Enhancement of the Solubility of Lipophilic Drug by Self-Micro Emulsifying Drug Delivery System (SMEDDS) For Oral Administration

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ABSTRACT

Aim: The aim of this research work is the formulation, development and evaluation of Self-Micro Emulsifying Drug Delivery System (SMEDDS).

Background: Zileuton, a drug that is poorly soluble in water, was formulated with Tween 20 in a 1:1 ratio as a surfactant. F1 formulation of SMEDDS was selected from the optimum concentration of oils, surfactant, and co-surfactants from pseudoternary diagrams. Materials and Methods: Enaltec Lab in Mumbai, India, provided Zileuton as a gift sample. Raj Chemicals in India provided the eucalyptus oil. Merk Private Ltd., INDIA provided a gift sample of Tween 20. N.R. Traders, INDIA, provided polyethylene glycol 300 (PEG 300). Result: For the optimized formulations, the mean globule size of SMEDDS was found to be below 107 nm, and the zeta potential was negative. The formulations were subjected to various accelerated physical stability tests and self-emulsification evaluations. For investigating drug-excipient interactions, FTIR analysis was carried out. Zileuton in SMEDDS dissolved rapidly and completely in the phosphate buffer pH 7.4 which was used as the dissolution medium, according to the in vitro dissolution data. Conclusion: From the droplet size analysis and zeta potential values confirm the reduction in particle size to nano range which definitely improves the solubility and the dissolution rate.

Keywords: SMEDDS, Zileuton, Zeta potential.

INTRODUCTION

In the last few years, there has been a lot of emphasis on increasing the drug absorption and solubility of less water soluble drug by using an oral dosage form with a Self-Micro Emulsifying Drug Delivery System (SMEDDS).¹ Numerous ways are used to improve the oral bioavailability of a poor aqueous soluble medication.² The oral route of drug delivery has the most important method of medication administration for the long-term therapy of several disorders. However, the medicine's high lipophilicity makes it difficult for half of the therapeutic components to be distributed orally.³

SMEDDS which are isotropic combinations of surfactants (solid or liquid), natural/ synthetic oils, and co-solvents/surface active agents with one or more hydrophilic solvents that are capable to create fine Oil-in-Water (o/w) microemulsion after light stirring and dilution in aqueous media, such as Gastrointestinal fluids.⁴ Since most BCS class II medicines have poor water solubility and permeability, they have short oral bioavailability, substantial variability within and across subjects, and dose inequity.⁵,⁶ This technology can be used to formulate a hydrophobic medication that is soluble in oil. The oil in the combination must have a droplet with a diameter of less than 100 nanometers. The SMEDDS come into contact with the lumen of the GIT and form a microemulsion with the GI fluid without forming a microemulsion. The use of lipid as a carrier and surface active agents to generate a w/o microemulsion in the GIT lumen is advantageous for poorly water-soluble medicines is shown in Figure 1.⁷,⁸

The rational of this research is to develop and evaluate stable SMEDDS formulation, with a low-solubility and high bio membrane permeability BCS class II medication. In this case, Eucalyptus oil was screened for oil, and Tween 20 and PEG 300 were utilized as surfactants and co-surfactants, respectively.⁹ Dilution with aqueous phase or evaporation of any volatile elements frequently causes phase transition in microemulsion systems. In alcohol-free microemulsion systems, relatively minor changes in the water content can have a great impact on the ternary systems' phase behaviour.¹⁰ SMEDDS are simple to make and physically stable compositions. As a result, these systems
may increase the rate and extent of absorption for lipophilic medicines, leading to more consistent plasma concentrations.11

MATERIALS AND METHODS

Enaltec Lab in Mumbai, India, provided Zileuton as a gift sample. Raj Chemicals in India provided the eucalyptus oil. Merk Private Ltd, India provided a gift sample of Tween 20 of loba grade. N.R. Traders, India, provided loba grade polyethylene glycol 300 (PEG 300). All of the other reagents were of analytical quality.

Preformulation study

Identification of drug

Melting point measurement, UV-spectroscopy, and Fourier Transformation infrared spectroscopy were used to identify Zileuton.

Selection of Solvents

Different solvents such as methanol, phosphate buffer, acetonitrile were tried for estimation of Zileuton in formulation. Maximum solubility was found in Phosphate buffer. Hence, phosphate buffer was selected as a solvent for study.

