Development Of Nutmeg Oil Based Snedds Formulation of Nisoldipine: Characterization of Phase Behavior & Dissolution Rate

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ABSTRACT

The aim of the present investigation is to improve the dissolution rate of Nisoldipine through Nutmeg oil based SNEDDS formulation. Nisoldipine is an antihypertensive drug belonging to BCS Class II category and has impaired bioavailability due to its poor water solubility. To locate the nanoemulsion region a pseudoternary phase diagram was constructed using Nutmeg oil, Tween 80 and PEG600 acts as oil, surfactant and cosurfactant respectively. Six formulations were prepared and were evaluated for droplet size, transparency, percentage transmittance, conductivity, refractive index, and in-vitro drug release.

Results: Nutmeg oil, Tween80 and PEG600 were selected amongst different surfactant/co surfactant and oil combinations led to form clear dispersion. Optimized formulation had a droplet size of 13.89nm, with PDI of 0.241, and was almost clear (% transmittance 98.36). Conductivity and refractive index data showed that F2 showed gradual increment with aqueous dilution and the values are stagnant. conductivity is 0.204 and refractive index is 1.406. In vitro dissolution characterization showed that the drug has been enhanced in the medium.

Conclusion: SNEDDS provides delivery system for nisoldipine for the enhancement of its dissolution rate

Keywords: SNEDDS, Dissolution, Phase behaviour Hypertension, Nisoldipine, nanoemulsion

I. INTRODUCTION

SNEDDS based formulation approach brings forth a prominent way to achieve solubilization of poorly water-soluble drugs. A combination of oil, surfactants and cosurfactants results in formation of SNEDDS. SNEDDS spontaneously generates oil/water nanoemulsion and the droplet size ranging from 20-200 nm or less follows aqueous addition and mild agitation (as in the case of GIT). A spontaneous emulsification appears when the entropy deviates which promotes dispersion. SNEDDSs have demonstrated an enormous capacity to overcome different compounds orally. SNEDDS improved the drug absorption by GI can be used with superfluous and lipid components. In addition, these components can be easily adjusted to ensure that SNEDDS is used in hydrophilic and hydrophobic medicines. Recent studies showed that, prevention against GI degradation and increased bowel permeability, SNEDDS can be efficient oral carriers of peptides and proteins. SNEDDSs are typically manufactured by means of short- and long-chain triglycerides (TGs), which contain oils with different levels of saturation. The oil with maximum solubility is typically chosen because of its significant influence both in the load capacity and in the absorption of drugs. The rational and desired oil ingredients remain the food-safe oils (e.g. beaver oil, soybean oil, cocoon oil etc.), while their potential for drugs is relatively low and their emulsification efficiency is weak. Tensile substances are also the second compulsory components of SNEDDS. The surfactants are found on the oil side of water because of their amphiphilic characteristics and help to stabilise the nanoemulsion by suppressing surface tension. Tensile substances are generally classified according to load and hydrophilic-lipophilic (HLB) value. Non-ionic surfactants are usually used because they exhibit low toxicity and high capability to
stabilize nanoemulsion through an increased range of pH and ionic strength in comparison with ionic surfactants.[1,2,3]

One surfactant seldom has a low interface tension; thus, additional surfactant (cosurfactant) or cosolvent is usually sufficient. They should synergistically work together to develop the solutions and dispersal of medicinal products into oil, thereby facilitating healthy and homogeneous nanoemulsion. By increasing the interface fluidity, the application of cosurfactants or cosolvents will minimise local surfactant irritability and variability in formulation dosage. The weight ratio of the surfactant-cosurfactant or cosolvent was also shown to have a significant impact on the distribution of size and the magnitude of the nanoemulsion area. Propylene glycol, ethanol, poly(ethylene glycol) (PEG) and other more recent cosolvents, including Transcutol® HP, are widely used cosolvents. The oral route is the preferred mode of administration because of its security, convenience, low cost and better patient conformity. Oral care has been recognised as the most attractive method among different routes, particularly because of its long shelf life, long distribution, ease of administration and increased immune response. Due to its specific benefit: longer and more controllable delivery, ease of administration, sound formulations are feasible, compliance with patients and enhanced immune response in the event of vaccinations, the oral route has been the most focused on various delivery methods for medicinal goods. Hypertension can also be called high blood pressure. It can cause serious health problems and put the person at risk of heart failure, ischemia and even death. The force of blood on the blood vessels is called blood pressure or hypertension. Resistance of the blood vessels can determine the stress. About half the population of adults in the United States are suffering from elevated blood pressure. Hypertension is a leading cause, including a stroke, heart failure, and aneurysm, of cardiovascular disease. It is essential to maintain health and reduce the chances of these dangerous conditions by controlling blood pressure.[4,5,6]

II. MATERIAL AND METHOD

1.1 Material
Chemicals used in the study were purchased from Sigma-Aldrich (Munich, Germany). Nisoldipine was received from SherniCorps Solutions Inc. (Airen Height Block -B Scheme No.54 Vijay Nagar).

