

## Development of solid SEDDS, III: application of Acconon<sup>®</sup> C-50 and Gelucire<sup>®</sup> 50/13 as both solidifying and emulsifying agents for medium chain triglycerides.

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### ABSTRACT

Solid self-emulsifying drug delivery systems (SEDDS) for medium chain triglycerides (Captex<sup>®</sup> 355, ABITEC) were developed using stearyl polyoxyl glycerides (Acconon<sup>®</sup> C-50, ABITEC and Gelucire<sup>®</sup> 50/13, Gattefosse) as both solidifying and emulsifying agents. Different mixtures of the lipid and each solidifying agent were heated to 65°C until homogeneously mixed clear liquids were formed. Probuco<sup>l</sup> was dissolved as the model drug. The molten mass was then filled into hard gelatin capsules, which upon cooling to room temperature converted to a solid mass inside capsules. The triglyceride could be incorporated into the system to a concentration as high as 80% w/w, still maintaining the solid or semisolid consistency of the system. Powder XRD, DSC, microscopy (cross-polarization and confocal fluorescence techniques), dispersion test and particle size analysis of the solid systems with, and without, drug were conducted to characterize different formulations. The solidifying agents maintained their crystallinity in solid systems, while the lipids were interspersed in between crystalline regions. The drug remained solubilized in the lipid phase. The formulations dispersed almost completely in 2 hours with particle size of the dispersed lipid in the range of 250 to 500 nm when the lipid content in the formulation was up to 50% w/w. Thus, a novel method of developing solid formulations of liquid triglycerides by incorporating lipids in stearyl polyoxyl glycerides has been developed.

**KEY WORDS:** Solid SEDDS, stearyl polyoxyl glycerides, Acconon<sup>®</sup> C-50, Gelucire<sup>®</sup> 50/13, probu<sup>l</sup>, dispersion testing

### INTRODUCTION

In recent years, there has been a great interest in the development of lipid-based drug delivery systems by solubilizing poorly water-soluble and lipophilic drugs in lipids or in mixtures of lipids and surfactants (1-5). For the release of drugs from lipids into the gastrointestinal fluids

after oral intake of such formulations, it is essential that the lipids emulsify in aqueous media to increase the surface area for the partitioning of drugs into aqueous media or for the enzymatic digestion of lipids to enable drug release. Depending on whether they spontaneously form an emulsion or microemulsion in presence of water, they are called self-emulsifying or self-micro emulsifying drug delivery systems (SEDDS or SMEDDS, respectively) (6, 7). They are also referred to as emulsion or microemulsion pre-concentrates since they form an emulsion or microemulsion

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in contact with aqueous media. Since the commonly used lipids and surfactants are liquid at room temperature, they usually result in liquid products.

In recent years, there has also been much interest in the development of lipid-based drug delivery systems that are solid at room temperature (8, 9). There are, however, potential stability issues with such dosage forms as the drugs may crystallize out from solid matrices. Li *et al.* (10) reported a novel method of developing solid lipid-based formulations where the mixture of lipid and surfactant exists as a separate phase interspersed in the solid matrix of polyethylene glycol (PEG) 3350. Later, Shah and Serajuddin (11) reported that lipids alone may be incorporated into the solid matrix of poloxamer 188, where the matrix serves as both solidifying and emulsifying agents. However, in both of these studies only the monoesters of fatty acids (monoglycerides or propylene glycol monoesters) could be solidified using PEG 3350 or poloxamer 188. More recently, it has been reported that a triglyceride may also be solidified by using lauroyl polyoxyl glycerides (Acconon<sup>®</sup> C-44, ABITEC, Gelucire<sup>®</sup> 44/14, Gattefosse) as the solidifying agent (12). As much as 70% w/w of a medium chain triglyceride, Captex<sup>®</sup> 355, could be incorporated into the formulation and still maintain its solid or semisolid consistency such that the formulation could be developed as hard gelatin capsules. It was, however, noted in this study that, despite being amphiphilic in nature, lauroyl polyoxyl glycerides were unable to disperse or emulsify the triglyceride present when the solid formulation was brought in contact with aqueous media. A second surfactant, Cremophor<sup>®</sup> EL, was necessary to develop a solid formulation that was self-emulsifying. However, there was a maximum amount of liquid component that could be present in the solid system, and therefore, the addition of Cremophor<sup>®</sup> EL reduced the amount of Captex<sup>®</sup> 355 present. For example, the maximum amount of the triglyceride present in the formulation was only 35% w/w if Acconon<sup>®</sup> C-44 or Gelucire<sup>®</sup> 44/14 could accommodate 70% w/w liquid in the solid

system and the liquid was a 1:1-mixture of Captex<sup>®</sup> 355 and Cremophor<sup>®</sup> EL.

