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Design and evaluation of self-nanoemulsifying drug delivery systems (SNEDDS) for cefpodoxime proxetil☆

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Abstract

Self-nanoemulsifying drug delivery systems (SNEDDS) were developed with the objective to overcome problems associated with the delivery of cefpodoxime proxetil (CFP), a poorly bioavailable high dose antibiotic having pH dependant solubility. Solubility of CFP in oily phases and surfactants was determined to identify components of SNEDDS. Various surfactants and co-surfactants were screened for their ability to emulsify selected oily phases. Ternary phase diagrams were constructed to identify area of nanoemulsification for the selected systems. The influence of CFP and the pH of dilution medium on the phase behavior of selected system were assessed. The globule size of optimized CFP SNEDDS in various dissolution media was determined to check the effect of pH on its behavior. The optimized CFP SNEDDS needed surfactant content less than 40% and yielded nanoemulsion of mean globule size 170 nm, which was not affected by the pH of dilution medium. The optimized SNEDDS released CFP completely within 20 min irrespective of the pH of dissolution medium.

Keywords: Cefpodoxime proxetil; SNEDDS; pH dependant solubility

1. Introduction

Cefpodoxime proxetil (CFP) is an orally absorbed, broad spectrum, third generation cephalosporin ester implicated in treatment of upper respiratory tract and urinary tract infections. The prodrug ester is hydrolyzed *in vivo* to its active metabolite, cefpodoxime. Absolute bioavailability of cefpodoxime proxetil administered as a 130 mg tablet (equivalent to 100 mg of cefpodoxime) in humans is only about 50% (Borin, 1991). The low bioavailability of CFP is mainly attributed to the degradation of its ester side chain by cholinesterases present in the intestinal lumen. In addition, poor water solubility (400 μg/ml), which may also be responsible for its poor bioavailability, as dissolution is a rate-limiting factor in intestinal absorption of poorly water-soluble drugs (Finsher, 1968). An approach, which will increase drug solubility and protect from degradation by cholinesterase in intestinal washings is highly desirable for optimizing the therapeutic performance of CFP.

Lipid based systems are anticipated to improve the bioavailability of CFP by protecting it from cholinesterase attack, as Cholinesterases which are reported to cause degradation of CFP are unable to hydrolyze triglycerides (Crauste-Manciet et al., 1998). Nicolaos et al. (2003) have evaluated potential of submicronic emulsions of medium chain mono-, di- and triglycerides in improving the oral bioavailability of CFP. Interestingly, submicronic emulsions were found to increase the bioavailability of CFP from 50 to 98%, after oral administration. Submicronic emulsion is an attractive approach if the quantity of submicronic emulsions for administration of single dose of CFP and palatability related issues associated with CFP and lipid excipients could be overcome for improving patient compliance. Development of lipid-based drug delivery strategy that will retain all the bioavailability related advantages associated with the submicronic emulsion and improve patient compliance by overcoming limitations associated with submicronic emulsion will be advantageous for optimizing CFP delivery. Self-nanoemulsifying systems would be one such approach to achieve optimum CFP delivery.

Self-nanoemulsifying drug delivery systems (SNEDDS) are isotropic mixtures of oil, surfactant, co-surfactant and drug that form fine oil-in-water nanoemulsion when introduced into aqueous phases under gentle agitation (Nazzal et al., 2002).

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Self-nanoemulsifying system of CFP would be an efficient, convenient and more patient compliant approach in comparison to submicronic emulsions as SNEDDS can be filled in hard gelatin capsules due to their anhydrous nature enabling its administration as unit dosage form.

To design a self-nanoemulsifying formulation containing substantial quantity of active like CFP is a challenging task as self-nanoemulsifying systems have been investigated or recommended for delivering potent lipophilic drugs like Ubiquinone and Retinol acetate (Nazzal et al., 2002; Taha et al., 2004). These investigations present successful design of SNEDDS that can deliver relatively high dose drug CFP in unit dosage form and would release CFP rapidly independent of pH. The investigation also reports the influence of drug (CFP) and pH on the phase behavior of SNEDDS.