1.2 Method
1.2.1 Preformulation Study
Preformulation study aims to optimise drug delivery by identifying the physicochemical properties of the new compound which can affect drug performance and developing efficient, stable, safe dosage forms. Preformulation study Various preformulation studies are discussed in the following section .[7]

1.2.2 Identification
1.2.2.1 Determination Of Melting Point
The nisoldipine melting point was established by the digital melting point appliance using open capillary tube method.[8]

Method
Then a gentle heating was used for the capillary tube from one end. Nisoldipine was then filled in small amounts into the capillary. A capillary was attached to the oil stage tube to plunge the sealed portion of the nisoldipine capillary into the oil. The oil bath was gently heated. The heat stopped and the powder started melting and the temperature was recorded so quickly.[9]

1.2.2.2 Fourier Transmittance Infra-Red (FTIR)
In combination with a pure drug and other excipients, the integrity (compatibility) of the medication was checked with a Shimadzu FTIR spectrophotometer in spectra FTIR formulations. Pellet method for potassium bromide has been used in this study (KBr). The specimens were combined thoroughly with dry powder KBr crystals. The blend was drawn in a disc. The disc is inserted into the spectrometer and the spectrum is recorded.[10]

1.2.2.3 DSC
The differential calorimeter or DSC scan is a thermal analysis technique which measures the heat difference required to increase the temperature of the sample and the reference to it depends on the temperature. The sample and reference was referred to at almost sample temperatures during the entire experiment.

Method
Nisoldipine has been precisely weighed with the thermal analyzer system (DSC60 Shimadzu Corporation, Japan). The analyses were conducted. All samples were screened and drilled aluminium panels. In this experiment. The temperature calibration was done standard with Indium. A blank pane, screened in the same way as the sample, was used as a reference. The complete samples were performed at the 10oC/min scan rate of 500- 300oC.[11]

1.2.3 Standard Curve for Nisoldipine
1.2.3.1 Determination of λmax
Dissolving 5 mg nisoldipine in 50 ml ethanol in 50 ml volumetric flask to dissolve the drug and obtain a concentration of 100 mg/ml produced a standard stock solution containing nisoldipine. Furthermore ethanol is used for the preparation of 10μg/ml of concentration for the stock solution. The result has been scanned for maximum absorption (Ƞmax) by using ethanol as blank in a range of 200-400 nm of UV spectrophotometer (UV-1700 Shimadzu Corporation, Japan). The maximum wave absorption length for future studies is considered.[12]

2.2.3.2 Preparation of standard curve
A solution was developed using ethanol from the aforementioned stock solution, which contains concentrations between 1 to 4 μg/ml. UV spectrophotometer is measured μmax to absorb those solutions.[13]

2.2.4 Formulation Of Nisoldipine Snedds:
The SNEDDS of nisoldipine were prepared by following steps:-
● Selection of oil, surfactant and co-surfactant based on the miscibility of each other.
● Construction of a pseudo ternary phase diagram.
● Formulation of SNEDDS by dissolving the drug in a mixture of oil, surfactant and cosurfactant.[14]

2.2.4.1 Screening Of Excipients:
2.2.4.1.1 Screening Of Oil
Suitable petroleum of a high miscible capacity was discovered for a weighing emulsifier of 300 mg co-surfactant and then for two minutes to twist and for 30 seconds to warm at 40-45 C. So a mixture of isotopes is possible. 50 mg isotropic mixture have been diluted with dual distillation water before for clear formulations with a different surfactant and co-surfactant oil the quantities for the bottle were visually observed (clove oil, cardamom oil, peppermint oil, nutmeg oil) 300 mg of oil and 300 mg of surfactant.

