Research Article

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Effect of Octyl Salicylate With Respect To the Physical Appearance of Mono/Di Caprylic and Capric Fatty Acids Formulations

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Abstract
Caprylic and capric acids are classified as medium-chain fatty acids. In this study, the behavior of the caprylic and capric acids formulations containing octyl salicylate were investigated. The formulations were prepared using homogenization proses. The characteristics of the formulation such as particle size, flow behavior, microscopic view and absorbance of the formulations were investigated. Particle sizes of the formulations were found ranging from 352.7 - 704.2 nm. The viscosity of the formulations changed as the shear rate was varied and could be classified as non-Newtonian fluids. The viscosity decreases when the fluid undergoes longer shear stress with time. The formulations containing octyl salicylate shows higher absorbance as compared to the formulations without octyl salicylate. The addition of octyl salicylate affected the system in terms of behavior, appearance and stability.

Keywords: Mono/diglyceride, Capric acid, Caprylic acid, Octyl salicylate.

Introduction
Medium-chain fatty acids (MCFAs) comprise saturated fatty acids with 6-10 carbons and could be found in several oil and fat such as coconut oil, palm kernel oil and dairy fat [1]. Caprylic acid (C8) (Figure 1) and capric acid (C10) (Figure 2) have been classified as Medium-chain fatty acid (MCFAs); they have 8 and 10 carbon, respectively and have unique physical and chemical characteristics with differences in absorption, transport and metabolism. The structure of caprylic and capric acids were shown in Figure 1 and Figure 2.

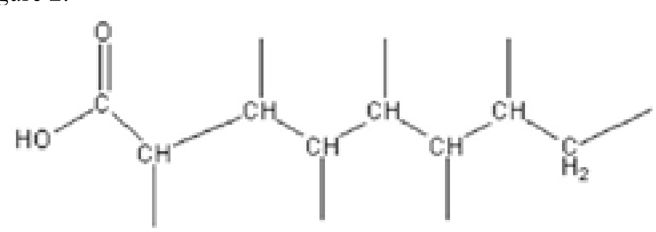

Figure 1: Caprylic Acid.

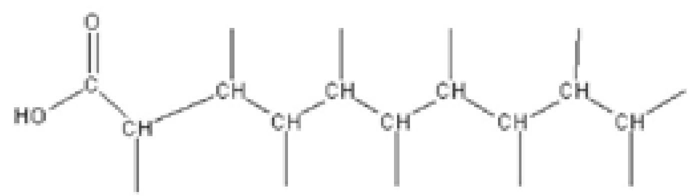

Figure 2: Capric Acid.

Guenther reported that capric acid can also be found in several essential oil including lemongrass, chamomile, pha-chium and fusel oil from grape bagasse. They are more easily and quickly absorbed the intestine than any of the conventional fats and oils [2]. They hydrolyzed quickly and absorbed into intestinal cells without micellar solubilization in intestinal lumen [3]. Thus, they become the established oral and parenteral treatments for variety of malabsorption cases such as chyluria, steatorrhea, hyperlipoproteinemia and other related condition [3].

Several reports suggested that MCFAs offer the therapeutic advantage of preserving insulin sensitivity in animal models and patients with type 2 diabetes [4]. They have been reported to have an anti-parasitic effect against other parasites and are essentially non-toxic in acute toxicity tests conducted in several species of animals [5]. They exhibit virtually no potential as ocular or dermal irritants, even with prolonged eye or skin exposure and also exhibit no capacity for induction of hypersensitivity [6]. In cosmetics field especially for dermal or topical application, MCFAs researches have a lot of potential to be explored.

Octyl salicylate is one of the organic sunscreen. The ester form of salicylate was proven to have less penetration into the stratum corneum of human skin as compared to the carboxyl form, salicylic acid. The salicylate provide a homologous series with calculated log actanol/water coefficients (Hansch group contribution method) ranging from 2.62 for the methyl analogue to 6.19 for the octyl analogue. These calculations suggest that the amount of salicylate crossing the skin will decrease with increasing alkyl chain length and that octyl (2-ethylhexyl) salicylate would be least permeable [7,8]. Furthermore, the combination of salicylate portion and ethylhexanol (octyl) portion give better effect on the skin as sunscreen and emollient. Salicylate portion absorbs ultraviolet (UV) light and ethylhexanol portion becomes emollient, give oil-like properties, prevent the water loss from the inner layer of the skin to the surrounding.

