# Formulation and Evaluation of Quercetin loaded self-emulsifying drug delivery system

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## ABSTRACT

The plant-derived flavonoid quercetin is well-known for its anti-inflammatory and antioxidant qualities, but because of its extremely low oral bioavailability, it is challenging to evaluate its potential for therapeutic use. The development of a self-emulsifying drug delivery system (SEDDS) to increase quercetin's oral bioavailability was the primary goal of this effort. Solubility of quercetin was determined in various vehicles. SEDDS is mixture of oils, surfactants, and co-surfactants, which are emulsified in aqueous media under conditions of gentle agitation and digestive motility that would be encountered in the gastro-intestinal tract. A series of formulations with different compositions were selected in the microemulsion region for assessment of self-emulsification time and droplet size. Emulsification time and the mean droplet size were found to be 1minute and 18.0 ± 0.25 nm, respectively, for the optimum formulation. Dilution study was also performed for optimization of formulation**.** The absorption of quercetin from SEDDS form resulted about 3.5-fold increase in bioavailability compared with the pure drug solution. The formulation is suitable for oral administration of quercetin. It would be useful to conduct efficacy studies of quercetin in diseased animal models and subsequently for toxic kinetics studies.

**Keywords**: Emulsifying, quercetin, flavonoids, bioavailability, hydrophobic, surfactants.

# 1. INTRODUCTION

One of the most often utilized methods for medication delivery and administration is the oral route. The slow start time, potential for irregular absorption, and the potential for digestive enzymes to break down some particular medications are the primary drawbacks of this approach. Drugs that are not well soluble in water, such HIV protease inhibitors, glycoprotein inhibitors, and anticancer medications, have difficulty being produced and being well soluble in the gastrointestinal system.

The drug delivery industry scientists are used a wide range of methods to improve the dissolution rate of poorly water-soluble drugs, including formulations containing nanoparticles, a solid solution formulation or self-emulsifying drug delivery system (SEDDS), and stable amorphous form of the drug.[1] In recent years, however, much attention has been focused on lipid-based formulations, with particular emphasis on self-emulsifying drug delivery system (SEDDS) and self-micro emulsifying drug delivery system (SMEDDS). [2] SEDDS is an isotropic mixture of oil, surfactant and/or co-surfactant can be used for formulations to improve the absorption of drugs in gastrointestinal tract and solve the solubility problems. SEDDS can produce fine oil/water emulsion after dilution in gastrointestinal fluids and provide large interfacial area for drug partitioning between oil and water phases and so increase in solubility rate and extent of absorption.[3]

### 1.1 For selecting a suitable self-emulsifying vehicle, it is important to assess:

a. the drug solubility in various components;
b. the area of self-emulsifying region in the phase diagrams;
c. droplet size distribution following self-emulsification.

### 1.2 Various modes of enhanced drug absorption from the SEDDS formulation can be hypothesized as follows:

- The chylomicron production of the fatty components of the digestible oil phase of an emulsion might facilitate the lymphatic absorption of drugs. In reality, bile salt micelles may be used to absorb a lipophilic medication which ideally stays in the oil droplets along with the lipid carrier's metabolite.[4]
- Bates and Sequeria proposed that prolonged medication dissolution and absorption from the lipid phase of the emulsion may be possible due to the reduction of stomach motility brought on by its presence.
- Increase mucosal permeability via incorporation of lipid from mixed micelles and enhanced mesenteric lymph flow may be responsible for the enhanced drug absorption.[5]
- A hydrophilic medication may diffuse straight into the portal supply rather than being absorbed via the lymphatic (chylomicron) system. Therefore, in this instance, increased medication absorption may be a result of increased dissolution from the wide surface area provided by the emulsion.[6]
- A relatively less focused consideration is the presence of surfactant in formulation, which may also play a role in increasing the absorption of the drugs.

For selecting a suitable self-emulsifying vehicle, it is important to assess:
a. the drug solubility in various components;
b. the area of self-emulsifying region in the phase diagrams;
c. droplet size distribution following self-emulsification (Kang, Lee, Cho, Jeong, Yuk, Khang, Lee, & Cho, 2004).
Most edible fruits and vegetables contain quercetin (QT, 3,3,4,5,7-pentahydroxyflavone), a plant flavonoid that was isolated and extracted from Sophora japonica L. It has a wide range of physiological activities, including anti-inflammatory and anti-proliferative effects on a variety of human cancer cell lines, osteoporosis, and inhibition of glycolysis, macromolecule synthesis, pulmonary and cardiovascular diseases, as well as anti-aging properties. [7]