2.2.4.1.2 Screening Of Surfactant
An emulsifying capacity for the different surfactants was evaluated with screened oil and co-surfactant for the appropriate surfactants with a good miscible capacity (between 20, tween 60, tween 80 and span 80). It
was weighed for about two minutes, with a 30- second heating rate of 40-45C at 300 mg of oil, 300 mg of surfactant and 300 mg of co- factant. So a mix of isotopes can be obtained. 50 mg isotropic blend with dual distillation water and previously diluted Visually, with the number of flask inversions, a clear formulation is observed.

2.2.4.1.3 Screening Of Co-Surfactant
The screened oil and surfactant examined adequate co-surfactor with good miscible abilities to detect the emulsifying capacity of the different co-factant (Propylene glycol, polyethylene glycol 400, PG 200,PG 600). 300 mg oil and three hundred mg 300 mg co-surfactant for two minutes and for 30 seconds warming at 40-45 C. Weighing and sprinkling So a mix of isotopes can be obtained. The 50 mg isotropic mix with double distilled water was taken and previously diluted Views for the clear formulation of flask reversals were observed.[15,16]

2.2.4.1 PSEUDO TERNARY PHASE DIAGRAM
Phase diagram represents the percentage of components which may lead to the SNEDDS maximum area. These diagrams were drawn using the oil, surfactant/co-factant ratio and water using water titrations method at room temperature. The method involved preparing solutions of various ratios, as 1:1, 2:1, 1:2 etc., by weight, which were subsequently rotated over 5 minutes to produce the isotropic mixture for an hour at 50 degrees C. All these solutions were used in weight ratios of 17: 1, 11:1, 3:1, 13:5 and 5 minutes of vorted preparation (mixture of surfactant and co-foil) and 1 hour in the oven at 50o C. At room temperature all combinations were set for 24 hours. For its appearance, water was observed at 5 to 95% of blends (turbid or clear). Indication of turbidity in the samples shows coarse emulsion formation, while clear area formation indicates clear isotropic. The percentage of oil, mixed water, was chosen and values were used for the composition of the ternary phase graph.[17,18]

2.2.4.2 Formulation Of Snedds
Ternary phase diagram optimised the ratio of surfactant to surfactant. Selected formulations with a different oil to Smix ratio were then prepared. The formulations were first prepared by precisely preparing the selected Smix ratio, then weighed 5-10minutes by vortex for that surfactant and co-factant. In oil with a different ratio, Smx Was added. These formulations will then be vortexed into an isotropic blend for 5-10 minutes. At the end of the drug, the isotropic mixtures have been loaded and then vortexed for a clear solution. [19,20]

- SELECTION OF SIX FORMULATIONS FROM THE TERNARY PHASE DIAGRAM
on the basis of high drug solubility, high Smix and least Smix amount, high oil and least oil amount and intermediates of Smix and oil from the pseudoternary phase diagram.

<table>
<thead>
<tr>
<th>S.NO.</th>
<th>FORMULATIONS</th>
<th>SELECTION RATIO BASIS OF FORMULATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F1</td>
<td>High Smix (65%)</td>
</tr>
<tr>
<td>2</td>
<td>F2</td>
<td>Least Smix (13%)</td>
</tr>
<tr>
<td>3</td>
<td>F3</td>
<td>High oil (10%)</td>
</tr>
<tr>
<td>4</td>
<td>F4</td>
<td>Least oil (1%)</td>
</tr>
<tr>
<td>5</td>
<td>F5</td>
<td>Smix intermediate (29%)</td>
</tr>
<tr>
<td>6</td>
<td>F6</td>
<td>Oil intermediate (5%)</td>
</tr>
</tbody>
</table>
2.2.5 CHARACTERIZATION OF SNEDDS FORMULATIONS:

2.2.5.1 Visual assessment
Diluted with purified water of 5 ml Nisoldipine SNEDDS was stirred gently by a magnetic agitation agitator. 370°C should be the temperature.[21]

2.2.5.2 Conductivity test:
The formulated electro-conductivity was measured by a conductivity measurement electrical conductometer, the SNEDDS tested by the oil smix was produced and distilled water. [22]

2.2.5.3 Refractive index and percent transmittance
The refractive index and percent transmission demonstrated the transparency of wording. The index was calculated by the Abbe's refractometer. UV spectrophotometers that keep ethanol white are the percentage of system transmission. Dilution with 100 ml of distilled water and spectrophotometer for 1ml of formulation for measuring SNEDDS stability. Transmission samples are measured with 638 nm and for each sample three replicate tests are performed.[23]