Walters reported that the permeation of octyl salicylate via in vitro human skin relatively low but it was higher than the predicted of physic-chemical data reported that octyl salicylate had been predicted to have slow penetration which is approximately 3.0 µg in 12 hour based on a total body application of 40 $\mu g/cm^2$ sunscreen agent as a 2% formulation respectively [7]. The average total absorption of two different vehicles of finite and infinite of octyl salicylate at 48 hours were 0.59 ± 0.09% (n = 12) and 0.23 ± 0.05% (n = 11) respectively [7].

Atmospheric Pressure Chemical Ionization (APCI) performed the analysis of salicylate derivatives (include octyl salicylate) in negative ion mode while the camphor derivatives in positive ion mode in order to determine the current used UV-filters that may present in human placental tissue samples. ACPI was selected due to its higher sensitivity after evaluation with electro-spray ionization (ESI) in both positive and negative modes. All of them do not inhibit cytotoxic activity including octyl salicylate using 5-diphenyltetrazolium bromide (MTT) test assessed in the concentration range tested (0.01-10 µm). Octyl salicylate also did not induce human breast cancer MCF-7 cell proliferation in the same range of concentration. In this study, the behavior of the capric and caprylic acids formulations with and without octyl salicylate were investigated.

Methods

Materials injured

Olive oil, Propylene glycol mono oleate, mono/diglyceride of capric acid and caprylic acid, Brij56, Octyl salicylate were purchased from Sigma-Aldrich, United Kingdom.

Formulation of emulsions

The mixing of compositions was carried out by emulsification method using hot-hot process. The total amount was 10 g. All of the ingredients excluding octyl salicylate were heated using a water bath at ± 70ºC for 5 min. By using high shear homogenizer the mixture was homogenized at 8 000 rpm until the temperature of the mixture dropped to room temperature (± 25ºC). Finally, octyl salicylate was added into the formulation and stirred for ± 2 minutes. The formulations were coded as 10a (containing capric acid without octyl salycilate), 10b (containing caprylic acid without octyl salycilate), 10a with OS (containing capric acid with octyl salycilate) and 10b with OS (containing caprylic acid with octyl salycilate), respectively. The compositions of the formulations were depicted in Table 1.

Ingredient	10a (% w/w)	10b (% w/w)	10a with OS (% w/w)	10b with OS (% w/w)
Mono/diglyceride of capric acid	5	-	5	-
Mono/diglyceride of caprylic acid	-	5	-	5
Olive oil	6	6	6	6
Glycerol monooleate	4	4	4	4
Brij 56 (polyoxyethylene (10) cetyl ether)	8	8	8	8
Propylene glycol monocaprylate	1	1	1	1
Octyl salicylate (OS)	-	-	5	5
Deionized water	76	76	71	71

Table 1: Compositions of The Formulations.

Stability Study

The assessment of product stability was carried out by centrifuging test. It was centrifuged at 10 000 rpm at 25ºC for 15 min. The samples were centrifuged in an attempt to observe their physical appearance or stability in a short time without storing for a long time.

Particle size Analysis

Particle size distributions of samples were measured by diffusion method using particle size analyzer. The sample was diluted into deionized water as dispersing medium in the ratio 1:100 (w/w). Then the solution was transfer into the cuvette. The measurement was performed at 25°C.

Flow Behavior Study

The rheological properties of the formulations were measured using the Modular Compact Rheometer (Paar Physica 300, Austria) with a cone-plate configuration and connected to software program in computer. The flow behaviors of the formulations were determined at 25ºC. The apparent viscosity and shear stress values of the samples were taken at different range of shear rate from 0s-1 to 100s-1. The flow index was mathematically calculated by the Ostwald law.

Transmission Electron Microscope (TEM) Analysis

A drop of the sample was swiped on a formvar coated copper grid. The sample on the copper grid was stained using 2 %

phosphotungstic acids (PTA) for 10 minutes. The copper grid was dried by evaporation at room temperature. The morphology of the samples was viewed by Transmission Electron Microscopy (Hitachi H-7100, Japan).

UV Absorption Studies

Sample (0.03 g) was dispersed in 30 ml of deionized water. The dispersed sample was shaken and transferred into the cuvette. Measurement of sample absorbance was performed in the range of wavelengths 290 nm to 410 nm (wavelength of UVA and UVB) at 25°C. UV absorption analysis was conducted using UV-vis spectrophotometer, UV-1650PC (Shimadzu, Japan).