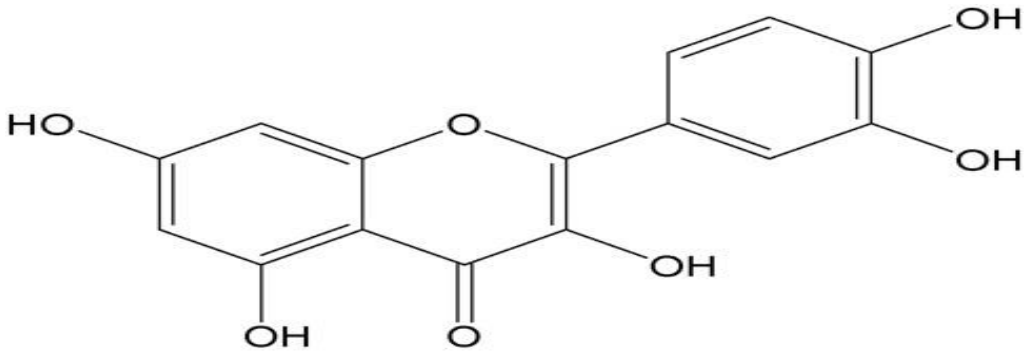


FIGURE 1. The Structure of quercetin

However, QT has a very low oral bioavailability (16.2%) due to its low solubility in water (0.17–7.7g/ml) and artificial gastric juice (5.5 ssg/ml) and artificial intestinal juice (28.9 g/ml) So its application is restricted in clinic.[8] Therefore, formulation strategies have been designed to increase the solubility and improve the oral absorption of QT. At micromolar concentrations, studies have shown that quercetin can stimulate cell differentiation and enhance cell death in a variety of cancer cell types, including lung cancer, colon cancer, prostate carcinoma, and pancreatic tumour cells.[9]

In this study, Oil (Castor oil) a non-ionic surfactant (Tween 80) and cosurfactant (PEG) were used to formulate a SES for Quercetin (QT), a poorly water-soluble drug. The objectives of this study were to develop and characterize the optimal formulation of SEDDS containing quercetin for to increase absorption leading to improvement in bioavailability, to reduce dose leading to reduction in dosing frequency, to achieve sustained release effect. Its bioavailability compared with pure drug solution in male albino rats.[10]

## 2. MATERIALS AND METHODS

### 2.1 Materials

QT was purchased from Sigma–Aldrich Chemical Co. Tween 80, castor oil and PEG 600 was purchased from Lob chem. (Mumbai, India). Potassium dihydrogen orthophosphate, HCL, and NaOH were purchased from Loba chem. (Mumbai, India). Methanol (HPLC grade) was also from Loba chem. Ltd, (Mumbai, India). All other Chemicals were reagent grade.

### 2.2 Solubility of QT in oils and surfactants

To find out the suitable oil and surfactant as compositions of SEDDS, the solubility of QT in various oils such as paraffin oil, castor oil, peanut oil, ethyl oleate, and surfactants including Cremophor EL-40, Tween 80, poloxamer 188 and emulsifier OP was measured. An excess amount of QT was added to 3 g oil or 20 ml 12.5% (w/v) surfactant solutions and then the resulting mixture was shaken in a water bath at 37˚C for 24 h followed by centrifugation for 10min at 12,000rpm [11]. The supernatant was diluted with ethanol appropriately and the drug concentration was determined by high performance liquid chromatography (HPLC) analysis. The oil and surfactant that showed higher solubility for QT were selected as the compositions of SEDDS. [12]

### 2.3 Fourier Transform Infrared Spectroscopy

The FT-IR spectra of the samples were obtained on a Perkin- Elmer 2000 spectrophotometer (Perkin-Elmer, Norwalk, CT, USA). Each sample and potassium bromide were mixed by an agate mortar and compressed into thin tablets. The scanning range was 370–4000 $cm^{-1}$ and the resolution were 1 $cm^{-1}$. Each sample was measured and recorded in triplicate. [13]

### 2.4 Compatibility tests

Cosurfactants were screened by the compatibility tests with the tested cosurfactants mixing with the systems of different oils and chosen surfactant solution. 6ml Tween 80 micelle solution (10%, w/v) was mixed with 0.05 g oil, and then the resulting mixture was titrated by cosurfactant under proper magnetic stirring till the appearance of resulting solutions was subjected to a change from turbid to clear and transparent. Samples were left to equilibrate for at least 10min before being examined for transparency. The added amounts of cosurfactant were recorded. The transparency of resulting solution was determined by ocular inspection and was used as an index to evaluate the compatibility of oil, cosurfactant and surfactant solution.[14] Under same conditions of clearance and transparency of obtained solution, the less amounts of added cosurfactant showed better compatibility with the oil and surfactant solution. Co-surfactants such as dehydrated ethanol, 1,2-propylene glycol, glycerine and PEG400 were chosen to drop to the mixed systems composed of emulsifier Tween 80 (10%, w/v) and oil such as ethyl oleate, paraffin oil, castor oil or peanut oil, and the results were recorded as shown in table-1