Melting point determination

The melting point of the medication was determined using a melting point instrument. In a capillary tube that is closed on one end, a little amount of drug was taken. The temperature at which the drug melted was measured using a capillary tube in a melting point instrument. This process was repeated three times, with the average range value being recorded.

Determination of λ max and plotting of Zileuton’s calibration curve

In Methanol

To get 1000 µg/ml, around 10 mg of Zileuton was accurately weighed and diluted in 10 ml of methanol. Take 1 ml of the above solution and dilute it in 100 ml of distilled water. Further dilutions were performed to generate Zileuton concentrations of 2, 4, 6, 8, and 10 µg/ml. From 400 to 200 nm, all dilutions were scanned against a blank of methanol and distilled water. To validate λ max, the drug’s spectra was examined, and an absorbance vs concentration calibration curve was constructed.

In phosphate buffer pH 7.4

About 10 mg of Zileuton was accurately weighed and diluted in 10ml of phosphate buffer pH 7.4 to obtain a 1000 µg/ml concentration of drug (Stock solution). From the stock solution, concentrations of 2, 4, 6, 8, and 10µg/ml of Zileuton were obtained. All dilutions were scanned with a phosphate buffer pH 7.4 as a blank from 400 to 200nm. To validate λ max, the drug’s spectrum was examined, and a calibration curve was established between absorbance and concentration.

Drug and excipient interaction study

Fourier Transformation Infrared Spectroscopy (FTIR)

Excipients including PEG 300, Tween 20, and Eucalyptus oil were tested for compatibility with Zileuton in this study. It also aids in determining the acceptability of excipients for SMEDDS preparation. A Shimadzu FTIR spectrometer was used to investigate the FTIR spectra (IR Affinity 1Model, Japan). The researchers looked at pure pharmacological samples as well as physical mixtures including Zileuton and PEG 300, Tween 20, and Eucalyptus oil. The scanning range was maintained between 4000 and 500 cm⁻¹.

Solubility studies12-15

The drug’s solubility was investigated in different oils, surfactants, and co-surfactants using the flask shake method. Each 0.1ml of the filtrate was diluted in 10 mL of methanol before being analysed at 200nm with a UV-Spectrophotometer to determine amount of zileuton was present (UV-1800, Shimadzu, Japan).

Pseudo-ternary phase diagram construction16-18

The Eucalyptus oil, Tween 20 (surfactant), and PEG 300 (co-surfactant) were dispersed in various vials with different weight ratios (9:1, 8:2, 7:3, 6:4, 5:5, 4:6, 3:7, 2:8, 1:9). Water was titrated in each vial containing the liquid combination. After each addition of water, the mixture was vortexed to homogenize and checked the sample visually for any changes in visual transparency. The points achieved between single-phase clear and two-phase translucent area at this stage of essential shift in transparency. The data from this titration is used to create the pseudo-ternary phase diagram shown in Table 4.

FTIR

FTIR spectroscopy was utilized for investigating the presence and amount of PDN interaction with oil and surfactant/co-surfactant of SMEDDS. An FTIR spectrophotometer was used to obtain FTIR spectra (Shimadzu, Japan). With a resolution of 4 cm⁻¹ and...
40 scans, transmittance (% T) was measured in the spectral band 500–4500 cm\(^{-1}\).

**SMEDDS formulation**

Selected ratios of Oil: Smix (Mixture of surfactant and co-surfactant) of Smix (3:1) were used to create the formulations. Depending on the percent transmittance, the chosen ratios are (9:1), (8:2), and (3:7) shown in Table 1.

<table>
<thead>
<tr>
<th>Sl.No.</th>
<th>Ingredients</th>
<th>F1 (9:1)</th>
<th>F2 (8:2)</th>
<th>F3 (3:7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Zileuton</td>
<td>20 mg</td>
<td>20 mg</td>
<td>20 mg</td>
</tr>
<tr>
<td>2</td>
<td>Eucalyptus oil</td>
<td>2 gm</td>
<td>2 gm</td>
<td>5 gm</td>
</tr>
<tr>
<td>3</td>
<td>Tween 20</td>
<td>6 gm</td>
<td>12 gm</td>
<td>8 gm</td>
</tr>
<tr>
<td>4</td>
<td>PEG 300</td>
<td>12 gm</td>
<td>6 gm</td>
<td>7 gm</td>
</tr>
</tbody>
</table>

Table 1: Formulation of SMEDDS.