2. Materials and methods

2.1. Materials

Cefpodoxime proxetil (CFP) was a generous gift from Glenmark Pharmaceuticals Ltd. (Nashik, India). Solutol HS-15 (SHS-15), Cremophore-EL (Cr-EL), Poloxamer 188, Poloxamer 407 (BASF, Mumbai, India), Transcutol, Plurol Oleique, Capryol 90 (CAE), Lauroglycol 90, Labrafac CC, Labrasol, Labrafac lipophile WL1349 (Colorcon Asia Pvt. Ltd., Mumbai, Inida) Akoline-MCM (Ak-MCM), Akomed E (Karlshamns AB, Sweden), Imwitor-742 (S. Zaveri & Co., Mumbai, India), and Hard gelatin capsules (Associated Capsules, Mumbai, India) were obtained as gift samples. PEG 400, propylene glycol, Tween 80 and Tween 20 were purchased from s.d. fine chemicals (Mumbai, India). All the excipients and reagents were used as received. Double distilled water was prepared freshly whenever required.

2.2. Solubility studies

The solubility of CFP in various modified oils, buffers and 10% (w/w) surfactant solutions was determined by using shake flask method. Briefly, an excess amount of CFP was added to each vial containing 1 g of the selected vehicle, i.e., either oil, surfactant solution or buffer. After sealing, the mixture was vortexed using a cyclomixer for 10 min in order to facilitate proper mixing of CFP with the vehicles. Mixtures were then shaken for 48 h in a water bath shaker (Remi, Mumbai, India) maintained at room temperature. Mixtures were centrifuged at 5000 rpm for 5 min, followed by filtration through membrane filter (0.45 μ, 13 mm, Pall Life sciences, Mumbai, India). Filtrate was suitably diluted with methanol and CFP dissolved in various vehicles was quantified by a validated HPTLC method developed in house (Date, 2006).

2.3. Screening of surfactants for emulsifying ability

Emulsification ability of various surfactants was screened (Date, 2006). Briefly, 300 mg of surfactant was added to 300 mg of the selected oily phase. The mixture was gently heated at 45–60 °C for homogenizing the components. The isotropic mixture, 50 mg, was accurately weighed and diluted with double distilled water to 50 ml to yield fine emulsion. The ease of formation of emulsions was monitored by noting the number of volumetric flask inversions required to give uniform emulsion. The resulting emulsions were observed visually for the relative turbidity. The emulsions were allowed to stand for 2 h and their transmittance was assessed at 638.2 nm by UV-160A double beam spectrophotometer (Shimadzu, Japan) using double distilled water as blank.

2.4. Screening of co-surfactants

The turbidimetric method was used to assess relative efficacy of the co-surfactant to improve the nanoemulsification ability of the surfactants and also to select best co-surfactant from the large pool of co-surfactants available for peroral delivery (Date, 2006). Surfactant, 0.2 gm was mixed with 0.1 gm of co-surfactant. Capryol 90 (CAE), 0.3 gm, was added to this mixture and the mixture was homogenized with the aid of the gentle heat (45–60 °C). The isotropic mixture, 50 mg, was accurately weighed and diluted to 50 ml with double distilled water to yield fine emulsion. The ease of formation of emulsions was noted by noting the number of flask inversions required to give uniform emulsion. The resulting emulsions were observed visually for the relative turbidity. The emulsions were allowed to stand for 2 h and their transmittance was measured at 638.2 nm by UV-160A double beam spectrophotometer (Shimadzu, Japan) using double distilled water as blank. As the ratio of co-surfactants to surfactant/s is the same, the turbidity of resulting nanoemulsions will help in assessing the relative efficacy of the co-surfactants to improve the nanoemulsification ability of surfactant/s.

2.5. Construction of ternary phase diagrams

Ternary diagrams of surfactant, co-surfactant and oil were plotted; each of them, representing an apex of the triangle (Kommuru et al., 2001). Ternary mixtures with varying compositions of surfactant, co-surfactant and oil were prepared. The surfactant concentration was varied from 30 to 75% (w/w), oil concentration was varied from 25 to 75% and co-surfactant concentration was varied from 0 to 30% (w/w). For any mixture, the total of surfactant, co-surfactant and oil concentrations always added to 100%. For example, in the experiment, first mixture consisted of 75% of surfactant (either Cr-EL or SHS 15), 25% of the oily phase (CAE) and 0% of co-surfactant (Ak-MCM). In the further experiments, the co-surfactant was increased by 5% for each composition, oily phase concentration was kept constant and the surfactant concentration was adjusted to make a total of 100%. Forty-two such mixtures with varying surfactant, co-surfactant and oil concentrations were prepared in this investigation. The percentage of surfactant, co-surfactant and oil used herein was decided on the basis of the requirements stated by Pouton (2000) for the spontaneously emulsifying systems. Compositions were evaluated for nanoemulsion formation by diluting 50 mg of each of the 42 mixtures to 50 ml with double distilled water. Globule size of the resulting dipersions was deter-

mined by photon correlation spectroscopy (Beckman Coulter N-5, Wipro, Mumbai). Dispersions, having globule size 200 nm or below were considered desirable. The area of nanoemulsion formation (NE) was identified for the respective system in which nanoemulsions with desired globule size were obtained.