### 2.5 Pseudo ternary phase diagram study

Pseudo ternary phase diagrams of oil, surfactants/cosurfactant or cosolvents, and water were developed using the water titration method. The mixtures of oil and S/CoS at certain weight ratios were diluted with water in a drop wise manner. For each phase diagram at a specific ratio of oil and Smix, i.e. (1:9 to 9:1) and S/CoS (i.e. 1:1, 2:1, 3:1, 4:1 and 5:1 wt/wt), a transparent and homogenous mixture of S/CoS was formed.[15] Then, each mixture was titrated with water and visually observed for phase clarity and flow ability. After the identification of microemulsion region in the phase diagrams, the microemulsion formulations were selected at desired component ratios. In order to form the stable microemulsion, a series of SEDDS formulations were prepared [16]

### 2.6 Preparation of SEDDS formulations

A series of SEDDS formulations were prepared using castor oil as the oil, Tween 80 as surfactants, and PEG 600 as cosurfactant shown in (Table 2). In all the formulations, the level of Quercetin was kept constant. Accurately weighed QT was placed in a glass vial, and oil (castor oil) was added and mixed by gentle stirring on a magnetic stirrer at 40°C until QT was completely dissolved. The remaining components, i.e. Tween 80, and PEG 600 (Smix) were added with constant stirring at 40°C until stable mixture was formed.[17]

TABLE 2
Formulation table

| Components | Smix(3:1)F(A) | Smix(4:1)F(B) | Smix(5:1)F(C) |
|---|---|---|---|
| QT(w/w) | 10 | 10 | 10 |
| Castor oil(w/v) | 10% | 18.36% | 9.09% |
| Tween 80(w/v) | 67.5% | 65.32% | 75.69% |
| PEG 600(w/v) | 22.5% | 16.32% | 15.22% |

## 3.0 Characterization and evaluation of the formulation

### 3.1 Dilution study

SEDDS formulations containing 10 mg of QT (1 part) were diluted with 10 parts of distilled water, 0.1 N HCl and Phosphate buffer of pH 6.8 and visually observed drug content

0.1 ml volume was extracted from final preparation and poured into 10 ml volumetric flask volume was make up by adding methanol. QT content in the methanolic extract was analysed spectrophotometrically at 370 nm, against the standard methanolic solution of QT [18]

### 3.2 Self-emulsification and precipitation assessment

Assessment of the self-emulsifying properties of SEDDS formulations were performed by visual assessment. Different formulations were categorized on the basis of Speed of emulsification, clarity, and apparent stability of the resultant emulsion. Visual assessment was performed by dropwise addition of the SEDDS into 250 mL of distilled water at room temperature, and the contents were gently stirred magnetically at ~ 100 rpm.[19] Precipitation was evaluated by visual assessment of the resultant emulsion after 24 h. The formulations were then categorized as clear (transparent or transparent with bluish tinge), non-clear (turbid), stable (no precipitation at the end of 24 h), or unstable (showing precipitation within 24 h)

### 3.3 Viscosity determination

SEDDS (1 mL) was diluted 10 and 100 times with the distilled water in beaker with constant stirring on magnetic stirrer. Viscosity of the resultant microemulsion and undiluted SEDDS was measured using viscometer (Brookfield-DV-E).[20]

### 3.4 Droplet size analysis

The Malvern Particle Size Analyzer, Model No. 2600 (Malvern Inst., South borough, MA), with a 63 mm lens was used to measure emulsion droplet size. The average droplet size is indicated as d (0.5). The instrument is based on the principle of laser diffraction. The system inherently measures the integral light scattering from all particles present in the beam. As material flows through the beam, the measured light scattering is continuously changing to give the instantaneous integral of the material illuminated by the analyzer beam. Approximately 0.002 % of emulsion concentration in water was incorporated into a 15 mL volume cell, and under slow agitation, the scattered light intensity was measured.[21]

### 3.5 Zeta-potential determination

SMEDDS (1 mL) was diluted 10 times and 100 times with distilled water in beaker with constant stirring on a magnetic stirrer. Zeta-potential and electrophoretic mobility of the resulting microemulsion was determined using the Zetasizer. (Malvern Instruments) [22]

### 3.6 In vitro dissolution studies

The purpose of in vitro dissolution study was to check the dissolution rate of SEDDS.
The quantitative in vitro release test was performed in 900 mL of phosphate buffer pH 6.8 maintained at 37 ± 0.5°C using USP XXIV type II dissolution apparatus (Electrolab TDT-08L, India). The paddles were rotated at 100 rpm. The SEDDS formulations were filled into transparent hard gelatin capsules (0 sizes) and used for drug release studies. Five mL aliquots were collected periodically and replaced with fresh dissolution medium. Aliquots, after filtration through Whatman filter paper (No. 41), were analysed spectrophotometrically at 270 nm for QT content [23].

