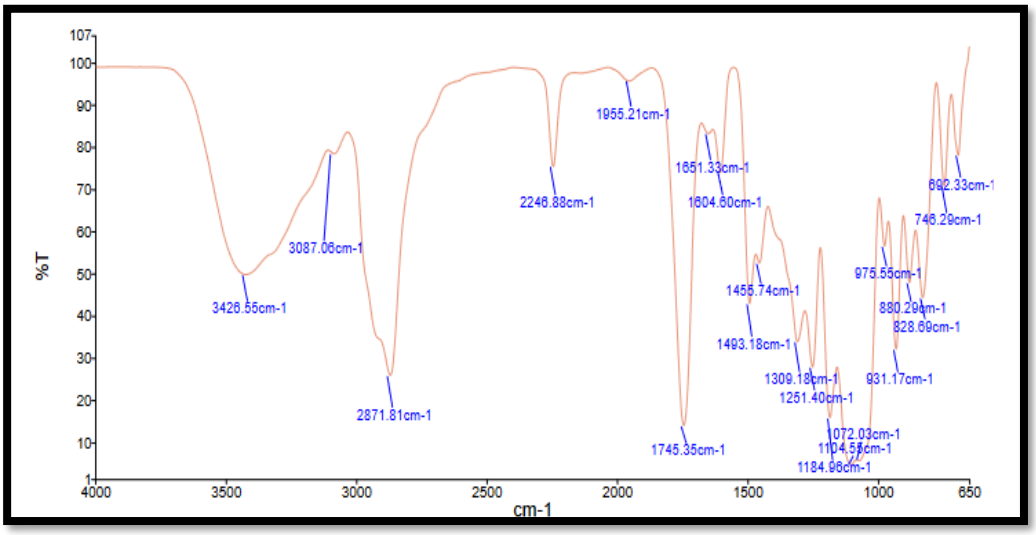
F.T.I.R spectra of preparation was compared with that of the F.T.I.R spectra of the pure drug Efavirenz to see the presence of the functional groups of the drug in the formulation. The spectra of formulation showed the presence of following functional groups which are within the frequency range indicating that no interaction was found in the formulation. There was no appearance of any new peak in the spectra.

a. The spectra was collected between 4000cm^{-1} to 450cm^{-1}.
b. Peak at 1745.35cm^{-1} carbonyl group showed intense clear peak (C=O)
c. Frequency range of 3300-3500cm-1 indicates stretching band of –OH and -NH_2 groups. (3426.55 cm^{-}).
d. 3087.06 cm^{-1} confirms the NH group.

e. 1190-1000cm^{-1} frequency range shows the stretching band for CF group. Peak at 1651.33cm^{-1} confirms the CF group.

f. Band at 2246.88 cm^{-1} is because of stretching, vibration of triple bond.

g. Stretching vibration of C=C in aromatic ring occur at 1604.60 and 1493.18 cm^{-1}



F.T.I.R spectra of the EFV loaded nanoemulsion

Viscosity

The result of viscosity measurement of nanoemulsion was determined to be 10.2±0.31 cP. The viscosity is low by reason of the nanoemulsion is O/W type which has higher water quantity when compared to that of the oil. The less viscous nanoemulsion can administered easily through oral route.

Conclusion

The most frequent dosage type that is accessible is a tablets, which has an inconveniently big mass that may severely influence a patient's ability to stick to their medication regimen. The suggested dose of EFV for adults is 600 milligrams administered once daily. The design of Nanoemulsion centered on separating the releasing characteristics from the gastrointestinal physiology as well as the fed-fasted condition of the person and in a dosage-form size that is compatible with the patient's gastrointestinal physiology would be beneficial to the patient if it could be used easily and would not require a large footprint. Because of the significant drug loading capabilities displayed, the administration of EFV with this NE would need a minute unit size of the dose form. This might result in a dosage form that is easier to use due to its more manageable size. It is possible to utilize co-solvents and co-emulsifying agent s to increase the thermodynamic stability of preparations, which would then result in improved therapeutic effectiveness. These formulations demonstrate a higher solubilization capacity. Due to the fact that macrophages are able to recognize and consume negatively charged particles, the negative Z.P of nanoemulsion droplets might be advantageous for directing macrophages.Grapeseed oil, Tween-80, and Transcutol P emulsifying agent and co-emulsifying agent with methanol were effectively synthesized into low-energy nanoemulsions, and these nanoemulsions were shown to be kinetically stable. The release profile, as observed visually, was much superior to that of the commercially available formulation when the two were compared. These can be utilized for the purpose of further optimizing formulations in order to develop ones that are appropriate for carrying out in vivo and pharmacokinetic research. By utilizing nanoemulsions to control release, it may be possible to lessen the adverse effects of EFV that are linked with dosage-dumping.Grapeseed-oil is an inexpensive renewable raw material for dosage-forms, and it may be useful to patients if it is used in dosage forms designed for oral-delivery because of the health benefits associated with the usage of polyunsaturated fatty acids. Although the nanoemulsion strategy shows promise, it is important to investigate the stability of gelatin or other encapsulated forms, in which crystallization of EFV from solution is minimized.

REFERENCES

[1] Powderly, William G., and Kenneth H. Mayer. 2003. "Editorial Commentary: Centers for Disease Control and Prevention Revised Guidelines for Human Immunodeficiency Virus (HIV) Counseling, Testing, and Referral: Targeting HIV Specialists." *Clinical Infectious Diseases* 37 (6): 813–19.