2.6. Effect of CFP and pH of the aqueous phase on ternary phase diagrams of the selected system

The drugs as well as pH of the vehicle have considerable influence on the phase behavior of the spontaneously emulsifying systems (Pouton, 1985; Kim et al., 2000; Kawakami et al., 2002). In view of this, the effect of CFP and pH of the aqueous phase on the phase behavior and area of nanoemulsion formation was studied.

In these investigations, CFP was dissolved in the CAE at ratio is 2:1 was treated as an oily phase and various compositions, 42 in number, were prepared in the similar fashion as described in Section 2.5. The influence of the pH of aqueous phase on the phase behavior and area of nanoemulsion formation was investigated by diluting 50 mg of oily mix to 50 ml with various vehicles viz. water, buffer pH 1.2, buffer pH 3.0 and buffer pH 6.8. The mean globule size of the resulting dispersions was measured by using photon correlation spectroscopy (PCS) and the data obtained was used to identify the area of nanoemulsion formation.

2.7. Optimization of formulae

SNEDDS were optimized for following parameters:

- Drug loading.
- Amount of oily phase.
- Effect of pH on globule size.

2.8. Evaluation of CFP loaded SNEDDS

Optimized SNEDDS were evaluated for robustness to dilution, globule size, effect of CFP loading and *in vitro* dissolution profile.

2.8.1. Robustness to dilution

Robustness of CFP SNEDDS to dilution was studied by diluting it 50, 100 and 1000 times with various dissolution media viz. water, buffer pH 1.2, buffer pH 3.0 and buffer pH 6.8. The diluted nanoemulsions were stored for 12 h and observed for any signs of phase separation or drug precipitation.

2.8.2. Globule size analysis

The formulation, 50 mg, was diluted to 50 ml with media like double distilled water, buffer pH 1.2, buffer pH 3.0 and pH 6.8 buffer. Visual observations were made immediately after dilution for assessment for self-nanoemulsification efficiency, appearance (transparency), phase separation, and precipitation of drug. The mean globule size and polydispersity index (P.I.) of the resulting nanoemulsions were determined by PCS. Measurements were obtained at an angle of 90°. Nanoemulsions were diluted respective vehicles to ensure that the light scattering intensity (between 6E+004 to 1E+006), was within the instrument's sensitivity range. The resultant nanoemulsions were also allowed to stand for 6 h at room temperature to assess dilution stability.

2.8.3. Effect of CFP loading

The increase or decrease in the amount of CFP would influence the globule size of the resultant nanoemulsions if CFP were participating at interface of nanoemulsion. In order to investigate role of CFP, various formulations were prepared containing varying amount of CFP from 20 to 5% (w/w). SNEDDS, 50 mg, was diluted to 50 ml with different media viz. double distilled water, buffer pH 1.2, buffer pH 3.0 and pH 6.8 buffer and the mean globule size of resulting nanoemulsions was determined by PCS.

2.8.4. In vitro dissolution profile

SNEDDS of CFP was filled in size '0' hard gelatin capsules. *In vitro* release profile of SNEDDS was studied using USP XXIII apparatus I at 37 ± 0.50 °C with a rotating speed of 100 rpm in dissolution media namely, pH 1.2, 3.0 and 6.8 buffer so as to evaluate the effect of pH on *in vitro* dissolution. During the study, 1 ml of aliquots were removed at predetermined time intervals (10, 20, 30 and 45 min) from the dissolution medium and replaced with fresh buffer. The amount of CFP released in the dissolution medium (Table 5) was determined by UV spectrophotometer at λ_{max} = 263 nm.

3. Results and discussion

3.1. Solubility studies

Solubility studies were aimed at identifying suitable oily phase and surfactant/s for the development of CFP SNEDDS. Identifying the suitable oil, surfactant/co-surfactant having maximal solubilizing potential for drug under investigation is very important to achieve optimum drug loading (Pouton, 1997, 2000). It is even more important for CFP, as the target dose is substantially high.