### 3.7 In vitro drug diffusion studies

The purpose of in vitro diffusion study was to check the permeation of drug through biological membrane. In vitro diffusion studies were carried out by using the dialysis technique. One end of pretreated cellulose dialysis tubing (7 cm in length) was tied with thread and 0.5 mL of self-emulsifying formulation (equivalent to 10 mg QT) was placed in it along with 0.5 mL of dialyzing medium (phosphate buffer pH 6.8). The other end of tubing was also secured with thread and was allowed to rotate freely in the dissolution vessel of a USP XXIV type II dissolution test apparatus that contained 900 mL dialyzing medium (phosphate buffer pH 6.8) maintained at 37 ± 0.5°C and stirred at 100 rpm. Placebo formulation (blank SEDDS, without drug) was also tested simultaneously under identical conditions so as to check interference, if any.[24] Aliquots were collected periodically and replaced with fresh dissolution medium and analysed spectrophotometrically at 270 nm for QT content.

### 3.8 Stability studies

Chemical and physical stability of optimized QT SEDDS formulation was assessed at 40°C, 60°C, 93% Rh, 75% Rh, and 33% Rh as per ICH Guidelines SEDDS equivalent to 10 mg QT was filled in 5ml glass bottle, packed in aluminium strips and stored for three months in stability chamber Samples were analysed at 0, 15 and 30 days for drug content, disintegration time and in vitro dissolution profile.[25]

# 4.0 RESULTS AND DISCUSSION

## 4.1 Solubility studies

The solubility of QT in various vehicles was analysed in order to screen suitable components for ME. In four tested surfactant solutions (12.5%, w/v), QT had the highest solubility in Tween 80 solution (887.7µg/ml), followed by Cremophor EL (522.4µg/ml) and Poloxamer (320.8µg/ml). It was almost insoluble in poloxamer 188 (73.3g/ml). Therefore, Tween 80 was chosen as surfactant for emulsion. In the four tested oils, the solubility of QT was highest in castor oil (835.1 µg/ml), followed by peanut oil (772.4 µg/ml), and the solubility of QT in paraffin oil or ethyl oleate was 702.3 µg /ml. So castor oil was initially considered as a good oil phase. [26]

When the mixture of Tween 80 and castor oil was titrated with different cosurfactants the stability of ME varied greatly. In tested cosurfactants, PEG 600 can form stable ME chosen as cosurfactant Since PEG 600 has a good ability in forming ME with castor oil and Tween 80. In conclusion, Castor oil, Tween 80 and PEG 600 were subsequently chosen as the oil phase, surfactant and cosurfactant for the formulation of QT-loaded SEDDS in this study. [27]

TABLE 3

Solubility in various vehicles

| Name of vehicles | Solubility µg/mL |
|---|---|
| Castor oil | 832 µg/mL |
| Mustard oil | 443 µg/mL |
| Sun flower | 726 µg/mL |
| Peanut oil | 772 µg/mL |
| Ethyl oleate | 702 µg/mL |
| Tween 80 | 887 µg/mL |
| Cremophor EL | 522.4 µg/mL |
| Poloxamer | 73.3 µg/mL |
| PEG 600 | 452 µg/mL |

## 4.2 Fourier Transform Infrared Spectroscopy

FIGURE 2. Fourier Transform Infrared Spectroscopy of Quercetin

IR spectroscopies of the quercetin and its complex were achieved by Perkin-Elmer, Norwalk CT, USA, in order to gain more information about the complex structure. The presence of peak at 424.81 $cm^{-1}$ in IR spectrum of the complex indicates formation of (O–Sn) bond through the complex. The C=O stretching mode of the free ligand (Fig.2) occurs at 1666.41 $cm^{-1}$. By the interaction of ligand with stannous chloride it has been shifted to 1642.90 cm-which can be explained by coordination of carbonyl oxygen with metal ion.[28] The bands located in 1611.0 $cm^{-1}$ and 1262.64 cm-1, respectively are related to ν(C=C) and ν(C–O–C) vibration frequencies in ligand spectrum which are slightly shifted after complexation with tin. Moreover, an increase in bond order (from 1319.09 cm-1 in the ligand to 1341.85 cm-1 in the complex) indicates involving of ν(C–OH) deformation mode, which is obvious when ortho-dihydroxy group in quercetin B ring coordinates in metal chelation. The big bound of ν (O–H) vibration frequency (from 3408.10 to 3384.82 $cm^{-1}$) indicates the existence of water in the compound.[29]