**Method of preparation of SMEDDS**

In an isothermal water bath at 50°C, 20mg of Zileuton was weighed precisely and dissolved in a mixture of 6 gm Tween 20 and 2gm Eucalyptus oil.

When the medication solubilized in an oil and-co-surfactant mixture, 12gm of PEG300 was added.

The vortexing of this combination was continued until a translucent preparation was achieved.

**Evaluation of SMEDDS**

**Centrifugation study**

The formulation was centrifuged for 30 min at 5000 rpm in a centrifuge for this study (REMI, India). Instability in the formulations was seen for example phase separation, creaming, and cracking. Formulations without phased separation, cracking and creaming were chosen for the heating-cooling cycle.

**Thermodynamic stability study**

This research covers six temperature cycles range from 4 to 40°C, for a minimum of 48 hrs at each temperature. Creaming, cracking, and phase separation were investigated in the formulations.

**Percentage Transmittance Study**

In this study, 0.1 ml formulation was mixed with 100 ml of distilled water. Using water as a blank, percentage transmittance was determined spectrophotometrically at 228 nm.

**Drug content analysis**

Take 10 mg of formulated SMEDDS and dissolved in 10 ml phosphate buffer, (pH 7.4). 1 ml of the above sample was dissolved in 100 ml of distilled water. Using correct dilution, the resultant sample is examined for absorbance in UV at 228 nm, and the % drug content is computed.

**In vitro dissolution profile**

A Dissolution Test Apparatus, USP standard, was used to conduct in vitro drug dissolution analysis of the SMEDDS formulation. The experiment was conducted in 900 ml of 6.8 Phosphate buffer, with 2ml of formulation inserted in a Dialysis bag and placed in 500ml dissolving media circulated at 50 rpm and kept at 37±0.5°C. Aliquots were taken at 5, 10, 15, 20, 30, 45, and 60 min intervals and examined using UV-spectroscopy at 228 nm.

**Viscosity measurement**

A Brookfield viscometer was used to determine the viscosity. The viscosity was measured at 27°C at 60 rpm using spindle no. 61.

**Globule Size Analysis and Zeta Potential measurement**

By analyzing the variations in light scattering caused by the Brownian motion of particles, Photon Correlation Spectroscopy (PCS) was used to quantify the droplet size distribution and Poly Dispersity Index (PDI) of the formulation. For measurement 100 ml of water and 0.1 ml of the formulation were mixed gently by inverting the flask 4 to 5 times. Then an aliquot of a few ml was taken and transferred to the sample cell for droplet size analysis.

Light scattering was measured in the zeta potential experiment at 25°C and a 90°angle. At room temperature measurement were taken in triplicates.

**Motic microscopic analysis**

Motic microscopy was used with a motic digital microscope to determine the development and arrangement of the globules in the SMEDDS F1 formulation (DMWB series, PAL System).

**Scanning Electron Microscopy**

Using a Scanning Electron Microscope (SEM) Model JSM6100 (Jeol) with Image Analyzer, Elemental Analyzer for CHN at (Thermo Scientific), SAIF Punjab, for the optimized SMEDDS formulation, the shape of the emulsion droplet was investigated.

**Stability Study**

In an ICH-certified stability chamber, the stability both chemical and physical of Zileuton SMEDDS F1 was examined under varied conditions of storage as per ICH requirements (ICH Q1A(R2)) (REMI, India). In storage circumstances up to three months, zileuton SMEDDS equal to 25 mg were put in a glass vial with a rubber seal and an aluminum-crimped top. After a 3-month
interval, samples were removed and tested for Zileuton drug content, centrifugation, heating cooling cycle, and dissolution study.

RESULTS

Solubility studies
Solubility of Zileuton's was found to be more in Eucalyptus oil i.e. 0.974. In surfactant Tween 20 has maximum solubility of Zileuton i.e. 0.853, PEG 300 has solubility of 0.821 shown in Table 2.