Results and Discussion

After centrifuging for 15 minutes at 10 000 rpm at 25ºC, formulations 10a, 10b and 10a with OS were found stable and remain homogenized without separation as depicted in Figure 3. Unfortunately, formulation 10b with OS was found separated with a very little amount of water phase on the top of the sample. Oil droplets in emulsions, during and after homogenization are constantly moving due to gravity, Brownian motion or the mechanical action of homogenization. The emulsifier, Brij56 help to bind the oil phase and water phase together and generate steric stability, thus the oil droplets were repealing each other [9]. Formulation 10b with OS involved the gravitational separation of the oil phase which is dispersed phase, from the water phase which is the continuous phase due to the lake of steric stability. Brij56 could not hold firmly the polar portion and effect the separation of little amount of water from the formulation 10b with OS system.

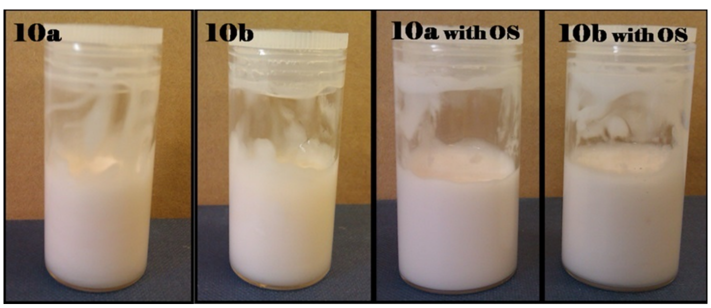

Figure 3: The Pysical Appearance of the Formulations.

The particle size of the formulations 10a, 10b, 10a with OS and 10b with OS were depicted in the Table 2. The particle size of formulation 10a was 448.1 nm. With the addition of octyl salicylate the particle size of the formulation 10a with OS increased to 542.3 nm. The particle size of formulations 10b and 10b with OS were 352.7 nm and 704.2 nm respectively. The corresponding mean particle sizes of the formulations were increased with the addition of octyl salicylate into the systems. The particle size of the sample formulated using capric acid was larger as compared to the sample formulated using caprylic acid because capric acid has 2 carbons more than caprylic acid. Due to the instability of formulation 10b with OS, the oil droplet agglomerate when OS was mixed into the system, thus gave big particle size of the droplet. The count rates of all formulations are in the range of 130 kcps to 208 kcps with the polydispersity index below than 1.0. The emulsifier used in this study was sufficient enough to emulsify the water and oil composition thus resulting in reduction the interfacial tension [10].

Item	10a	10b	10a with OS	10b with OS
Particle size (nm)	448.1	352.7	542.3	704.2
Count rate (kcps)	134.6	164.6	247.5	207.7
PDI (polydipersity index)	0.893	0.433	0.182	0.581

Table 2: The Particle Size of the Formulations.

Figures 4 and 5 depict the flow curves of shear stress (τ) and apparent viscosity (η) versus shear rate (γ) for formulations 10a, 10a with OS, 10b and 10b with OS. From the flow curve graphs, the flow behaviors of substances over a wide range of shear rate and appearance viscosity were shown. All of these four formulations were classified as pseudo-plastic materials under non-Newtonian fluid (shear thinning) behavior where the viscosity decreases as the shear rate applied increases. Furthermore, the viscosity was inversely proportional with time. The viscosity is getting low when the fluid is undergoing long shear stress with time [11]. Increasing shear rate resulted in greater molecular structure breakdown [12]. Formulation 10 a is more viscose as compared to the formulation 10b. Capric acid chain length is longer than the caprylic acid chain length, thus make the system more viscose and harder to flow [13]. The curves of the flow curves show that at low shear rates, the formulations fluids were more viscous than the Newtonian fluid. At high shear rates, the samples were less viscous [14,15]. These pseudo-plastic groups of material are acceptable in cosmeceutical field where it is important for application on the skin uniformly.