### 4.3 Pseudo ternary phase diagram

When self-emulsifying systems are added to aqueous medium, they create fine oil-water emulsions with very little agitation. At the contact, surfactant and co-surfactant are preferentially adsorbed, lowering the interfacial energy and acting as a mechanical barrier to coalescence. The microemulsion formulation's thermodynamic stability is subsequently enhanced by the reduction in the free energy needed for emulsion formation. As a result, the choice of surfactant and oil, as well as the proportion of oil to S/CoS, are crucial for the microemulsion's creation.[30] After performing solubility studies, components in which drug showed more solubility put forwarded for phase behaviour study. In the present study, combinations of surfactants (Smix) with high and low HLB values were used. PEG 600 has low HLB value (5–6) and Tween 80. The combination of low and high HLB surfactants leads to more rapid dispersion and finer emulsion droplet size on addition to aqueous phase.[31] PEG 600 and Tween 80 in the ratio of 3:1, 4:1 and 5:1 showed wider microemulsion existence area and rapid emulsifications compared with 1:1 and 2:1. Shown in (Fig 3, Fig 4 and Fig 5) Respectively. An increase in the microemulsion area as increase in S/Cos ratio from 3:1 to 5:1. But in 1:1 and 2:1 ratio the concentration of surfactants goes beyond limit, hence authors selected 3:1, 4:1 and 5:1 S/Cos ratio for formulation. PEG 600 is reported to be incompatible with hard gelatin capsules when used in high concentrations (> 15% W/W of total formulation). Thus PEG 600 concentration was kept below 15% w/w in formulation.[32]