Study of a pseudo-ternary phase diagram
$S_{\text{mix}}$: Co-surfactant in the ratio of (3:1) shows highest % transmittance 60.42% ± 0.9590. Oil: Surfactant ratio 9:1, 3:7 and 8:2 were showed maximum % transmittance of 78.96%, 59.51% and 60.86% respectively in less quantity of water as shown in Figure 2 and Table 3.

Centrifugation study
The centrifugation test passes as no phase separation occurs in F1 Formulation.

Heating and cooling cycle
No phase separation occurs in heating and cooling cycle.

Percentage Transmittance Study
The % transmittance of F1 formulation was near 100 % i.e 91.02% ±0.8241. F2 shows 65.23% ± 0.5470 and F3 shows 53.19% ± 0.3219. Percentage transmittance of formulations were shown in Table 5.

Analysis of droplet size and Zeta potential
Formulation F1 and F2 had droplet sizes of 107 nm and 801 nm, respectively shown in Figure 3.

The formulations F1 and F2 have zeta potentials of -13.0mV and -15.0mV, respectively shown in Figure 4.

Microscopic image of SMEDDS F1
The image showing the formation of globules of 18.23µm radius having uniformity and spherical shape and were arranged properly shown in Figure 5.

FT-IR analysis
The drug and formulation ingredients were found compatible with each other shown in Figures 6 and 7.

Drug Content
The percent drug content of F1 formulation was found to be greater than F2 and F3 formulation i.e. 96.65%±0.8650, 89.08%±0.5112, 83.20%±0.4975 respectively shown in Table 6.

Viscosity
Viscosity of F1, F2,F3 was found to be 89±0.086, 62±0.052 and 46±0.037 respectively x shown in Table 7.

In vitro dissolution profile
The drug release profile of three formulation F1, F2 and F3 was studied and shown in Figure 8.

SMEDDS F1’s drug release kinetics was zero order kinetics shown in Figure 9.

Scanning Electron Microscopy
Scanning electron microscopic representation of Zileuton SMEDDS F1 and F2 shown well separated dense spherical particles with a smooth surface as the exterior morphology in Figure 10.

Table 2: Absorbance observed in solubility studies of oils.

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Vehicle</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Eucalyptus Oil</td>
<td>0.974</td>
</tr>
<tr>
<td>2</td>
<td>Tween 20</td>
<td>0.853</td>
</tr>
<tr>
<td>3</td>
<td>PEG 300</td>
<td>0.821</td>
</tr>
</tbody>
</table>

Figure 2: Graph of eucalyptus oil, Smix/CS, and water in pseudo-ternary phase (a) 3:7 ratio; (b) 8:2 ratio; (c) 9:1 ratio.
**Post Stability Studies**

**Centrifugation study**

After centrifugation for 5000 rpm for 30 min, there was no phase separation, creaming or cracking observed in SMEDDS F1 formulation.

**Heating and cooling cycle**

The formulation showed no phase separation, creaming, or cracking.

**Motic image of SMEDDS F1**

The image showing formation of globules of 18.43µm radius having uniformity and spherical shape and were arranged properly.

**Drug Content**

Drug content was estimated by extracting Zileuton from SMEDDS and was found to be 97.46±0.6250 shown in Table 8.

**Viscosity measurement**

At 25°C, the viscosity was measured at 60 rpm with spindle no. 61 was found to be 88±0.068 for F1 formulation shown in Table 9.

**DISCUSSION**

**Solubility studies**

Since eucalyptus oil demonstrated the highest solubility of zileuton among the evaluated oils, it was selected for further study. Amongst surfactants tested, Tween 20 had the maximum Zileuton solubility. Few surfactants are capable of generating temporary
negative interfacial tension and fluid interfacial film required to boost up the stability of microemulsion. Co-surfactant decreases interface bending stress along with that it gives interfacial film enough elasticity to take on the various curvatures required to generate microemulsion in a wide variety of composition. This is due to co-surfactant molecules penetrating the interfacial film, leaving free space between surfactant molecules. PEG 300 is being investigated as a co-surfactant for further study because of its ability to more effectively solubilize zileuton.