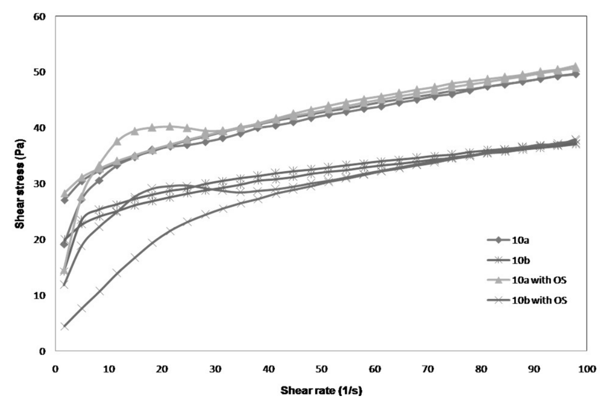

Figure 4: The Flow Curves of Shear Rate (1/s) Versus Shear Stress (Pa) of the Formulations.

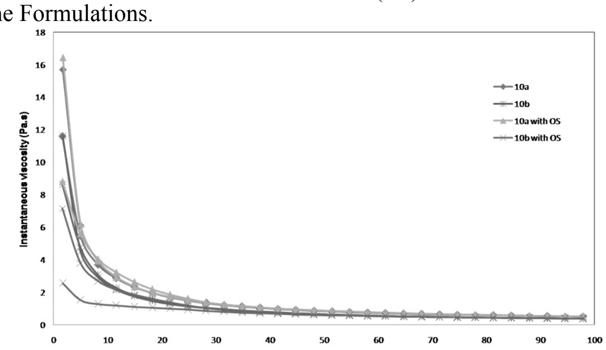

Figure 5: The Flow Curves of Shear Rate (1/s) Versus Instantaneous Viscosity (Pa.s) of the Formulations.

Figures 6 and 7 show the TEM micrograph of the particles of and mono/diglycerides of capric and caprylic acid that were dispersed in the distilled water without octyl salicylate. Figure 9 and Figure 10 depict the particle distribution of mono/ diglycerides of capric acid and caprylic acid with octyl salicylate. The dispersion of the oil droplets was visualized in the water system via transmission electron microscopy. The oil droplet was distributed properly in the system containing mono/diglyceride of capric acid with or without the present of octyl salicylate. These were shown clearly in both Figures 6 and 8 respectively. The micrograph images in Figure 9 show that a higher degree of nano-emulsion stability was achieved in the presence of oil phase concentration and the surfactants. There are a few possible explanations behind this experiment. The droplets size might becoming closely packed leading to increase the droplet concentration.

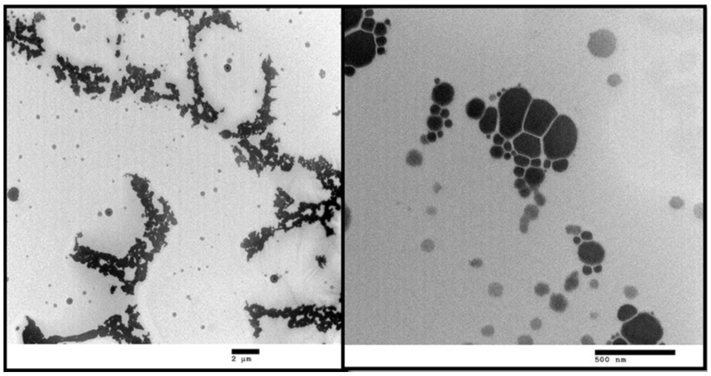

Figure 6: TEM Micrograph of the 10a Formulation without OS.

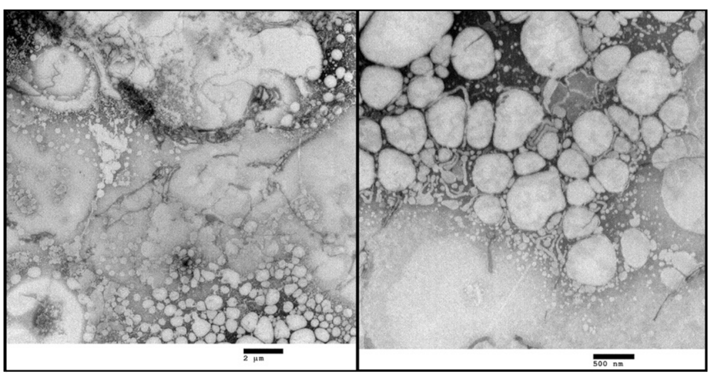

Figure 7: TEM Micrograph of The 10b Formulation Without OS.