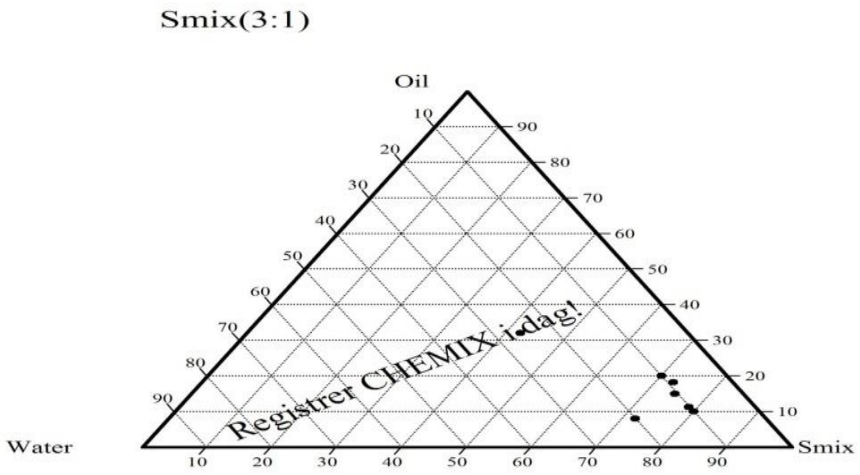


**FIGURE 3. Smix (3:1) Formulation (A)**

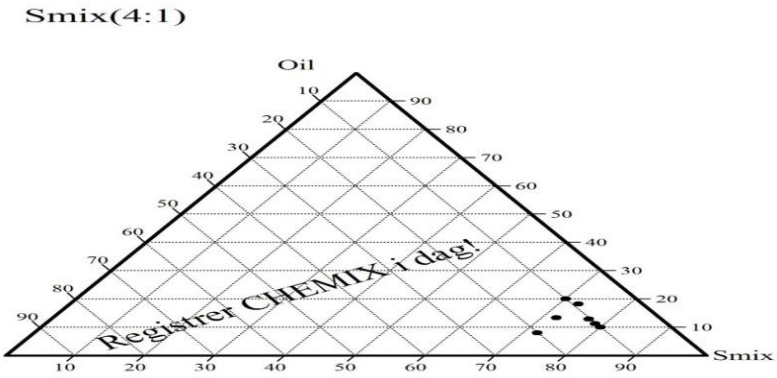


**FIGURE 4. Smix (4:1) Formulation (B)**

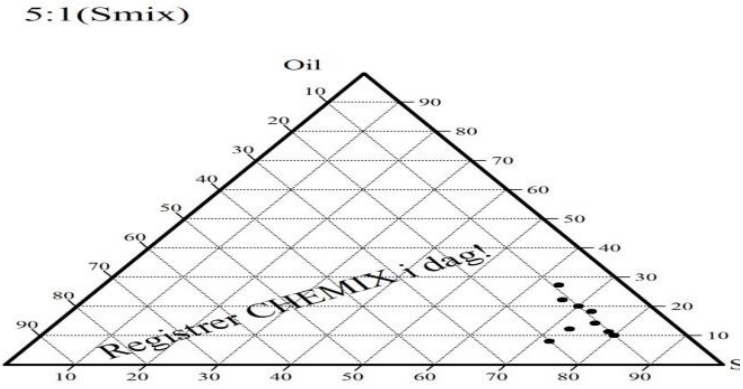


**FIGURE 5. Smix (5:1) Formulation (C)**

## 4.4 Characterization and evaluation of the formulation

### 4.4.1 Dilution study

The objective of the dilution study was to study the degree of emulsification and recrystallization of the drug, if any Viscosity of diluted and undiluted SMEDDS was measured to study the effect on emulsification time. Dilution may better mimic conditions in the stomach following oral administration of SMEDDS pre- concentrate. Dilution study was carried out to access the effect of dilution on SMEDDS pre-concentrates. Accurate mixture of emulsifier is necessary to form stable microemulsion, for the development of SEDDS formulation when one part of each SEDDS formulation was diluted with 10 parts of distilled water, 0.1 HCl and phosphate buffer 6.8 pH (Table 4). It implies that the formulation (A) 1:9 of Smix 5:1 was more stable because there was no precipitation or crystallization of drug.[33]

TABLE 4
Dilution study

| Vehicles | Smix(3:1)F(A)1:9 | Smix(4:1)F(B)2:8 | Smix(5:1)F(c) 1:9 |
|---|---|---|---|
| Distil water | Stable up to 5 hrs | Stable up to 5 hrs | Stable up to 5 hrs |
| 0.1N HCL | Stable up to 5 hrs | Stable up to 3 hrs | Stable up to 5 hrs |
| Phosphate buffer 6.8 | Stable up to 1 hrs | Stable up to 1 hrs | Stable up to 5 hrs |

### 4.4.2 Drug content

Drug content of the SEDDS formulations is shown in (Table 5) which was in the limit (98–102%).

TABLE 5
Characterization and evaluation parameter

| **Parameters** | **Smix (3:1) F(A)** | **Smix(4:1)F(B)** | **Smix (5:1) F(c)** |
|---|---|---|---|
| Drug content (%) | 80.8 | 81.5 | 85.6 |
| Precipitation | Stable | Unstable | Stable |
| Clarity | Bluish | Turbid | Stable |
| Viscosity (Cp) (1:50) | 1.6347 | 1.8670 | 1.3926 |
| Droplet size(micron) | 68.0828 | 90.2016 | 63.7696 |

### 4.4.3 Self-emulsification and precipitation assessment

It was discovered that there was turbid and unstable dispersion above and below the 49% surfactant concentration threshold, at which point the self-emulsification time (SET) decreased. This might be because of excessive water evaporation into the oil, which disrupts the interfacial layer and ejects droplets into the bulk aqueous phase. Higher surfactant levels, however, lower the drug's solubility limit and may therefore cause precipitation. Given the proportional increase in surfactant concentration, it is reasonable to presume that the self-emulsification time has decreased. Because low HLB surfactants acted as coupling agents for high HLB surfactants, a mixture of high and low HLB value surfactants was employed.

Furthermore, using a blend of low and high HLB surfactants may also lead to more rapid dispersion and finer emulsion droplet size on addition to an aqueous phase.[34] As concentration of surfactant increases the molecular volume increases which affects penetration at the interface hence SET decreases. Therefore, we were found formulation(A) of Smix 5:1 takes less time to emulsifying compare to other two optimize formulation. (Table 5)

### 4.4.4 Viscosity determination

As SEDDS was diluted 10 and 100 times with water, viscosity of the system was decreased, which indicates that oral administration of SEDDS formulation will be diluted with the stomach fluid and viscosity will be decreased and therefore absorption from the stomach will be fast.

### 4.4.5 Droplet size analysis

The droplet size of the emulsion is a crucial factor in self-emulsification performance because it determines the rate and extent of drug release as well as drug absorption. Also, it has been reported that the smaller particle size of the emulsion droplets may lead to more rapid absorption and improve the bioavailability. It was observed that increasing the S/CoS ratio led to decrease in mean droplet size. It is well known that in microemulsion systems the addition of surfactants stabilizes and condense the interfacial film, while the addition of cosurfactant causes the film to expand; thus, the relative proportion of surfactant to cosurfactant has varied effects on the droplet size. The SEDDS was found to be clear transparent after the 100 times dilution with distilled water and remained stable.