Solubility of CFP in various buffers, oily phases and 10% (w/w) surfactant solutions is presented in Figs. 1–3, respectively. Solubility studies (Fig. 1) clearly indicated that CFP has pH dependant solubility. Amongst the various oily phases that were screened, Capryol 90 (CAE) (Fig. 2) could solubilize target amount of CFP (130 mg) at relatively small concentration of 300 mg. The selection of surfactant or co-surfactant in the further study was governed by their emulsification efficiency rather than their ability to solubilize CFP.

3.2. Screening of surfactants for emulsifying ability

The % transmittance values of various dispersions are given in Table 1. Emulsification studies clearly distinguished the ability of various surfactants to emulsify CAE. These studies indicated that Cr-EL and SHS-15 had very good ability to emulsify CAE followed by Tween 20 and Tween 80, whereas, Labrasol

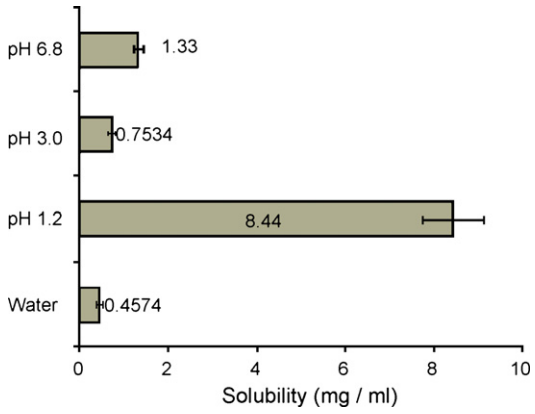

Fig. 1. Solubility of CFP in various buffers. Data are expressed as mean ± S.D. ($n = 3$).

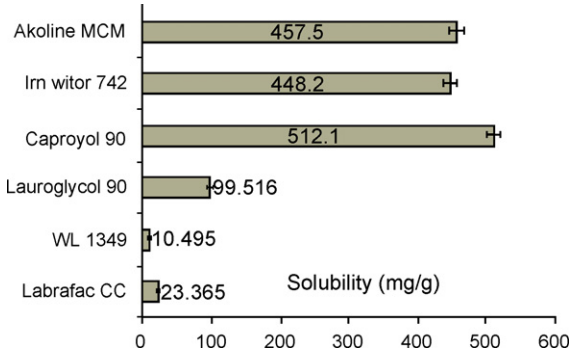

Fig. 2. Solubility of CFP in various oily phases. Data are expressed as mean ± S.D. ($n = 3$).

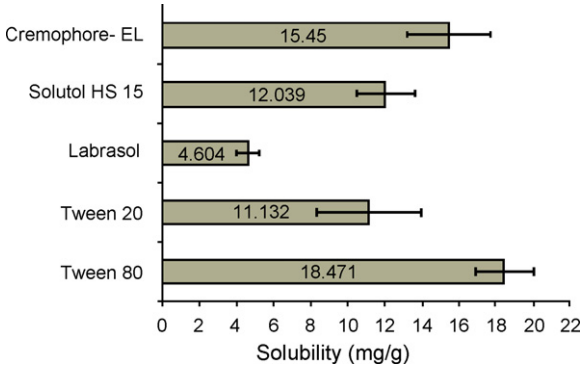

Fig. 3. Solubility of CFP in various 10% (w/w) surfactant solutions. Data are expressed as mean ± S.D. ($n = 3$).

Table 1
Emulsification efficiency of various non-ionic surfactants

Surfactant	% Transmittance[a]
Tween 20	94.6
Tween 80	93.3
Cremphore EL	99.4
Solutol HS 15	97.9
Labrasol	59.9
Poloxamer 407	97
Poloxamer 188	65.1

[a] Data expressed as mean ($n = 2$).

Table 2
Emulsification studies on surfactant/co-surfactant combinations

Co-surfactant	% Transmittance[a]	
	Cremophore EL	Solutol HS 15
Transcutol	99.7	98.7
Propylene glycol	99.6	98.6
Polyethylene glycol	99.5	98.3
Labrafil 1944 CS	99.2	97.9
Plurol Dioleique CC 497	91.2	73.7
Lauroglycol FCC	98.6	85.5
Lauroglycol 90	98	63.3
Imwitor 742	99	95.5
Akoline MCM	99.2	95.1
Akomed E	99.7	99.1

[a] Data expressed as mean ($n = 2$).

appeared to be poor emulsifier for CAE. Although, the HLB values of the surfactants used in the investigation were in the range of 13 to 16 except for Poloxamers and Tween 20, there was a great difference in their emulsification ability. This observation is in line with the investigations reported by Malcolmson et al. (1998) and Warisnoicharoen et al. (2000) who concluded that microemulsification is also influenced by the structure and chain length of the surfactant. Cr-EL and SHS-15 rendered very good nanoemulsions requiring short time for nanoemulsification and were selected for further investigation.

