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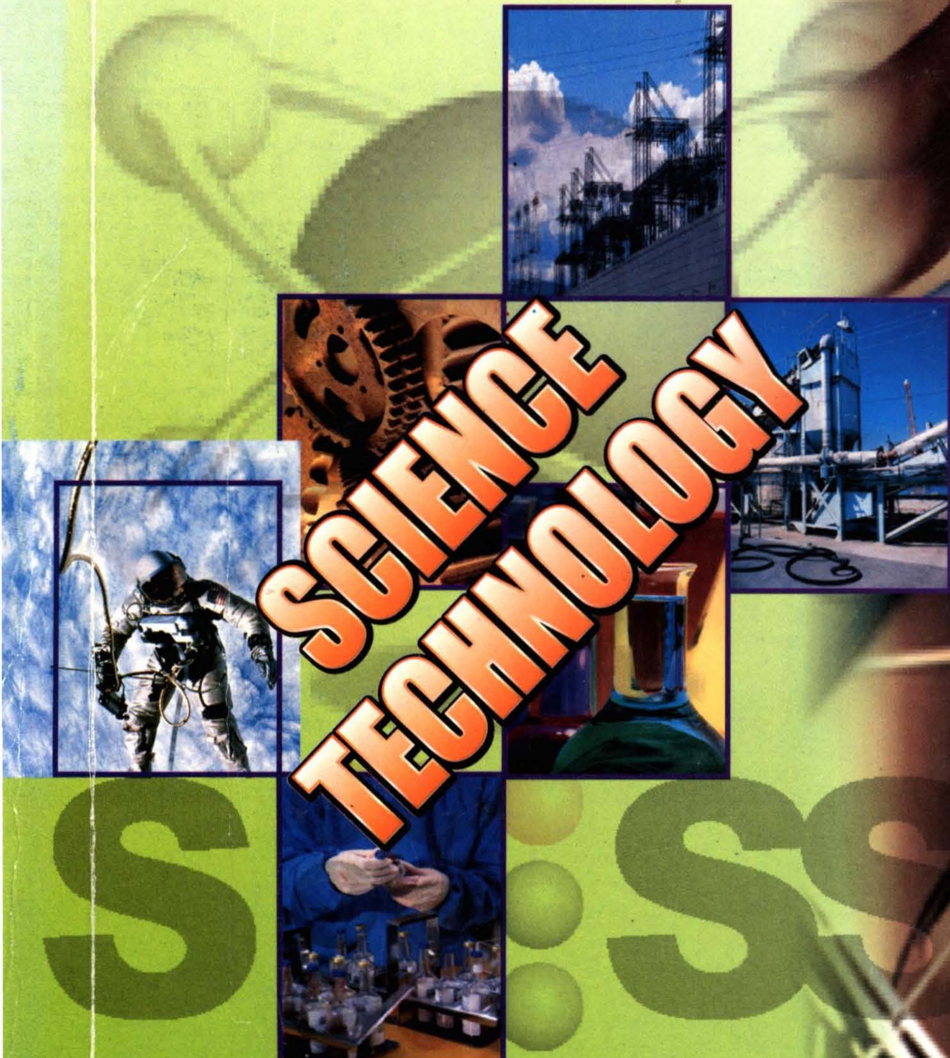

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Rheology of Palm Olein Emulsions Stabilized By Non-Ionic Surfactants as Potential Carriers for Drug Delivery

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ABSTRACT

Palm olein emulsions were prepared by homogenising the oil with varied ratios of sorbitan monolaurate (Span 20®) and polyoxyethylene 20 sorbitan monolaurate (Tween 20®). Viscosity changes of these emulsions with and without Tragacanth gum, were measured. The viscosity of emulsions increased drastically with increasing ratios of Span 20/ Tween 20, and decreased with increasing shear rate, indicating shear thinning. As the ratio of Span 20/Tween 20 increased to 1: 0.4 ratio, a small amount of hysteresis was observed. Significant thixotropic behaviour was noted with the addition of 0.01% Tragacanth gum into the oil emulsion.