**Study of a pseudo-ternary phase diagram**

To locate the self-emulsifying area and determine appropriate component concentrations for producing the SMEDDS formulation, a pseudo-ternary phase diagram was constructed. Oxyethylene chains, both long and short homolog mixtures of non-ionic surfactants are useful in enhancing the stability of microemulsion. The three ratios of Smix: Co-surfactant were prepared and studied for pseudo-ternary phase diagram determination. Addition of 1µl of water in each vial along with mixing and monitored visually for optical transparency, until a homogeneous and transparent solution obtained. As well as their % transmittance was measured by UV-spectroscopy.

From the observations, Oil: Surfactant ratio 9:1, 3:7 and 8:2 were showed maximum % transmittance of 78.96%, 59.51% and 60.86% respectively in less quantity of water. Hence these

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**Table 3: Observation table for water titration.**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Smix: Co-surfactant Ratio</th>
<th>Quantity of water for max. transmittance</th>
<th>% Transmittance Mean ±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1:1</td>
<td>1ml</td>
<td>41.12% ± 0.7325</td>
</tr>
<tr>
<td>2</td>
<td>2:1</td>
<td>1ml</td>
<td>53.166% ± 0.8652</td>
</tr>
<tr>
<td>3</td>
<td>3:1</td>
<td>1.4 ml</td>
<td>60.42% ± 0.9590</td>
</tr>
</tbody>
</table>

**Table 4: Observation table of water titration (3:1).**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Ratio</th>
<th>Quantity of water for max. transmittance</th>
<th>% Transmittance Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10:0</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>2</td>
<td>9:1</td>
<td>16.01ml</td>
<td>78.96% ± 0.9852</td>
</tr>
<tr>
<td>3</td>
<td>8:2</td>
<td>15.02ml</td>
<td>60.86% ± 0.7651</td>
</tr>
<tr>
<td>4</td>
<td>7:3</td>
<td>9.96ml</td>
<td>38.98% ± 0.0098</td>
</tr>
<tr>
<td>5</td>
<td>6:4</td>
<td>10.56ml</td>
<td>41.21% ± 0.0156</td>
</tr>
<tr>
<td>6</td>
<td>5:5</td>
<td>11.73ml</td>
<td>44.37% ± 0.0173</td>
</tr>
<tr>
<td>7</td>
<td>4:6</td>
<td>10.91ml</td>
<td>43.05% ± 0.01429</td>
</tr>
<tr>
<td>8</td>
<td>3:7</td>
<td>14.75ml</td>
<td>59.51% ± 0.6184</td>
</tr>
<tr>
<td>9</td>
<td>2:8</td>
<td>12.56ml</td>
<td>50.06% ± 0.5286</td>
</tr>
<tr>
<td>10</td>
<td>1:9</td>
<td>13.48ml</td>
<td>53.24% ± 0.6554</td>
</tr>
</tbody>
</table>

**Figure 5: Microscopic image of SMEDDS F1 formulation.**

**Table 5: Percentage transmittance study.**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Formulations</th>
<th>% Transmittance (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F1</td>
<td>91.02% ± 0.8241</td>
</tr>
<tr>
<td>2</td>
<td>F2</td>
<td>65.23% ± 0.5470</td>
</tr>
<tr>
<td>3</td>
<td>F3</td>
<td>53.19% ± 0.3219</td>
</tr>
</tbody>
</table>

**Table 6: Percent drug content of the formulation.**

<table>
<thead>
<tr>
<th>Batch</th>
<th>Drug Content±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>96.65%±0.8650</td>
</tr>
<tr>
<td>F2</td>
<td>89.08%±0.5112</td>
</tr>
<tr>
<td>F3</td>
<td>83.20%±0.4975</td>
</tr>
</tbody>
</table>
three were selected for formulation. The emulsion must show maximum transmittance after the minimum addition of water would be ideal.

**Centrifugation study**

There was no separation of phases, creaming, or cracking in the SMEDDS F1 formulation after centrifugation at 5000 rpm for 30 min. As a result, the centrifugation test is passed.

**Heating and cooling cycle**

After 6 cycles of 4°C and 40°C with storage at each temperature for 48 hr, there is no creaming, cracking, or phase separation of the SMEDDS F1 Formulation.