In vitro dissolution studies.[35]

Drug release from the SEDDS formulation 5:1(Smix) F (C) was found to be significantly higher as compared with other formulation ratio (Shown in Fig 5). The result indicates that 5:1(Smix) F (C) shows 14% of drug release within 10 min and 74% of drug release in 90 min, which is higher than the other formulation. It could be suggested that the SEDDS formulation resulted 5:1(Smix) F (C) in spontaneous formation of a microemulsion with a small droplet size, which permitted a faster rate of drug release into the aqueous phase, much faster than that of other formulation.

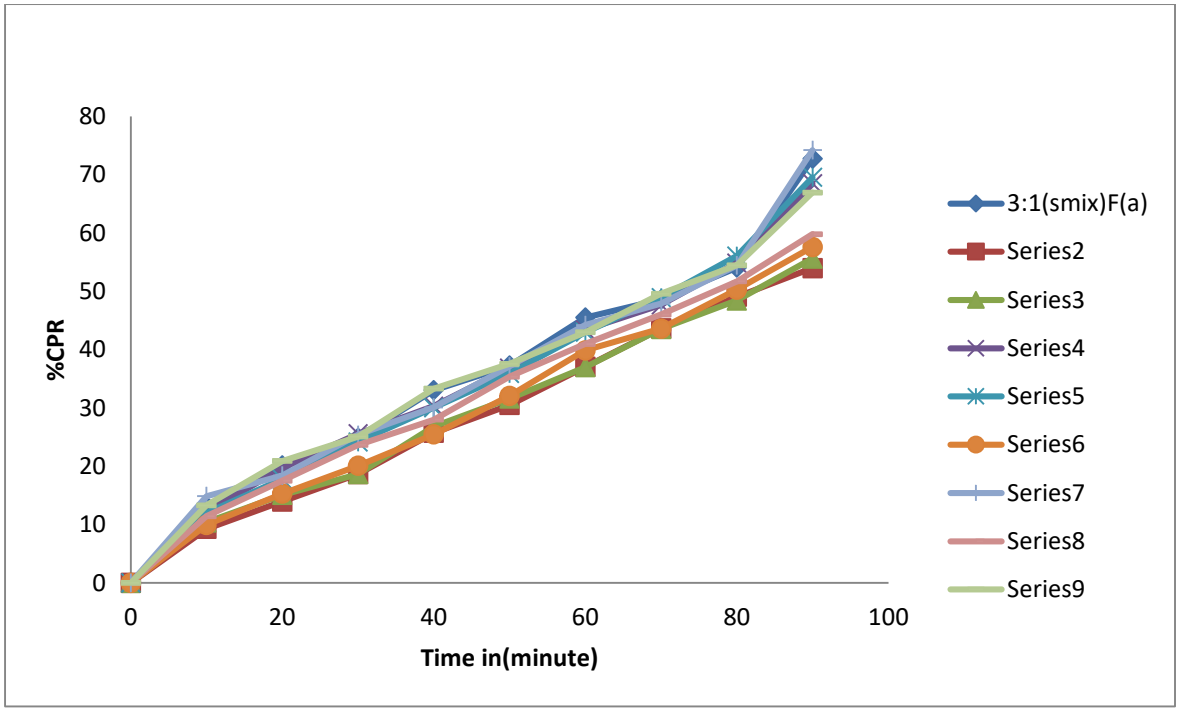


FIGURE 6. In vitro dissolution studies of developed formulations

### 4.4.6 In vitro drug diffusion studies

Conventional dissolution testing of SEDDS has a limitation in mimicking its real time in vivo dissolution and such a technique can only provide a measure of Dispersibility of SEDDS in the dissolution medium. Alternatively, for evaluating the in vitro performance of SEDDS, drug diffusion studies using the dialysis technique are very popular and well documented in many literatures. Diffusion studies were performed for SEDDS 3:1(Smix) F (A), 4:1(Smix) F (B) and 5:1(Smix) F(C). The release of QT from these dosage forms was evaluated in phosphate buffer pH 6.8; the release percentage of 5:1(Smix) F (C) was significantly higher than that of 3:1(Smix)F(A) and 4:1(Smix) F (B).