3.3. Screening of co-surfactants

The investigations clearly distinguished the ability of various co-surfactants, both hydrophilic and lipophilic, to improve the nanoemulsification of selected surfactant/s. All the co-surfactants increased the spontaneity of the nanoemulsion formation. Interestingly, all the hydrophilic co-surfactants appeared to be equivalent in improving nanoemulsification ability of Cr-EL and SHS 15. In case of lipophilic co-surfactants, good correlation was observed between the structure and chain length of co-surfactant (or molecular volume) of co-surfactant and the transmittance values of resulting dispersions. Larger the chain length or structure (or molecular volume) of the co-surfactant lesser was the transmittance value. This correlation was applicable to Ak-MCM, Imwitor 742, Lauroglycol 90, Lauroglycol FCC and Plurol oleique CC 497 (Table 2).

However, Akomed E and Labrafil 1944 CS did not follow this behavior. Among Akoline MCM, Imwitor 742, Lauroglycol 90, Lauroglycol FCC and Plurol oleique CC 497, Ak-MCM, a mixture of capric/caprylic acid mono-, di- and triglycerides, due to its smallest molecular volume appeared to be the best co-surfactant. Imwitor 742 and Ak-MCM were almost equivalent which is attributed to similarity in their mono-, di-, and tri-glyceride proportions of capric/caprylic acids. However, Lauroglycol 90, Lauroglycol FCC were less effective as co-surfactants. This was attributed to the presence of lauric acid backbone, which is longer in chain length than capric/caprylic acid. But they were more efficient than Plurol oleique, which has oleic acid backbone, which is longer in chain length than lauric acid. These observations are in line with the investigations

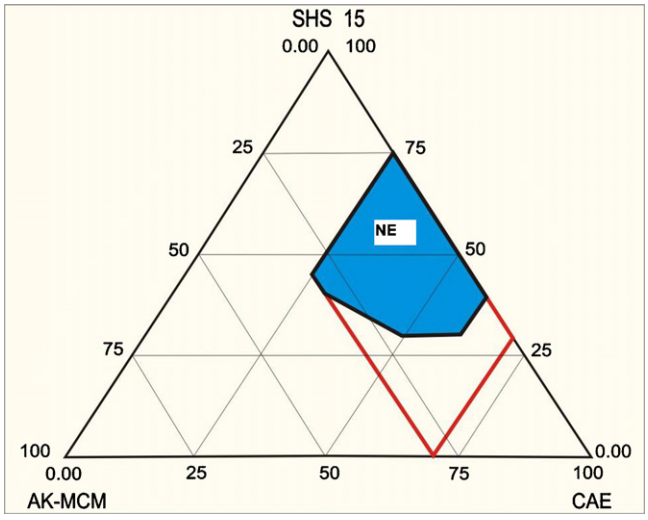

Fig. 4. Ternary diagram of SHS-15, AK-MCM and Capryol 90 (CAE).

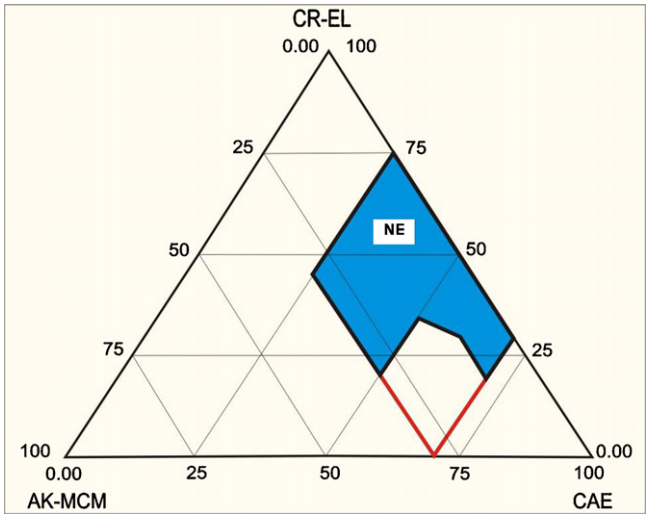

Fig. 5. Ternary diagram of CR-EL, AK-MCM and Capryol 90 (CAE).

reported by Malcolmson et al. (1998) and Warisnoicharoen et al. (2000).