Keywords: *palm olein emulsion, viscosity modifier, drug carrier, rheological properties*

Introduction

Lipid emulsions have been widely used in pharmaceutical and medical field as drug carriers (Chung *et al.*, 2001). There are growing interests in replacing petroleum-based ingredients to natural-based material because of their many advantages. Natural oil and their derivatives are renewable, biodegradable, harmless to the environment, and less of an irritant to the users (Raman *et al.*, 2003). However, the use of palm olein-based emulsions is still not common in the design of commercially available drug carriers. Palm olein seems attractive as an excipient in the drug carrier formulations. It is a vegetable oil and therefore renewable and inexhaustible. Most of all, it is relatively cheap compared to the other vegetable oil such as soy bean oil, corn oil or sunflower oil (Ahmad, 2002). There is thus, the possibility to replace these oils with palm oil as excipient in parenteral emulsion formulations for instance. To be applied as parenteral, oral, ocular (Roland et al. 2003) or topical formulation, emulsions must be physically stable (Chung et al., 2001, Roland et al., 2003), least irritant and non-toxic (Chung et al. 2001; Nielloud & Marti-Mestres 2000). The formulation of emulsions for pharmaceutical use requires a thorough understanding of the properties, uses and limitation of the emulsions (Bagwe et al. 2001).

Rheological properties give reliable and versatile information about the structural properties of the emulsions. Changes in the rheological properties may signify instability and provide qualitative and quantitative information about the structural, intermolecular properties of the emulsion (Korhonen, 2004). Understanding the rheological properties is essential for evaluation, development, performance of dosage form and application in industrial scale production of emulsions. In this respect, even though investigations had been done on the formation of palm oil-based emulsions stabilized by non-ionic surfactants (Raman et al. 2003; Ahmad, 2002; Julianto & Kubait, 2005), the rheological properties of the systems formed were not thoroughly studied. This is critical especially in view of the potential of palm olein emulsion in our local pharmaceutical manufacturing industries. The rheological properties are important to describe the flow of the emulsion through pipings and pumps, ease of transferring products from tubes or bottles and spreadibility on the skin as an example.

Materials and Methods

Materials

Oil: The commercially available refined, bleached and deodorized palm olein was used in this work. Oil from the same batch was used for each series of emulsification procedure to minimize possible compositional variations in oil properties such as iodine values and impurities present therein, which may influence the emulsion properties. The compositions of the oil are as described earlier (Ahmad, 2002).

Surfactants: Sorbitan monolaurate (Span 20) and polyoxyethylene sorbitan monolaurate (Tween 20) were purchased from Merck. Both oil and surfactants were used as received without further purification. The effective HLB values of the combination of surfactants were calculated.

Viscosity modifier: Tragacanth gum was used to increase the viscosity of the emulsions and was added at varied concentrations. A stock solution of 1% Tragacanth gum was prepared by dissolving the powder into reverse osmosis water at room temperature using a mechanical stirrer. The solution was used immediately.

Preparation of emulsions

For each emulsion, 50% w/w oil was homogenised with reversed osmosis water in the presence of 12% w/w mixed surfactants of Span 20 and Tween 20 using a high-pressure Ultra-Turrax homogenizer (T25 basic, Ika Labortechnik, Germany) at 9500 rpm for 30 minutes at room temperature (28°C). The various emulsions prepared containing different ratios of Span 20/Tween 20, and varied concentrations of Tragacanth gum, are indicated in Table 1. All emulsions were stable against creaming. Measurements were carried out after 24 hours.

Table 1: Formulations for emulsions

Sample	Palm olein (% w/w)	Surfactant (% w/w)	Span 20/Tween 20	HLB	Tragacanth gum (% w/w)
A1	50	12	0.6 : 1	13.7	nil
A2	50	12	0.8 : 1	13.1	nil
A3	50	12	1 : 1	12.6	nil
A4	50	12	1 : 0.8	12.2	nil
A5	50	12	1 : 0.6	11.6	nil
A6	50	12	1 : 0.4	10.9	nil
A1TG	50	12	0.6 : 1	13.7	0.01
A6TG	50	12	1 : 0.4	10.9	0.01

Determination of rheological properties

Rheological measurements were performed using controlled shear viscometer, Brookfield DV-II-Pro Programmable Viscometer, which uses a cone-and-plate system. All the measurements were taken using the same spindle CPE 40 and the temperature of the base plate was controlled at 25 ± 0.2°C using a thermostat water-bath. Controlled rate ramp test was performed to indicate the type and degree of non-Newtonian flow and yield value (dynamic yield value) of the sample. A continuous ramp with shear rate as the variable was applied. For each sample, the torque was maintained between 10% and 100%. The duration of spindle rotation was one minute before the reading was taken and before the shear rate was changed for subsequent measurement. Viscosity and shear stress readings were plotted against the shear rate.