One of the limiting factors in the development of lipid-based drug delivery systems is the limited solubility of drugs in lipids used. Most of the NCEs have relatively low lipid solubility. To maximize the drug load of a formulation, it is essential that the lipid content of the formulation should be as high as possible. In our continued efforts to develop solid SEDDS, we observed that stearyl polyoxyl-32 glycerides (Acconon<sup>®</sup> C-50, ABITEC or Gelucire<sup>®</sup> 50/13, Gattefosse) may serve as both solidifying and emulsifying agents for triglycerides. The excipient is primarily a mixture of PEG 1500 mono- and diesters with palmitic (C<sub>16</sub>) and stearic (C<sub>18</sub>) acid with an HLB value of ~13 (13). It was used for the development of solid dispersion hydrophobic drugs (14-18) with the potential of improving oral bioavailability (19, 20). However, it is possible that the drug crystallizes out from solid dispersion since both the drug and the carrier are solid at room temperature (8, 21). The present report describes a novel application of Acconon<sup>®</sup> C-50 and Gelucire<sup>®</sup> 50/13, where the drug remains in solution in the liquid triglyceride and the solution can be incorporated in the solid matrix as a dispersed but separate phase. After oral administration, the solid formulation would self-emulsify without the need for any additional surfactant. Stearyl polyoxyl-32 glycerides from two different manufacturers were used in the present study to determine whether materials from different sources behave similarly. Probutol, a practically water-insoluble compound (0.002-0.005 µg/ml at 25 °C) with high partition coefficient (LogP = 11), was used as the model drug (22, 23).

## MATERIALS AND METHODS

### Materials

Acconon<sup>®</sup> C-50 EP/NF and Gelucire<sup>®</sup> 50/13 EP/NF (stearyl polyoxyl-32 glycerides) were, obtained, respectively, from ABITEC Corp., Columbus, OH, USA and Gattefosse Corp., Paramus, NJ, USA. Captex<sup>®</sup> 355 EP/NF

(caprylic/capric triglyceride) was supplied by ABITEC Corp. ProbucoI was purchased from Sigma Aldrich, St. Louis, MO, USA. Nile red, a fluorescence probe for lipids, was purchased from MP Biomedicals, Solon, OH, USA. All other chemicals and reagents used were of analytical grade or better.

## Methods

### *Preparation of the Formulation*

The samples were prepared using Captex<sup>®</sup> 355 and Acconon<sup>®</sup> C-50 or Gelucire<sup>®</sup> 50/13 at ratios 8:2, 7:3, 6:4, 1:1, 4:6 and 3:7. A batch size of 4 grams was prepared in which each solidifying agent was weighed according to its ratios in the mixtures and then melted in glass scintillation vials on a hot plate until a clear solution (~65°C) was formed. The weighed amounts of lipids were equilibrated at the corresponding temperature and added to the melt. All samples were vortex mixed (2-3 minutes) in the molten state to ensure homogeneity. The molten mixtures were then manually filled into #00 hard gelatin capsules (~1g). Fill materials of capsules were allowed to solidify at room temperature and stored for at least 48 hours prior to analysis. The solubility of probucoI in Captex<sup>®</sup> 355 was determined to be 133 mg/g, and the drug concentration at only 80% of the saturation solubility in the lipid (106 mg/g) was incorporated in the formulation. Thus, when the lipid/solidifying agent ratio was 7:3 w/w, there was ~74 mg of drug per gram of the solid formulation, and it was ~53 mg/g of formulation at the lipid/solidifying agent ratio of 1:1 w/w.