Surprisingly, Akomed E, despite of its larger content of diglycerides and triglycerides of capric/caprylic acid as compared to Ak-MCM and Imwitor 742, appeared to be best among all lipophilic co-surfactants which can further be validated with the help of globule size analysis. Labrafil 1944 CS (PEG-8-oleate/linoleate), which has oleic and linoleic acid backbone showed superior performance over Plurol oleique, Lauroglycol FCC and Lauroglycol 90 probably due to more hydrophilicity and surfactant like properties. In conclusion, emulsification studies gave good insight into the efficiency of various co-surfactants.

Hydrophilic co-surfactants despite of their good potential were not investigated further as systems with higher lipid content will protect CFP from degradation by cholinesterases. Among lipophilic co-surfactants, Akomed E, Ak-MCM and Imwitor 742 exhibited superior profile with Akomed E showing the best performance. However due to its less solubilizing potential for CFP (data not shown), it was not used for further studies. Ak-MCM, a lipophilic co-surfactants with good solubilizing potential for CFP was selected and Cremophore EL-Akoline MCM-CAE and Solutol HS 15-Akoline MCM-CAE systems were developed for further studies.

3.4. Construction of phase diagrams

The phase diagrams of Cremophore EL-Akoline MCM-CAE and Solutol HS 15-Akoline MCM-CAE systems are shown in Figs. 4 and 5. The outer parallelogram indicates the area, which was explored for locating nanoemulsification region. The filled region indicated with NE indicates the region in which nanoemulsions of desired size were obtained. From Figs. 4 and 5, it is evident that Cr-EL-Akoline MCM-CAE system has larger nanoemulsification region as compared to Solutol HS 15-Akoline MCM-CAE system. Cremophore EL-Akoline MCM-CAE system yielded nanoemulsions for the compositions that had as high as 70% (w/w) of oily phase comprising of oil + lipophilic co-surfactant concentration, whereas, Solutol HS 15-Akoline MCM-CAE system yielded nanoemulsions for compositions having about 60% (w/w) of oily phase. These compositions had ability to solubilize various hydrophobic drugs like Cefuroxime axetil, Artemether, Simvastatin and Tacrolimus (data not shown) and have potential to become platform systems. In view of current investigation, due to larger nanoemulsion region and greater capacity for incorporation of oily phase, which is most desirable for CFP, Cremophore EL-Akoline MCM-CAE system was selected for further studies.

3.5. Effect of CFP and pH of the aqueous phase on ternary phase diagrams of the selected system

The phase diagrams indicating effect of CFP and pH of the aqueous phase on phase behavior and area of nanoemulsion existence are shown in Figs. 6–9. It was expected that CFP would influence the phase behavior and the area of nanoemulsion for-

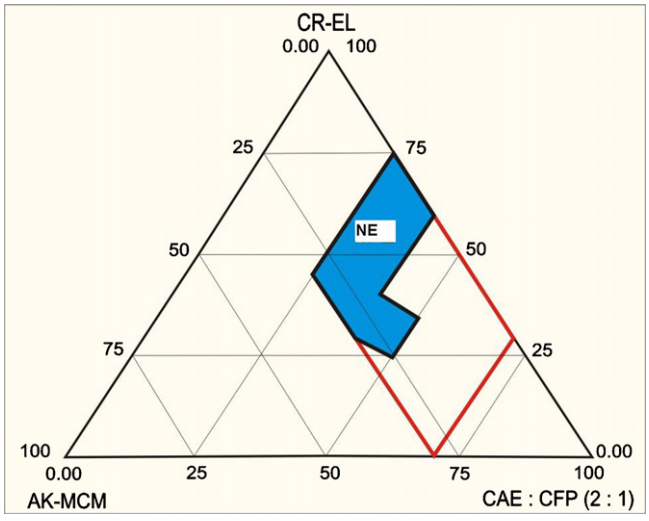

Fig. 6. Pseudo-ternary diagram of CR-EL, AK-MCM and CAE + CFP using water as dilution medium.