Results and Discussion

From Fig. 1, the results showed that at both shear rates of 56.3 s^{-1} and 112.5 s^{-1}, the viscosity decreased as the composition of Span 20 increased until the ratio of Span 20 to Tween 20 became 1:1. At this point the viscosity was the lowest where the readings were 44.0 cP and 41.0 cP at shear rates of 56.3 s^{-1} and 112.5 s^{-1} respectively. As the concentration of Span 20 increased above the 1:1 ratio, the viscosity increased drastically. Without any viscosity modifier, this increase in viscosity may be very much related to the decreasing size of oil droplets produced as the ratios of Span 20/Tween 20 increased. As indicated in Table 1, the HLB value decreased progressively with increasing Span 20/Tween 20 ratios. At the 1:0.4 ratio, the HLB value almost coincides with that of palm olein as inferred earlier (Ahmad, 2002). At this HLB value, the very favourable interaction at the oil-water interface allows significant reduction in interfacial tension and thus would promote smallest oil droplets compared to other emulsions at the varied ratios of Span 20/Tween 20.

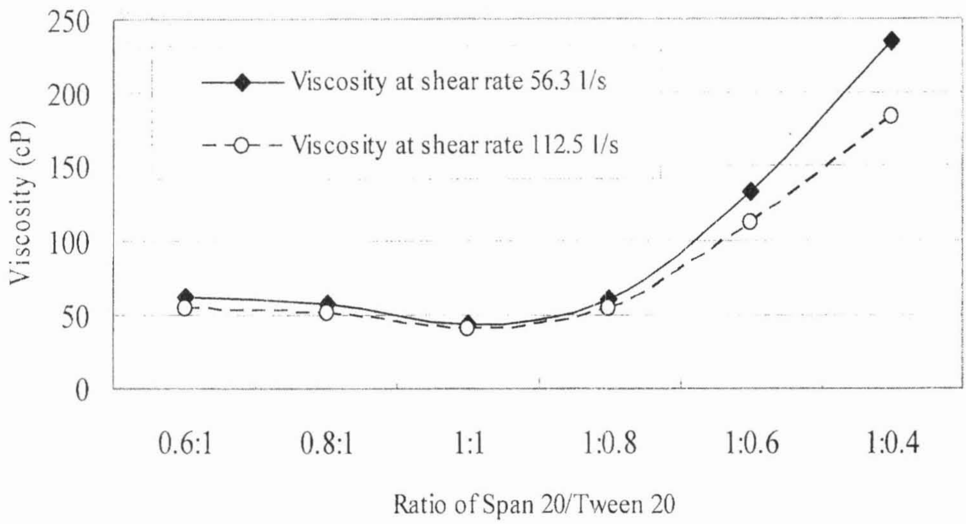

Fig. 1: Viscosities of palm olein emulsions prepared using different ratios of Span 20 and Tween 20 measured at shear rates of 56.3 s^{-1} (") and shear rate 112.5 s^{-1} (O)

From the results shown in Fig. 2, all the palm olein emulsions prepared using various ratios of Span 20/Tween 20 exhibit shear-thinning behaviour. This shear thinning behaviour, or pseudoplasticity, is non-Newtonian flow. The viscosity was not constant at constant temperature and composition, but decreased with increasing shear. The causes for pseudoplastic flow are the progressive breakdown of structure in the liquid medium by increasing shear, and the rebuilding of structure by Brownian motion (Alfonso, 2000). The emulsions form structures under rest that can be disaggregated under shear (Nielloud & Marti-Mestres, 2000). From a drug delivery point of view, adequate flow behaviour is often required to ensure good therapeutic or cosmetic function. For example, a cream should be strongly shear thinning such that it can be poured into and from the container, which is critical in processing and packaging, and to facilitate rubbing on the skin of the end user. On other hand, the cream, once spread, has to form a strong film that does not run and this allows the delivery of the active or cosmetic compound (Nielloud & Marti-Mestres, 2000).