### *Characterization of the formulation*

All of the solid systems, with and without drug, were characterized by powder-X-ray diffractometry and differential scanning calorimetry (DSC). Selected solid systems were also examined microscopically to ascertain the microstructure of the lipid within the solid emulsifier.

### *Powder X-ray diffractometry (P-XRD)*

The P-XRD patterns were measured using Shimadzu XRD-6000 (Shimadzu, Kyoto, Japan) using a voltage of 40kV and a current of 30mA over a 2 $\theta$  range of 10-80° using a step size of 0.02° at a scan speed of 4°/minute. The results were compared by measuring the approximate peak intensity at 2 $\theta$  = 23.3°.

### *Differential scanning calorimetry (DSC)*

The thermal characteristics of solidifying agents (neat Acconon<sup>®</sup> C-50 and Gelucire<sup>®</sup> 50/13) and formulations were determined using a differential scanning calorimeter (Pyris Diamond, Perkin-Elmer DSC-7, CA, USA). Samples were weighed accurately (2-5 mg) and sealed into aluminum pans by crimping. The scans for all samples were recorded by holding for 5 minutes at initial temperature (20°C) and then heating from 20-60°C (5°C/min) under an extra dry nitrogen gas purge (20 ml/min).

### *Microscopic Examination*

Solid pre-concentrates were analyzed using an optical microscope fitted with cross-polarizing lenses (Nikon Microscope Eclipse 50i, Morrell Instrument Co., Melville, NY, USA) and a confocal fluorescence microscope (Leica Microsystems Inc., Exton, PA, USA) with 514 nm excitation, 550-605 nm emission wavelength, and the bandpass filter of DD458-514 nm. For fluorescence microscopy, Nile red, a fluorescent probe for lipids (24), was dissolved in Captex<sup>®</sup> 355 and the colored lipid was then mixed with molten Acconon<sup>®</sup> C-50 or Gelucire<sup>®</sup> 50/13 at the 1:1 ratio. Two drops of the melt were placed on a glass slide and covered with glass cover slip, and edges of the cover slip were sealed with a nail polish. The slides were then allowed to cool in two different ways (a) under ambient condition (shock cooling) and (b) in an oven (GCA/Precision Scientific, Chicago, IL, USA) from 60 to 25°C at the rate of 0.1°C/min. Pictures from optical microscopy were captured using a

Nikon Digital Camera (100x, DS 5000, Nikon Inc., Melville, NY, USA).

### **Dispersion test**

The efficiency of the self-emulsification and the dispersion of the formulations were assessed using a USP apparatus II (50 rpm, 37°C, Paddle method; Distek Inc., NJ, USA) and 250 ml of 0.01N HCl (pH~2) per dispersion vessel. Glass pipettes with siliconized tips were used to withdraw aliquots from the dispersion vessels such that there was no loss of dispersed lipids through the adherence to the pipettes. The aliquots were withdrawn from each vessel at intervals of 10, 15, 30, 45, 60, 120 and 180 minutes for particle size analysis using a Delsa Nano C Particle Analyzer (Beckman Coulter, Beckman Coulter Inc., CA, USA) using disposable plastic cuvettes (Beckman Coulter disposable cell, Beckman Coulter Inc., CA, USA). The volume of the dispersion medium was kept constant by replacing the aliquot with an equal volume of 0.01N HCl. For formulations containing probucol, samples were also analyzed using an HPLC for drug concentration in the dispersion medium. Aliquots were not filtered prior to the analysis of the drug concentrations in the dispersion medium as it could reduce the content due to the retention of some lipid globules on the filters.

### **HPLC Analysis**

The samples without filtration were diluted with methanol, prior to the analysis, to dissolve the dispersed oil phase. The HPLC analysis system for probucol consisted of a quaternary pump, an Agilent 1100 autosampler and a photodiode array detector (HP 1100 series, Agilent Technologies, Wilmington, DE, USA). The chromatographic column used was a C8 Waters X-Bridge column (3.5 $\mu$ m) 4.6 mm x 150 mm. A methanol-water solution (95:5, v/v) was used as the mobile phase at a flow rate of 1 ml/min and the detection wavelength was set at 243 nm.