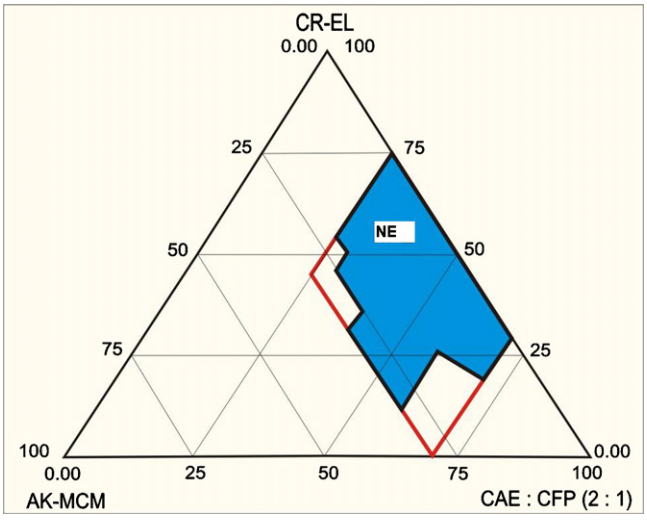

Fig. 7. Pseudo-ternary diagram of CR-EL, AK-MCM and CAE + CFP using pH 1.2 buffer as dilution medium.

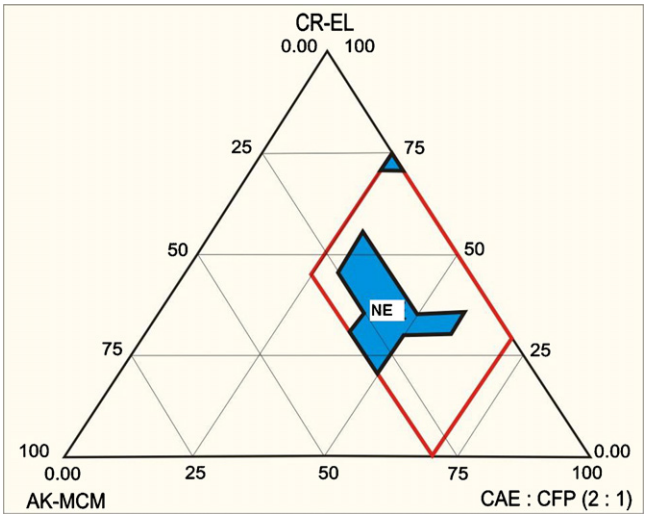

Fig. 8. Pseudo-ternary diagram of CR-EL, AK-MCM and CAE + CFP using pH 3.0 buffer as dilution medium.

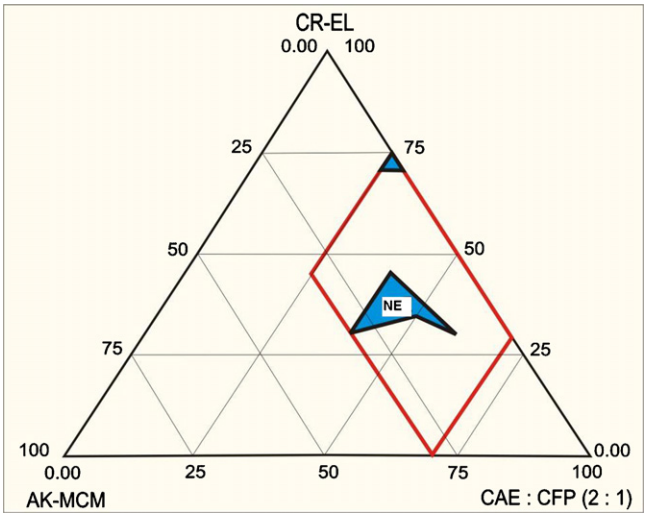

Fig. 9. Pseudo-ternary diagram of CR-EL, AK-MCM and CAE + CFP using pH 6.8 buffer as dilution medium.

Table 3
Composition of optimized CFP SNEDDS

Ingredient	Quantity (mg/capsule)
Cremophore EL	195
Akoline MCM	65
Capryol 90	260
CFP	130
Total	650

mation as in these formulae, CFP substituted one-third amount of CAE as compared to the systems without CFP. Phase diagrams studies indicated that there was remarkable influence of CFP and also the pH of dilution medium on the area of nanoemulsion formation of the Cremophore based system. Incorporation of CFP in CAE led to a considerable reduction in the area of nanoemulsion formation of Cremophore based SNEDDS when compared to the area in Fig. 4. CFP, due to its low aqueous solubility, is likely to participate in the nanoemulsion by orienting at the interface. The reduction in the area of nanoemulsion formation could be due to CFP influenced interaction of surfactant and co-surfactant with oil. Interestingly, area of nanoemulsion formation was largest at pH 1.2. This behavior supports the aforementioned hypothesis about the orientation of CFP. As CFP is having much more solubility in pH 1.2 than water, it likely to migrate more in the external phase leading to reduction in the amount present at interface. This may lead to increase in the effective concentrations of surfactant and co-surfactant available for nanoemulsion formation, which may be responsible for highest area of nanoemulsion formation at pH 1.2. The area of nanoemulsion formation reduced for buffer pH 3.0 and was least for buffer pH 6.8.