2.2.5.4 In vitro drug release
The triple in vitro release of prepared SNEDDS was assessed with the U.S. Pharmacopoeia (USP) Type II dissolution device (paddle type) at 37±0.5°C. SNEDDS containing 8.5 mg drug equivalents were added to the 900 ml dissolution medium (0.1 N HCL with 0.5 percent SLS). The revolutionary paddle speed was maintained at 50 minutes per hour. The medium was collected at a prescribed dissolution interval of 5 ml, filtered and refilled for the same volume of fresh dissolution media to keep sinking conditions, and the medicine was monitored for 10 to 60 minutes. UP-VIS spectrophotometer samples at a concentration of 237 nm have been analysed for the drug.[24]

2.2.5.5 Determination of Particle size and Zeta potential:
The medium size (z average) and zeta potential of the nisoldipine SNEDDS formulas are determined by using a zeter size analyser. A technique of light dispersion (Nano ZS 90, Malvern Instruments Ltd., UK).[25]

2.2.5.6 Pharmacodynamic study
The research was conducted in Wistar rats of 150–200 g sex. Temperature of the animals (22 ± 2°C), 12 hours light / dark cycle, were maintained in conventional laboratory settings. For 1 week before the experiments all animals were kept in quarantine. Rat was fed conventional lab food and ad libitum water. The institutional animal ethics Committee examined and approved all experimental protocols. One night before the test, the animals were fasting. The animals were trained to stay in the container before research. This guaranteed a calm and ineffective rat during measurements of blood pressure (BP).
Subcutaneous methylprednisolone acetate (20 mg/kg/week) injection introduced hypertension during a 1 week period. The rats were then altered in three groups, each including one individuals. The group were (low dose nisoldipine SNEDDS + high dose nisoldipine SNEDDS + cmc suspension). After the last injection of methylprednisolone, drug administration start at 0 min. A dose of 0.9 mg/kg in nisoldipine was given orally, and a dose of 0.9 mg/kg/ml in solution was taken orally using Nisoldipine SNEDDS, utilising a cannula that is attached in the mouth of an animal. Based on an accepted clinical dose in humans, the nisoldipine dose was selected. This dose was converted on the body surface formula to the equivalent dose of rats. To assess systolic BP, a non-invasive tail cuff method approach has been used. BP was measured in all categories up to 30min, 1 hrs, 3 hrs, 6 hrs following drug use from 0 hrs. Six readings for each animal have been made at each stage.[26]
III. RESULTS AND DISCUSSION

3.1 STANDARD CURVES FOR NISOLDIPINE

3.1.1 Preparation of dissolution medium

The calibration medium (0.1 N HCL and 0.5% SLS) was prepared as per the literature survey. The result was shown in table 4.1 and figure 4.1.

Table 3.1: Calibration of nisoldipine using 0.1 HCL

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<tr>
<th>CONCENTRATION</th>
<th>ABSORBANCE</th>
</tr>
</thead>
<tbody>
<tr>
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<td>0</td>
</tr>
<tr>
<td>1</td>
<td>0.0295</td>
</tr>
<tr>
<td>2</td>
<td>0.0614</td>
</tr>
<tr>
<td>3</td>
<td>0.0953</td>
</tr>
<tr>
<td>4</td>
<td>0.1328</td>
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</tbody>
</table>

Figure 3.1: Calibration Curve for nisoldipine using 0.1 N HCL

Table 3.2: Calibration curve of nisoldipine using ethanol

<table>
<thead>
<tr>
<th>Concentration</th>
<th>Absorbance</th>
</tr>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>0.0754</td>
</tr>
<tr>
<td>2</td>
<td>0.1641</td>
</tr>
<tr>
<td>3</td>
<td>0.2196</td>
</tr>
<tr>
<td>4</td>
<td>0.2791</td>
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</tbody>
</table>
3.2 FTIR

Infrared (IR) spectroscopic studies have been confirmed to be compatible with medicaments and excipients of nisoldipine snedds. The IR studies for pure drugs, stabilisers and physical combinations were conducted. At 4500cm⁻¹ to 500cm⁻¹ the spectrum was demonstrated (Figure 4.4). The major drug pin points were observed at the 3226.69 cm⁻¹ and at the 836.08 cm⁻¹. Numbers, respectively. The results clearly showed that there was no unchanged interaction between the medicine and the excipients.