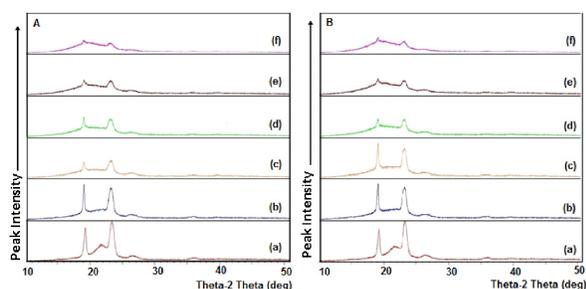
## **RESULTS AND DISCUSSION**

Preliminary experiments were conducted by incorporating monoglyceride (Capmul MCM) and triglyceride (Captex<sup>®</sup> 355) with Acconon<sup>®</sup> C-50 or Gelucire<sup>®</sup> 50/13 at different ratios. The physical consistency of the mixtures were then assessed visually. It was observed that the formulations containing monoglycerides did not solidify and there was phase separation of liquid lipid when the concentration of the liquid was >50% w/w. On the other hand, the triglyceride could be incorporated into the solid formulation to a concentration as high as 80% w/w, thus showing that stearyl polyoxyl glycerides are suitable solidifying agents for the triglyceride. The solid systems formed by Acconon<sup>®</sup> C-50 and Gelucire<sup>®</sup> 50/13 with up to 50% w/w triglyceride were waxy but sufficiently hard that it was difficult to scrape them off using a plastic spatula. As the concentration of lipid was further increased in the formulations, up to 80% w/w, the consistency of the formulations changed from solid to semi-solid. However, they were still sufficiently hard that they did not flow even when applying stress. Further studies were then carried out using the triglyceride.

### **Physicochemical characterization of the formulations**

#### **Powder X-ray diffractometry**

The P-XRD patterns of solid system containing varying ratios of Captex<sup>®</sup> 355 and Acconon<sup>®</sup> C-50 or Gelucire<sup>®</sup> 50/13 are shown in Figure 1. There was a gradual decrease in peak heights as the concentration of the lipid increased and, consequently, the concentration of the solidifying agent decreased in the formulations. The presence of the peaks in the mixtures at the same  $2\theta$  values as those of neat solidifying agents demonstrated that the crystallinity of Acconon<sup>®</sup> C-50 and Gelucire<sup>®</sup> 50/13 was maintained in the formulations. In addition, the decrease in XRD peak heights was proportional to the decrease in the concentration of the



**Figure 1** Powder-XRD patterns of solid system containing (A) Captex<sup>®</sup> 355:Acconon<sup>®</sup> C-50 and (B) Captex<sup>®</sup> 355:Gelucire<sup>®</sup> 50/13. Key: (a) 100% Stearoyl polyoxylglyceride (b) Captex<sup>®</sup> 355/ stearoyl polyoxylglyceride, 3:7 (c) Captex<sup>®</sup> 355/stearoyl polyoxylglyceride, 4:6 (d) Captex<sup>®</sup> 355/ stearoyl polyoxylglyceride, 1:1 (e) Captex<sup>®</sup> 355/stearoyl polyoxylglyceride, 6:4 and (f) Captex<sup>®</sup> 355:stearoyl polyoxylglyceride 7:3.

solidifying agent in the formulation, indicating that the presence of the lipid did not have an impact on the crystalline nature of the solid component. It was also observed that the presence of the drug did not have an impact on the P-XRD patterns of the formulations due to the lack of extra peaks and lack of changes in the existing peaks (data not shown).