[2] Celum, C. L., R. W. Coombs, W. Lafferty, T. S. Inui, P. H. Louie, C. A. Gates, B. J. McCreedy, et al. 1991. "Indeterminate Human Immunodeficiency Virus Type 1 Western Blots: Seroconversion Risk, Specificity of Supplemental Tests, and an Algorithm for Evaluation." *Journal of Infectious Diseases* 164 (4): 656–64.

[3] Chou, Roger, Shelley Selph, Tracy Dana, Christina Bougatsos, Bernadette Zakher, Ian Blazina, and P. Todd Korthuis. 2012. "Screening for HIV: Systematic Review to Update the 2005 U.S. Preventive Services Task Force Recommendation." *Annals of Internal Medicine* 157 (10): 706.

[4] Haehl, Manfred. 2001. "Nevirapine and Postexposure Prophylaxis for Human Immunodeficiency Virus." *JAMA* 285 (7): 883.

[5] Rodari, Anthony, Gilles Darcis, and Carine M. Van Lint. 2021. "The Current Status of Latency Reversing Agents for HIV-1 Remission." *Annual Review of Virology* 8 (1): 491–514.

[6] Fauci, Anthony S., and Gregory K. Folkers. 2012. "Toward an AIDS-Free Generation." *JAMA* 308 (4): 343.

[7] Deeks, Steven G, Sharon R Lewin, and Diane V Havlir. 2013. "The End of AIDS: HIV Infection as a Chronic Disease." *The Lancet* 382 (9903): 1525–33.

[8] Ravi T P U, Padma T (2011) Nanoemulsions for drug delivery through different routes. Res. Biotechnol. 2(3): 1-13.

[9] Kotta S, Khan AW, Pramod K, Ansari S H, Sharma R K, Ali J (2012) Exploring oral nanoemulsions for bioavailability enhancement of poorly water-soluble drugs. Expert Opin. Drug Deliv. 9(5): 585-598.

[10] Dixit RP, Nagarsenker MS (2008) Self-nanoemulsifying granules of ezetimibe: design, optimization and evaluation. Eur. J. Pharm. Sci. 35: 3183-3192.

[11] Shafiq S, Shakeel F, Talegaonkar S (2007) Development and bioavailability assessment of ramipril nanoemulsion formulation. Eur. J. Pharm. Biopharm. 66: 2227-2243

[12] Gasco MR, Gallarate M, Pattarino F (1991) In vitro permeation of azelaic acid from viscosized microemulsions. Int J Pharm 69:193–196

[13] Kriwet K, Muller-Goymann C (1995) Diclofenac release from phospholipid drug systems and permeation through excised human stratum corneum. Int J Pharm 125:231–242

[14] "Fiz. Khim. Mekh. Mater." 1993. *Metal Powder Report* 48 (2): 37.

[15] Mohr, K.-H. 1987. "High-Pressure Homogenization. Part II. The Influence of Cavitation on Liquid-Liquid Dispersion in Turbulence Fields of High Energy Density." *Journal of Food Engineering* 6 (4): 311–24.

[16] Stone, H. A., B. J. Bentley, and L. G. Leal. 1986. "An Experimental Study of Transient Effects in the Breakup of Viscous Drops." Journal of Fluid Mechanics 173 (December): 131–58.

[17] Abismaïl. B, J.P Canselier, A.M Wilhelm, H Delmas, and C Gourdon. 1999. "Emulsification by Ultrasound: Drop Size Distribution and Stability." Ultrasonics Sonochemistry 6 (1-2): 75–83.

[18] Alegria, Antonio E., Yves Lion, Takashi Kondo, and Peter Riesz. 1989. "Sonolysis of Aqueous Surfactant Solutions: Probing the Interfacial Region of Cavitation Bubbles by Spin Trapping." The Journal of Physical Chemistry 93 (12): 4908–13.

[19] Stone, H.A., A.D. Stroock, and A. Ajdari. 2004. "ENGINEERING FLOWS in SMALL DEVICES." Annual Review of Fluid Mechanics 36 (1): 381–411.

[20] Paquin, Paul. 1999. "Technological Properties of High Pressure Homogenizers: The Effect of Fat Globules, Milk Proteins, and Polysaccharides." International Dairy Journal 9 (3-6): 329–35.

[21] Utada, A. S., L.-Y. Chu, A. Fernandez-Nieves, D. R. Link, C. Holtze, and D. A. Weitz. 2007. "Dripping, Jetting, Drops, and Wetting: The Magic of Microfluidics." MRS Bulletin 32 (9): 702–8.

[22] Shinoda, K, and H Saito. 1968. "The Effect of Temperature on the Phase Equilibria and the Types of Dispersions of the Ternary System Composed of Water, Cyclohexane, and Nonionic Surfactant." Journal of Colloid and Interface Science 26 (1): 70–74.

[23] Shinoda, Kōzō, and Hiroshi Saito. 1969. "The Stability of O/W Type Emulsions as Functions of Temperature and the HLB of Emulsifiers: The Emulsification by PIT-Method." Journal of Colloid and Interface Science 30 (2): 258–63.

[24] Shinoda, K., M. Hanrin, H. Kunieda, and H. Saito. 1981. "Principles of Attaining Ultra-Low Interfacial Tension: The Role of Hydrophile—Lipophile-Balance of Surfactant at Oil/Water Interface." Colloids and Surfaces 2 (4): 301–14.

[25] Warson, H. 1987. "Emulsions and Solubilization: K. Shinoda and S. Friberg, Wiley-Interscience, New York, 1986. Pp. Xiii + 174, Price £43.25. ISBN 0-471-03646-3." British Polymer Journal 19 (6): 544–45.

[26] Taisne, L., and B. Cabane. 1998. "Emulsification and Ripening Following a Temperature Quench†." Langmuir 14 (17): 4744–52.