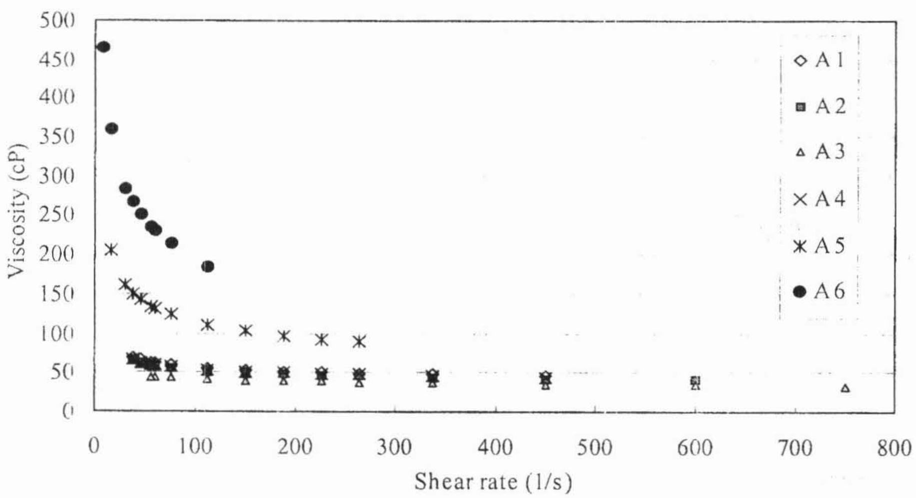

Fig. 2: Viscosities of palm olein emulsions emulsified with varied ratios of Span 20/Tween 20

Yield stress of the emulsions (Table 2) was obtained by extrapolating the flow curves of shear stress against shear rate to the stress axis as shown in Fig. 3 (Alfonso, 2000). Structural networks extending throughout an entire system usually cause yield stresses. To break such network requires stresses equal to or exceeding the yield stress. The yield stress of the emulsion prepared using 1:1 ratio of Span 20 to Tween 20 was the lowest, indicating that least stress was needed to initiate flow. Beyond this ratio however, with increasing concentration of Span 20, commencing at Span 20/Tween 20 ratio of 1:0.6, the yield stress increased. Above the yield stress value, all emulsions exhibited almost Newtonian flow. The possible reason that increasing yield stress was observed could be most likely due to the increasing hydrogen bonding present within the network as the Span 20/Tween 20 ratio increased, thereby the tendency of the oil droplets to flocculate. This may also explain the higher viscosities of emulsions prepared with increasing Span 20/Tween 20 ratios as shown in Fig. 1 and Fig. 2. Nonetheless, all the samples studied exhibited relatively low yield stress values, which are deemed suitable for application of the formulation as skin lotion or oral emulsion with little effort.

Table 2: Composition and yield stress values of the emulsions obtained from shear stress against shear rate plots.

Sample	Span 20/Tween 20	HLB	Yield stress (dynes/cm^2)
A1	0.6 : 1	13.7	7
A2	0.8 : 1	13.1	7
A3	1 : 1	12.6	5
A4	1 : 0.8	12.2	7
A5	1 : 0.6	11.6	13
A6	1 : 0.4	10.9	15

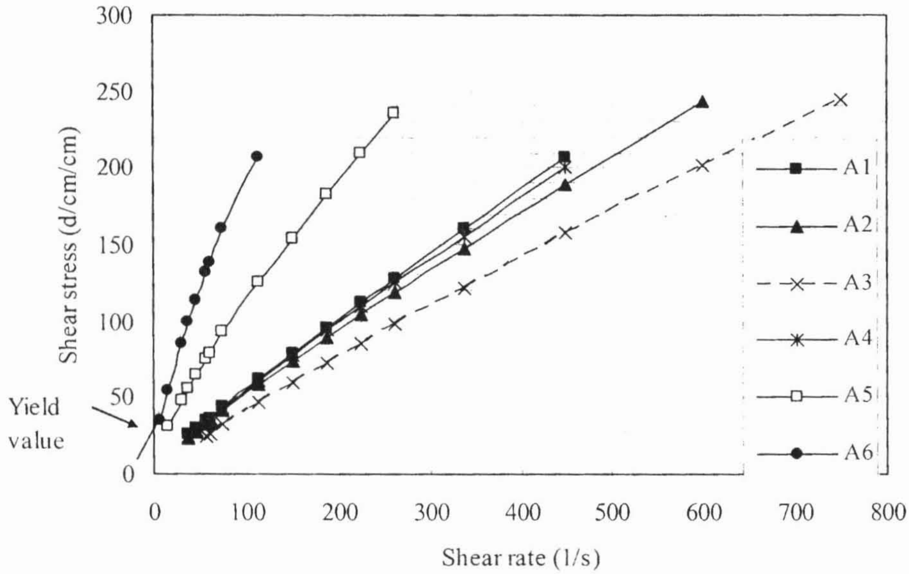

Fig. 3: Effect of shear rate on the shear stress of oil emulsion emulsified with varied Span 20/Tween 20 ratios without viscosity modifier