Figure 3.2: Calibration curve for nisoldipine using ethanol

Figure 3.3: Determination of λ max for nisoldipine

Figure 3.4: IR spectra of nisoldipine
3.3 DIFFERENTIAL SCANNING CALORIMETRY

The physical condition of nisoldipine with differential calorimetry scanning was characterised by SNEDDS. The DSC thermogram for nisoldipine snedds formulation is shown in Figure 4.5. Nisoldipine DSC thermogram shows that its melting point was typically strong endothermal (less than 148°C) and shows the substance’s crystalline nature. The melting point of nisoldipine was negligible for prepared nisoldipine snedds and no alterations or interactions between the drug and the excipient were demonstrated, in the presence of excipients.

3.4 FORMULATION OF NISOLDIPINE SNEDDS

Using a simple blending method, the SNEDDS Nisoldipine were prepared. Following steps are required in the preparation process.

- Oil and surfactants are selected based on each other's miscibility.
- Construction of a pseudo ternary phase diagram.
- Dissolving the drug in a combination of oil, surfactant and co-surfactant to formulate SNEDDS.

3.4.1 Screening Of Components:

Based on the miscibility research conducted in the tween 80-PEG 600 screened nutmeg oil from several oils, surfactants and co-factants, oils, surfactants and co-factants are selected to ensure the greatest miscibility in all. All three are therefore selected for development of the wording. Hence tween 80 have been chosen to form a stable emulsion. PEG 600 was chosen as a co-surfactant.

3.4.2 Construction of Pseudo ternary phase diagram:

Data were determined for the SNEDDS region in the pseudo ternary phase diagram. The selected oil, surfactants and co-surfactants were formulated by SNEDDS. All of these solutions were used for the preparation of the mixed oil and mixture (surfactant/co-fectant mixture) in the weight ratios of 17:1, 11:1, 31:5, 13:5. The 1:1, 2:1 and 1:2 ratio were selected. The diagrams appear in Figure 4.6(a,b,c).
Formulation Of Snedds

A formula containing (1-10%) Nutmeg oil and a mix from Tween 80 and PEG 600 were based on the phase diagram (1-65%). The formula contains the best self-emulsification properties (1-10%) fig.4.7( a, b ).

Figure 3.6(a, b,c): Pseudo ternary phase diagram

Figure 3.7(a,b) : Selected formulations from the phase diagram
3.5 Characterization Of Snedds:

3.5.1 Dispersibility test and Visual assessment
Diluted with purified water (5 mL), Nisoldipine SNEDDS (1ml) was stirred softly by a magnetic strutting device. 37 degree Celsius should be temperature. Figure 4.8 shows the results.

![Figure 4.8: Formulation Dilution With Water](image)

3.5.2 Conductivity test:
The electro-conductometer for the conductivity measurement has been measured by an electro-conductometer. Table 4.3 and Figure 4.9 showed the results.

![Figure 4.9: Values of conductivity](image)

<table>
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<tr>
<th>FORM.(mg)</th>
<th>WATER(mg)</th>
<th>CONDUCTIVITY</th>
</tr>
</thead>
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<tr>
<td>5000</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>5000</td>
<td>1000</td>
<td>9.2</td>
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<td>5000</td>
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</tr>
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<td>6000</td>
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<tr>
<td>5000</td>
<td>7000</td>
<td>0.265</td>
</tr>
</tbody>
</table>
3.5.3 Refractive index and percent transmittance:
The refractive index and percent transmission are determined to verify the transparency of the formulation. Refractometer measures the refractive formulation index and then compares the slide with the slide when the solution drops (RI=1.333). The formulations are transparent in nature if the refractive index is more than 90 percent similar to the refractive water Index and the transmission proportion. Results and percentage of Refractive Index in Table 4.4 and Figure 4.10, the transmissions are shown. The transmittance value of formulation F1-F2, F3, F4, F5 and F6 is greater than 90% and suggests its clarity. And the F1, F2, F3, F4, F5, and F6 refractive index has water values closest to RI.