#### Differential scanning calorimetry

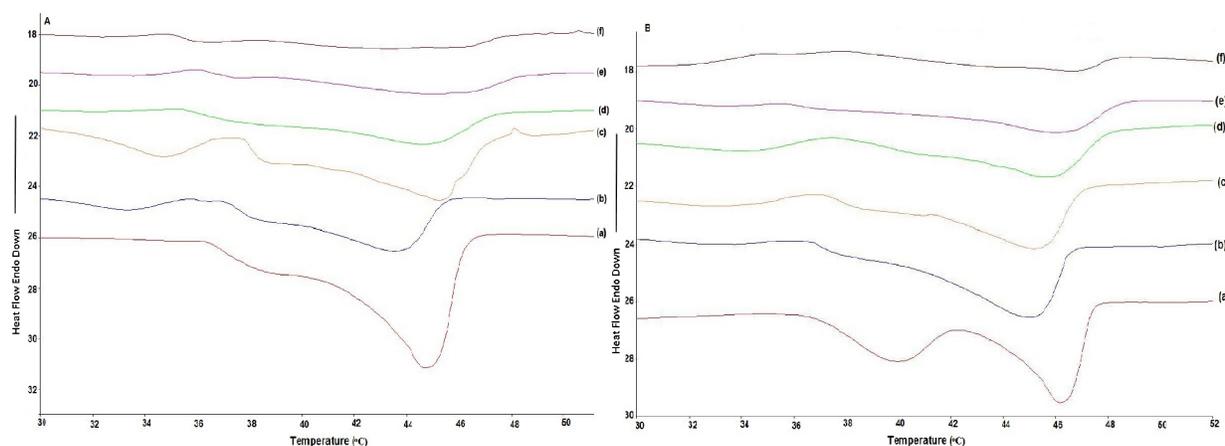
The DSC results were in agreement with those of the P-XRD analysis. Figure 2A shows the DSC scans of the solid system with varying concentrations of Acconon<sup>®</sup> C-50 and Figure 2B shows the same for the Gelucire<sup>®</sup> 50/13 formulations. A gradual decrease in melting endotherms was observed as the lipid content increased in the formulations. The decrease in enthalpy was, however, proportional to the decrease in the concentration of the solidifying agent. This again demonstrates that the solidifying agents crystallized at room temperature to the extent of their initial concentrations in the formulations.

Shallow exothermic peaks at about 35-38°C were observed in most DSC scans, which were then followed by the melting endotherms at about 42-45°C. The exotherms appear to be due to the partial recrystallization of Acconon<sup>®</sup>

C-50 or Gelucire<sup>®</sup> 50/13 from one form to another. As discussed in the next section, the microscopic examination revealed that smaller and irregular crystals of the solidifying agents were formed when the hot solutions were left to solidify at room temperature at an uncontrolled rate. For the preparation of materials for DSC studies, the normal manufacturing condition was mimicked by filling the capsules with the molten mass and then letting the capsule contents solidify at room temperature. It is possible that during such cooling, part of the solidifying agents did not crystallize properly, and they recrystallized when reheated and thus caused the exothermic peaks. The significance of such events on the performance of the formulations was not investigated here.

#### Microscopic examination

The results of the microscopic examination of solid pre-concentrates are shown in Figure 3. There are several reports in the literature indicating that PEG forms, from the melt when cooled, crystalline spherulites (25-27). Because of their PEG backbones, it appears that Acconon<sup>®</sup> C-50 and Gelucire<sup>®</sup> 50/13 also behave similarly. It may be observed from Figure 3A that the neat stearoyl polyoxyl glycerides (Acconon<sup>®</sup> C-50) is crystalline and form birefringent spherulites under the cross-polarized light of an optical microscope. Although some dark zones may be observed in the spherulites of Acconon<sup>®</sup> C-50, possibly due to the presence of amorphous regions in its structures, there were no obvious gaps between the spherulites. When Captex<sup>®</sup> was added to the formulations, the spherulites separated from each other and the lipid was interspersed in between the spherulites (Figures 3B and 3C). There was, however, a major impact of the cooling rates of molten liquids on the microstructure of solids formed. Figure 3B shows the optical photomicrograph of the 1:1-mixture of Captex<sup>®</sup> 355 and Acconon<sup>®</sup> C-50, where the molten liquid was cooled on a glass slide by exposing the slide to room temperature right after placing the drops of liquid and the