The stronger network formed within emulsions containing higher ratios of Span 20/Tween 20 may also be responsible for the observed time-dependent rheogram as indicated in Fig. 4. The down curve for emulsion A6 in both plots of viscosity and shear stress against shear rate was higher than the up curve. In Fig.5, addition of 0.01% tragacanth gum had a significant effect on the thixotropic behaviour of emulsion with Span 20/Tween 20 at 1:0.4 ratio (b), but did not alter the thixotropy of emulsion with 0.6:1 ratio (a). This indicates that it is critical to first understand the effect of concentrations of binary mixtures of surfactants on the rheological behaviour of emulsions, as the viscosity modifier, Tragacanth gum in this case, is not the only determining factor.

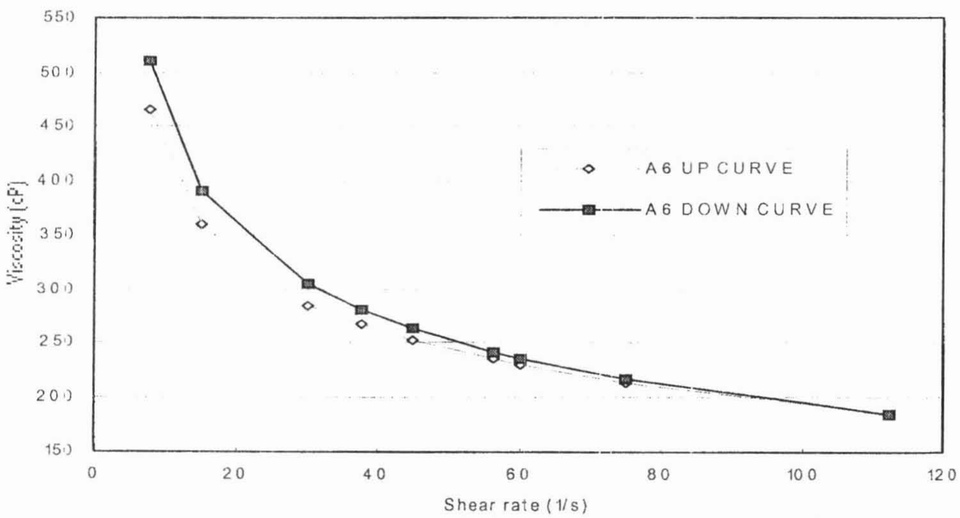

Fig. 4: Rheogram depicting time-dependent non-Newtonian behaviours of emulsion containing Span 20/Tween 20 at 1:0.4 ratio

(a)

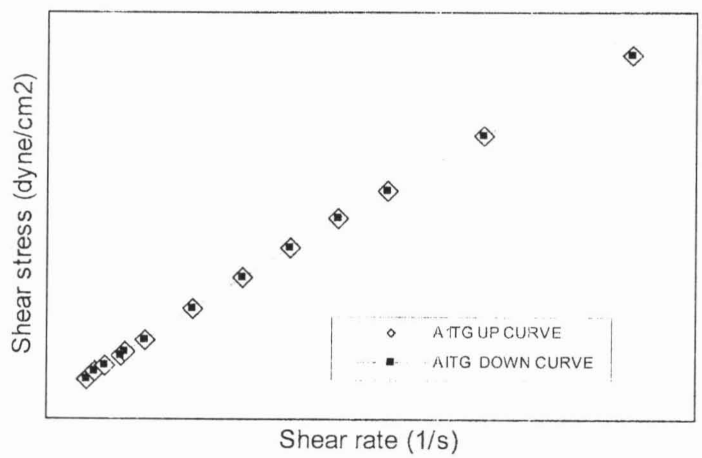

Fig. 5: Effect of the addition of 0.01% tragacanth gum on the thixotropic behaviour of palm olein emulsions prepared using Span 20/Tween 20 ratios of (a) 0.6:1 and (b) 1:0.4

Conclusion

The rheological properties of palm olein emulsions can be controlled by varying the concentrations of binary mixtures of non-ionic surfactants and by the addition of Tragacanth gum. Depending on the dosage form and design, the palm olein emulsions formed can be used for topical applications or as parenteral drug delivery systems.

Acknowledgment

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