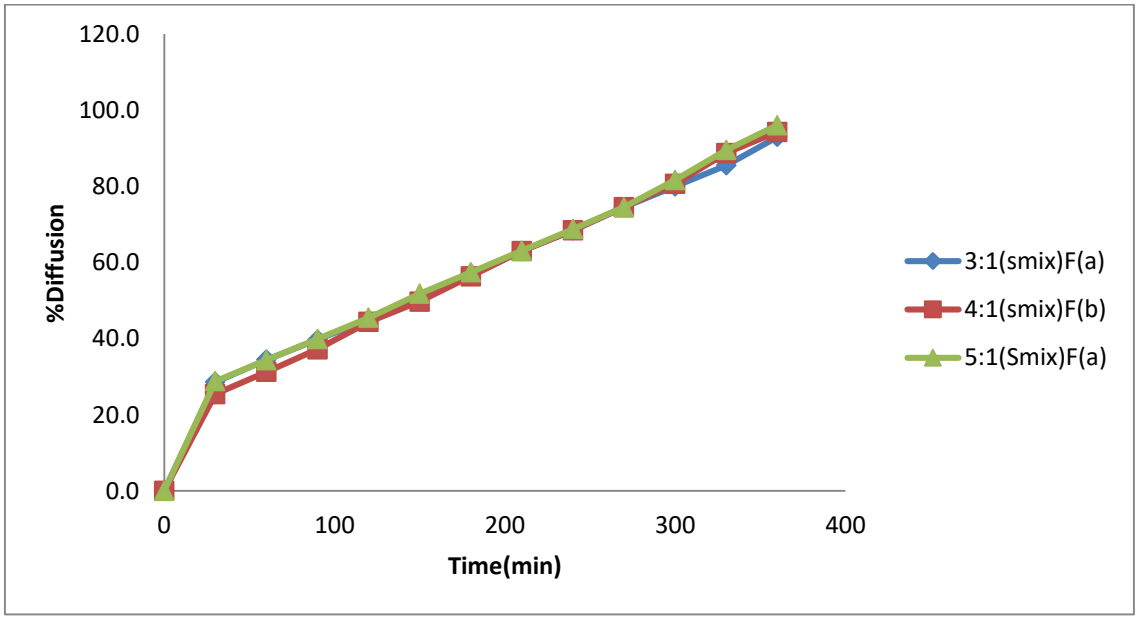


FIGURE 7. In vitro diffusion studies

### 4.4.7 Stability studies

TABLE 6 Stability study data

| At Room Temp RH | Time(days) | Colour | Clarity | PH | Emulsification time (Sec) |
|---|---|---|---|---|---|
| 33% | 0 | Golden Yellow | Clear | 8.4 | 48 |
| | 7 | Golden Yellow | Clear | 8.4 | 51 |
| | 15 | Golden Yellow | Clear | 8.4 | 43 |
| | 30 | Golden Yellow | Clear | 8.4 | 52 |
| 75% | 0 | Golden Yellow | Clear | 8.4 | 45 |
| | 7 | Golden Yellow | Clear | 8.4 | 53 |
| | 15 | Golden Yellow | Clear | 8.4 | 56 |
| | 30 | Golden Yellow | Clear | 8.4 | 47 |
| 93% | 0 | Golden Yellow | Clear | 8.4 | 49 |
| | 7 | Golden Yellow | Clear | 8.4 | 53 |
| | 15 | Golden Yellow | Clear | 8.4 | 51 |
| | 30 | Golden Yellow | Clear | 8.4 | 49 |

Optimized formulations 3:1(Smix) F (A), 4:1(Smix) F (B) and 5:1(Smix) F (C) are filled into 5 ml glass bottles the final dosage form. However, liquid-filled are prone to leakage, and the entire system has a very limited shelf life owing to its liquid characteristics and the possibility of precipitation of the drug from the system. Thus, the optimized formulations were subjected to stability studies to evaluate its stability and the integrity of the dosage form.[36] No change in the physical parameters such as homogeneity and clarity was observed during the stability studies. Shown in (Table 6). There was no major change in the drug content, disintegration time, and in vitro dissolution profile. It was also observed that the formulation was compatible. Also, there was no phase separation, and drug precipitation was found at the end of two -month stability studies indicating that QT remained chemically stable in SEDDS.

## 5.0 Summary & Conclusion

Bioavailability is major concern of the most therapy involving with hydrophobic drugs. The current study demonstrated a successful and simple method to prepare self-emulsifying delivery system produced emulsion with uniform droplet size to enhance its aqueous solubility and dissolution rate. Zeta potential of the optimal system was neutral so we can conclude that system is stable. SEDDS appeared to be an interesting approach to improve problems associated with oral delivery of Quercetin. Quercetin SEDDS formulation was superior to marketed formulation in respect to in vitro dissolution profile. It also shows better in vivo antioxidant activity than pure quercetin. Thus, there is improvement of oral bioavailability of quercetin was successfully achieved in SEDDS formulation as delivery system. Thus, SEDDS can be regarded as a novel and commercially feasible alternative to current quercetin formulations.

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