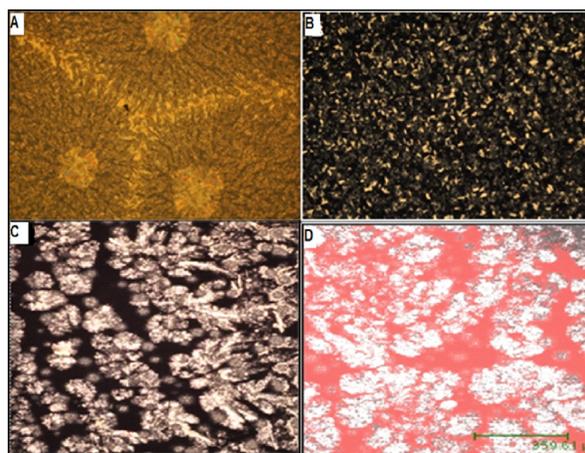
**Figure 2** DSC scans of solid system containing (A) Captex 355<sup>®</sup>/Acconon C-50<sup>®</sup> and (B) Captex 355<sup>®</sup>/Gelucire 50/13<sup>®</sup>. Key: (a) Neat stearyl polyoxylglyceride (Acconon C-50<sup>®</sup> or Gelucire 50/13<sup>®</sup>) (b) Captex 355<sup>®</sup>/stearyl polyoxyl glyceride, 3:7 (c) Captex 355<sup>®</sup>/stearyl polyoxyl glyceride, 4:6 (d) Captex 355<sup>®</sup>/stearyl polyoxyl glyceride, 1:1 (e) Captex 355<sup>®</sup>/stearyl polyoxyl glyceride, 6:4 and (f) Captex 355<sup>®</sup>/stearyl polyoxyl glyceride, 7:3.

material solidified in <1 minute. The quick cooling did not allow the spherulites to grow in a proper manner and thus irregular-needle shaped crystals of polyoxyl glycerides were observed. On the other hand, when the melt was cooled slowly in an oven from 60°C to room temperature (~ 25°C) at a rate of 0.1 C/min (Figure 3C), the spherulites grew. It was clearly visible that the liquid phase of Captex<sup>®</sup> 355 was trapped (dark zones) in between the crystalline solid structures of Acconon<sup>®</sup> C-50. The confocal fluorescence microscopic image in Figure 3D performed using Nile red as a fluorescent probe to visualize the non-crystalline region of the system confirmed that the lipid (shown in red) is located between the crystalline domains of the stearyl polyoxyl-glycerides.

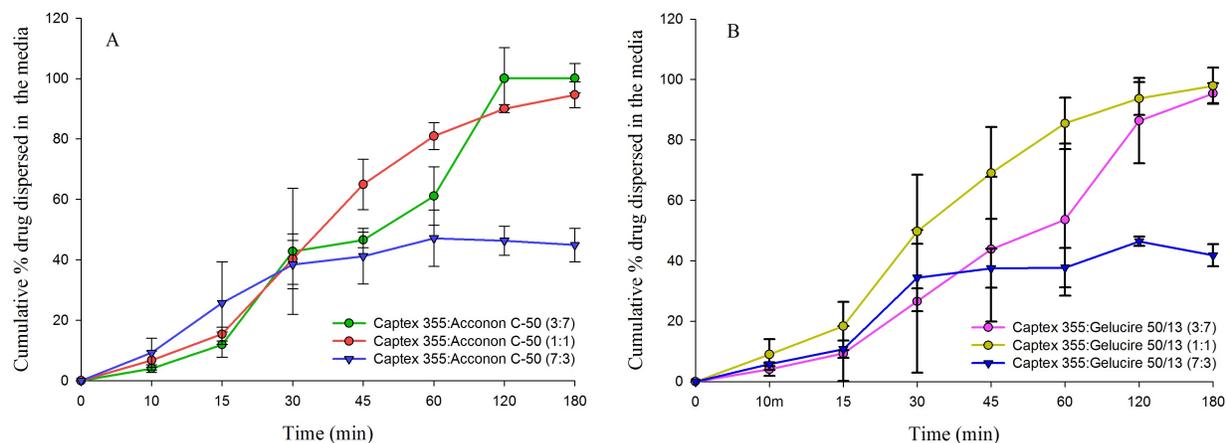
### Dispersion Test

Dispersion profiles of the triglyceride formulations in Acconon<sup>®</sup> C-50 and Gelucire<sup>®</sup> 50/13 are shown in Figure 4A and 4B, respectively. Three combinations of Captex<sup>®</sup> 355 to a solidifying agent was used, namely 3:7, 1:1 and 7:3 w/w. Exposure of the solid pre-concentrates to 0.01N HCl resulted in opaque emulsions within 20 to 25 minutes, and

the intensity of opaqueness increased with time. It was observed that the solid systems containing 30% and 50% triglyceride (3:7 and