3.6. Selection of optimized formulation

The optimized formulation was selected based on the drug loading efficiency and consistency in mean globule size at varying pH. The composition is given in Table 3.

3.7. Evaluation of CFP loaded SNEDDS

3.7.1. Robustness to dilution

Nanoemulsions resulting from dilution of CFP SNEDDS with various dissolution media were robust to all dilutions and did not show any separation even after 24 h of storage.

3.7.2. Globule size analysis

The mean globule size of CFP SNEDDS after dilution with various dissolution media is given in Table 4. The CFP SNEDDS showed fairly similar mean globule size within range of 150–170 nm when diluted with various dissolution media differing in pH. The time required for formation of nanoemulsions after dilution with various dissolution media was just 3 min. The resulting nanoemulsions were translucent in appearance and they did not show any signs of phase separation and drug precipitation even after 6 h.

Table 4
Globule size and polydispersity index of CFP SNEDDS at different pH conditions

Dissolution medium	Water	Buffer pH 1.2	Buffer pH 3.0	Buffer pH 6.8
Globule size (nm)[a]	165.2	154.8	156.8	162.2
Polydispersity index[b]	0.746	0.914	0.736	0.71

[a] Globule size expressed as mean ($n = 2$) where relative standard deviation was <10%.
[b] Data expressed as mean ($n = 2$).

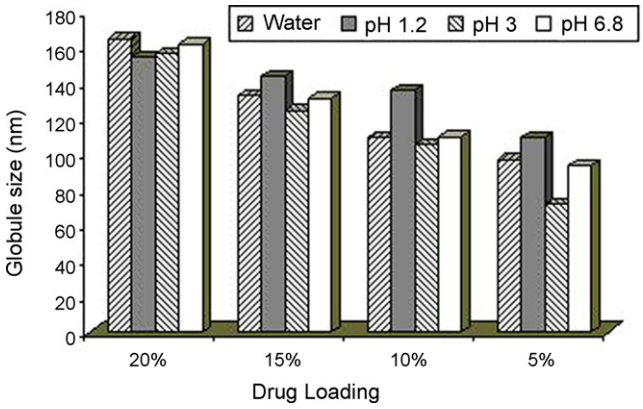

Fig. 10. Effect of CFP loading on mean globule size of SNEDDS. Data are expressed as mean ($n = 2$).

Table 5
In vitro dissolution profile of CFP SNEDDS

Time (min)	% Cumulative release[a]		
	Buffer pH 1.2	Buffer pH 3.0	Buffer pH 6.8
10	100.11 ± 2.0	101.49 ± 2.48	99.25 ± 3.48
20	101.81 ± 2.7	102.31 ± 1.11	101.23 ± 0.42
30	100.32 ± 1.18	102.1 ± 1.14	101.31 ± 0.84
45	101.21 ± 1.6	101.21 ± 0.49	101.1 ± 1.9

[a] Data expressed as mean ± S.D. ($n = 3$).

3.7.3. Effect of CFP loading

The amount of CFP influenced the globule size of nanoemulsions obtained after diluting CFP SNEDDS with various dissolution media. The globule size decreased with the decrease in the %CFP loading (Fig. 10).

3.7.4. In vitro dissolution profile

In vitro dissolution profile of optimized CFP SNEDDS in various dissolution media is given in Table 5. The dissolution profile of CFP SNEDDS in various dissolution mediums showed that 100% of CFP was released within 20 min irrespective of the pH of dissolution medium.

4. Conclusion

The method employed in the investigation for screening of SNEDDS excipients helped in understanding the emulsification efficiency of various surfactants for selected oily phase. It also helped in rapid screening of large pool of co-surfactants available for the peroral delivery. The potential of Ak-MCM, to act as a co-surfactant was established in the present investigation. Studies on ternary phase diagrams indicated that CFP and the pH of dilution medium significantly affects the area of the nanoemulsion formation for the selected system. SNEDDS of CFP could accommodate high dose of CFP (130 mg) and exhibited rapid release independent of pH of dissolution media.

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