Table 3.4: Values of refractive index

<table>
<thead>
<tr>
<th>FORM.(mg)</th>
<th>WATER(mg)</th>
<th>F1</th>
<th>F2</th>
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<th>F4</th>
<th>F5</th>
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<tbody>
<tr>
<td>500</td>
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<td>1.454</td>
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3.5.4 In vitro drug release
A 1-hour dissolution study was conducted on HCL and SLS. The in vitro dissolution studies of all formulations were compared with cmc suspension. The results of in-vitro drug release studies on nisoldipine SNEDDS have been demonstrated. All formulations showed a higher percentage of release than cmc suspension.
Figure 3.11: Graph of in vitro drug release

3.5.5 Pharmacodynamic study

<table>
<thead>
<tr>
<th>Sample (Low Dose)</th>
<th>Time (h)</th>
<th>Systolic Blood Pressure</th>
<th>Mean Blood Pressure</th>
<th>Diastolic Blood Pressure</th>
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<tbody>
<tr>
<td></td>
<td>0</td>
<td>138</td>
<td>117</td>
<td>107</td>
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<td>126</td>
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<table>
<thead>
<tr>
<th>Sample (High Dose)</th>
<th>Time (h)</th>
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<table>
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<th>Suspension</th>
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<th>Diastolic Blood Pressure</th>
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<td>6</td>
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<td>106</td>
<td>92</td>
</tr>
</tbody>
</table>

However, the self-nanoemulsifying drug delivery system f4 showed greater improvements in its bioavailability than drug in suspension.
Table 3.5: Characterization of SNEDDS

<table>
<thead>
<tr>
<th>FORMULATION</th>
<th>DROPLET SIZE (nm)</th>
<th>PDI</th>
<th>ZETA POTENTIAL (mv)</th>
<th>% TRANSMITTANCE</th>
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<tbody>
<tr>
<td>F1</td>
<td>1576</td>
<td>0.377</td>
<td>0.0290</td>
<td>99.85</td>
</tr>
<tr>
<td>F2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>93.61</td>
</tr>
<tr>
<td>F3</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>98.36</td>
</tr>
<tr>
<td>F4</td>
<td>13.89</td>
<td>0.241</td>
<td>1.94</td>
<td>98.36</td>
</tr>
<tr>
<td>F5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>100.43</td>
</tr>
<tr>
<td>F6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>99.072</td>
</tr>
</tbody>
</table>

Figure 3.12: Size distribution of optimized formulation (f4)
IV. SUMMARY AND CONCLUSION

- This study aimed at improving solubility and dissolution through the incorporation of the medicine in a lipid vehicle in the self nano emulsifying drug delivery system nisoldipine.
- Compatibility results from infrared spectroscopy and differential scanning calorimetry did not show interactions between drugs or excipients (DSC).
- Pseudo-ternary phase diagrams were designed to obtain the maximum self-emulsion range for SNEDDS with optimal oils of 10-20% and a 20-85% mixture.
- Microemulsion area was obtained from various proportions of oil, surfactant and co-surfactant for the preparation of nisoldipine SNEDDS.
- Prepared SNEDDS were evaluated in relation to their physicochemical parameters, (visual assessment, percentage transmission and refractive index).
- The formulation RI is between 1.391 and 1.461.
- The transmission value for all formulations varied between 93 and 100%. And it clearly indicates that the nanoemulsion are clear and stable against turbidity.
- In-vitro studies of all formulations have been shown to increase drug release. The dissolution rate for all formulations has been improved compared to pure medicines.
- Particle size analyser used for testing the particle size of nisoldipine snedds showed a suitable particle size for F1 and F4, respectively, of 1576 nm and 13,89 nm.
- The polydispersibility index was 0.377 and 0.241 in SNEDDS formulations (F1 and F4), indicating a broad distribution of the particles.
- The potential value of the nisoldipine snedds-Zeta has been negative (0.0290mv and 1.94mv).

V. CONCLUSION

Nisoldipine is a water-soluble medicine that has a bioavailability of only approximately 60% due to low solubility. Poor solubility results in its low bioavailability. A good approach has therefore been found in the self-nano emulsification based drug delivery system to improve the solubilities and dissolution effects of nisoldipine. The optimised formulation composition [f1 consist of nutmeg, co-surfactant and water (10 percent), tween 80 (21.6 percent) as surfactant (Propylene glycol 600(43.3 percent)]) The f4 are comprised of nutmeg oil (1%), Tween 80 (9.3%), Propylene glycol 600 (4.6%) and water (85%) which contains 8.5mg nisoldipine with SNEDDS formulation release (%), Particle size (1 576nm & 13,89nm), Zeta potential (0.0290 & 1.94mv), Compared to the cmc suspension and the in vitro release and pharmacodynamic study of f4 was highly significant. The admixture technique is successful in the preparation of SNEDDS.

REFERENCE