**Percentage Transmittance Study**

After dilution at different time intervals, the percent transmittance of optimal batches i.e. F1, F2 and F3 was investigated. In comparison to F2 and F3, formulation F1 with a Smix to co-surfactant ratio of 3:1 had a percentage transmittance closer to 100 percent. Even after 24 hr after dilutions, this data indicates that no aggregation or particle growth has occurred. A percentage transmittance near to 100% indicated a droplet size in the nanoscale region.

**Analysis of droplet size and Zeta potential**

The SMEDDS particle size is significant because it determine the rate and degree of drug release and absorption. The minor globule size allows for better absorption and dissolution. The higher the Smix proportion, the smaller the mean droplet size becomes. Formulation F1 produced the smallest particles, while Formulation F2 produced the largest droplets.
Microscopic image of SMEDDS F1

For determination of formation and arrangement of globules of SMEDDS F1 formulation, motic microscopy was carried out.

FT-IR analysis

The FTIR analysis of physical mixture, SMEDDS F1 formulation and the individual components shows that no interaction occurs between the components and drug.

Drug Content

Extraction of Zileuton from SMEDDS was used to evaluate drug content. In a suitable amount of methanol, SMEDDS was dissolved. The solution was sonicated 10-15 min and then filtered. The absorbance of the filtrate was measured at 228 nm using a UV-visible Spectrophotometer.

Viscosity measurement

Rotational viscosity measurement equipment with concentric cylinders was used to determine the viscosity (Brookfield viscometer DVII plus pro, Brookfield engineering laboratory, USA). At 25°C, the viscosity was measured at 60 rpm with spindle no. 61.

In vitro dissolution profile

The drug release profile of three formulations F1, F2 and F3 was studied. The small globule size and high percentage transmittance of SMEDDS F1 are responsible for its rapid release. SMEDDS F1’s drug release kinetics was zero order kinetics. As a result, this SMEDDS is expected to rapidly deliver Zileuton in a solubilized form in the GI fluid after intake, potentially leading to increased oral absorption.

Scanning Electron Microscopy

The SEM picture indicated well separated dense spherical particles with a smooth surface as the exterior morphology of the SMEDDS formulation.

Post Stability Studies

Centrifugation study

After centrifugation for 5000 rpm for 30 min, there was no phase separation, creaming or cracking observed in SMEDDS F1 formulation. Hence formulation passes the centrifugation study.

Heating and cooling cycle

After six cycles of 4°C and 40°C with storage at each temperature for 48 hr, the formulation showed no phase separation, creaming, or cracking.

Motic image of SMEDDS F1

For determination of formation and arrangement of globules of SMEDDS F1 formulation, motic microscopy was carried out. The image showing formation of globules of 18.43 µm radius having uniformity and spherical shape and were arranged properly.

Drug Content

Drug content was estimated by extracting Zileuton from SMEDDS.

Viscosity measurement

Rotational viscosity measurement equipment with concentric cylinders was used to determine the viscosity. At 25°C, the viscosity was measured at 60 rpm with spindle no. 61.
CONCLUSION
As a surfactant mixture, a SMEDDS of Zileuton, a weakly water soluble drug, was produced with Tween 20 in a 1:1 ratio. The water titration method was used to make Zileuton SMEDDS. Various physical stability investigations and self-emulsification assessment tests were performed on the produced and formulations. Based on percentage transmittance investigations, the formulations that passed the first two tests were further improved. The improved formulation had a drug content of roughly 96 percent of the added amount, suggesting the system’s aptitude for high entrapment in the internal phase. For globule size analysis, the SMEDDS F1 with a percentage transmittance of more than 90% was used. The creation of spherical globules can be seen in microscopic images. SMEDDS F1 had a faster in vitro dissolving profile, due to its minor particle size, the solubilizing capacity is larger, and the dissolution rate is faster. From the SEM image, the SMEDDS formulation revealed a well-separated intense spherical particle with a smooth surface. The zeta potential values and droplet size analysis confirm the reduction in particle size to the nanometer range, which improves solubility and thus the dissolving rate and absorption of otherwise poorly soluble drugs.

ACKNOWLEDGMENT
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CONFLICT OF INTEREST
The authors declare no conflict of interest.

ABBREVIATIONS
hr: Hours; min: Minutes; ℃: Degree celcius; SMEDDS: Self Micro Emulsifying Drug Delivery System; %: Percentage; GI Tract: Gastrointestinal Tract.

REFERENCES