**Figure 3** Photomicrographs of solid systems incorporating Captex 355<sup>®</sup> into stearyl polyoxylglycerides (Acconon C-50<sup>®</sup>). Key: (A) Photomicrograph of neat stearyl polyoxylglycerides obtained from cross-polarized optical microscope (B) photomicrograph under cross-polarized optical microscope of 1:1-Captex 355<sup>®</sup>/stearyl polyoxylglyceride cooled to room temperature by rapid cooling (C) photomicrograph under cross-polarized optical microscope of 1:1-Captex 355<sup>®</sup>/stearyl polyoxylglyceride cooled to room temperature at a controlled rate of 0.1 °C/min over a period of 4 hours (D) confocal fluorescence photomicrograph of 1:1-Captex 355<sup>®</sup>/stearyl polyoxylglyceride (1:1) cooled to room temperature at a controlled rate of 0.1 °C/min over a period of 4 hours.



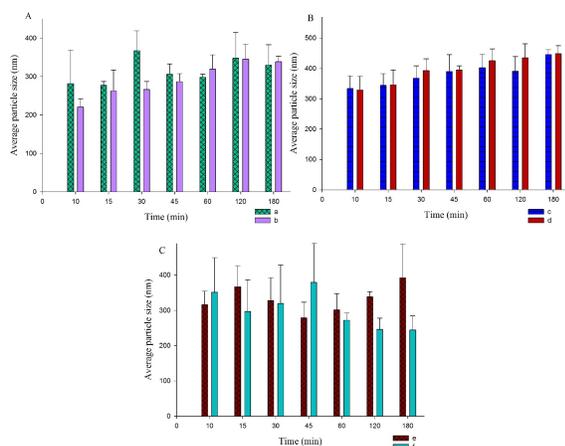
**Figure 4** Dispersion profile of solid system containing (A) Captex 355<sup>®</sup>/Acconon C-50<sup>®</sup> and (B) Captex 355<sup>®</sup>/Gelucire 50/13<sup>®</sup> using 250 ml 0.01N HCl as the dispersion medium at 37 °C.

1:1 w/w, respectively) resulted in the dispersion of more than 80% of the drug within 2 hours and almost complete dispersion in 3 hours. The solid masses did not disintegrate in the dispersion media, rather they remained as solid plugs and dispersed slowly by erosion. The relatively slow dispersion rates of the formulations appear to be dependent on their erosion rate. Since the intestinal residence time of a formulation ranges from 3 to 5 hours (28), it is expected that the drug will be fully released during the transit of the formulations to the GI tract. In the case of the 70% w/w triglyceride content in the formulation (7:3 w/w), the drug concentration in the dispersion medium almost leveled off in ~45 minutes after the dispersion of ~40% w/w drug. It appeared that 30% w/w Acconon<sup>®</sup> C-50 or Gelucire<sup>®</sup> 50/13 in the formulation was not able to emulsify the lipid completely and an additional surfactant could be necessary for complete dispersion of the lipid. Nonetheless, both Acconon<sup>®</sup> C-50 and Gelucire<sup>®</sup> 50/13 had superior emulsifying properties for Captex<sup>®</sup> 355 than those of Acconon<sup>®</sup> C-44 and Gelucire<sup>®</sup> 44/14, which required an additional surfactant at all lipid concentrations (12). Although only the results of the dispersion tests at pH 2 are presented in here, no change in the dispersion between pH 2 and 6.8 was observed in the preliminary studies as the drug and various excipients used are

nonionic.

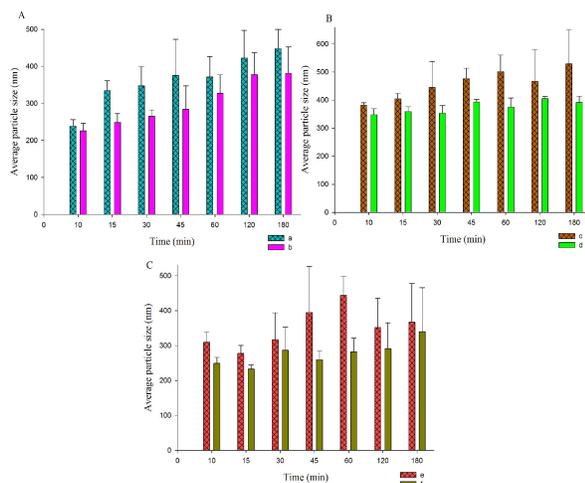
During the dispersion testing, particle size analysis of each sample was performed and the results are shown in Figures 5 and 6. Although microemulsions (<200 nm) were not formed, the particle size of the dispersed lipid phase from various formulations were still very fine, mostly in the range of 250 to 600 nm. There was also not much change in the particle size of the dispersed lipid as the concentration of the dispersed phase increased with time.

Another aspect of the dispersion test was to determine whether there was any crystallization of the drug in dispersion media. As mentioned previously in Methods, the probucol concentration at only 80% of the saturation solubility in the lipid content of the formulation was used. It was, therefore, expected that the drug would remain dissolved in the lipid phase, i.e., emulsion globules of the dispersions after mixing with water. Nonetheless, to determine whether any precipitation did at all occur, aliquots of the emulsions formed in dispersion media were periodically centrifuged (8000 rpm), and no separate solid precipitate was observed. There was also no change in the particle size with time (Figures 5 and 6), indicating the absence of any crystallization and particle size growth with time. Thus, the lack of



**Figure 5** Average particle size of emulsion of solid preconcentrate in aqueous media during dispersion test. Key: (a) 3:7-Captex<sup>®</sup> 355/Aconon<sup>®</sup> C-50 without the drug (b) 3:7-Captex 355<sup>®</sup>/Aconon C-50<sup>®</sup> with the drug (c) 1:1-Captex 355<sup>®</sup>/Aconon C-50<sup>®</sup> without the drug (d) 1:1-Captex 355<sup>®</sup>/Aconon C-50<sup>®</sup> with the drug (e) 7:3-Captex 355<sup>®</sup>/Aconon C-50<sup>®</sup> without the drug and (f) 7:3-Captex 355<sup>®</sup>/Aconon C-50<sup>®</sup> with the drug.

crystallization of the drug indicated that the drug remained dissolved in the fine lipid globules of the dispersed phase.



**Figure 6** Average particle size of the emulsion of solid preconcentrate in aqueous media during dispersion test. Key: (a) 3:7-Captex 355<sup>®</sup>/Gelucire 50/13<sup>®</sup> without the drug (b) 3:7-Captex 355<sup>®</sup>/Gelucire 50/13<sup>®</sup> with the drug (c) 1:1-Captex 355<sup>®</sup>/Gelucire 50/13<sup>®</sup> without the drug (d) 1:1-Captex 355<sup>®</sup>/Gelucire 50/13<sup>®</sup> with the drug (e) 7:3-Captex 355<sup>®</sup>/Gelucire 50/13<sup>®</sup> without the drug and (f) 7:3-Captex 355<sup>®</sup>/Gelucire 50/13<sup>®</sup> with the drug.

## CONCLUSION

This study presents a novel approach in developing solid self-emulsifying lipid-based drug delivery systems where a liquid medium-chain triglyceride may be incorporated into the solid microstructure of stearyl polyoxyl glycerides (Acconon<sup>®</sup> C-50 and Gelucire<sup>®</sup> 50/13). Acconon<sup>®</sup> C-50 and Gelucire<sup>®</sup> 50/13 not only served as solidifying agents, there was also no need for a liquid co-surfactant when the lipid content was used up to 60% w/w. The potential for physical instability of the formulations due to the crystallization of the drug from the solid systems was minimized as the drug remained dissolved in the lipid. The formulations may be filled into hard gelatin capsules in their molten state as they solidified as hard masses inside the capsules. The solid formulations formed very fine emulsions upon the dispersion in aqueous media.

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