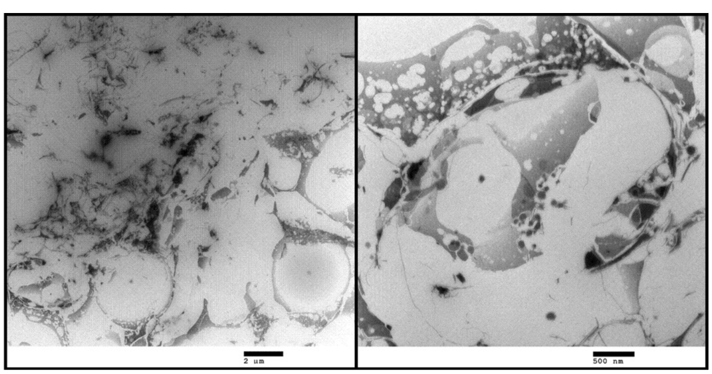

Figure 8: TEM Micrograph of the 10a Formulations with OS.

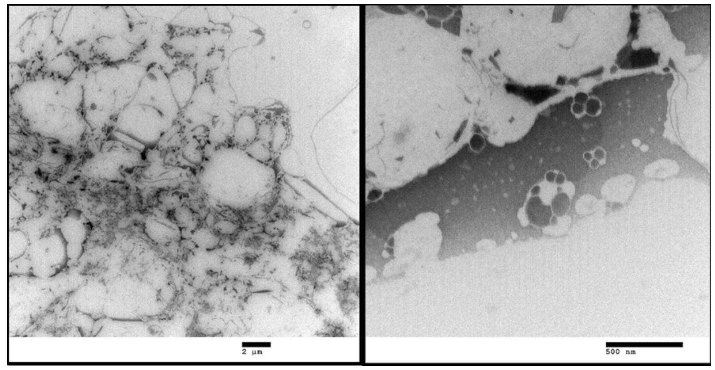

Figure 9: TEM Micrograph of the 10b Formulations with OS.

Figure 10 depicts the absorption spectra of the formulation 10a, 10a with OS, 10b and 10b with OS using dilute-solution method. The four spectra illustrated are for formulations which are primarily considered to be UVB absorber due to the present of octyl salicylate those formulations covered the UVB (280 nm to 320 nm) and small range of UVA which is 320 nm to 335 nm. The UV absorption dropped drastically starting from the wavelength 335 nm as octyl salicylate has an ability to absorb UVB only in both capric and caprylic fatty acid formulations. The UV absorption for the formulation without octyl salicylate remains static at 1.9 abs for 10a and 1.5 abs in the UVA range. While, the absorbance value slightly decreases in both formulation 10a and 10b in the UVA range respectively. In both UVA and UVB, the formulation without octyl salicylate absorbance value was lower than the formulation containing octyl salicylate as octyl salicylate leads to a synergistic effect and the UV scattering by the particles.

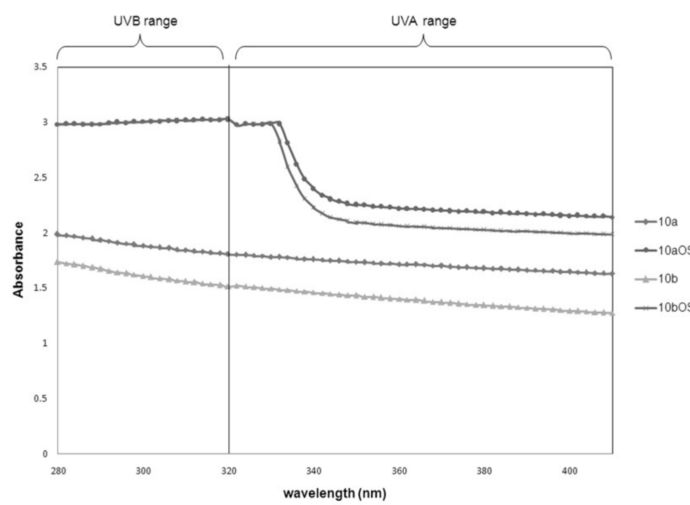

Figure 10: The Absorption Spectra of the Formulations.

Octyl salicylate acts as physical sunscreens on their own to achieve improved photo protection that showing a UV-blocking potential. The UV protection increases in the formulation containing octyl salicylate as compared to the formulation without octyl salicylate might be explained by the applied lipid layers that covering fully or partially the surface of pigments that are believed it were responsible for UV absorption enhancement. As the conclusion, formulations containing capric and caprylic acid with and without octyl salicylate were successfully obtained and characterized. The addition of octyl salicylate affected the system in terms of behavior, appearance and stability. These formulations were suitable for use in cosmeceutical industry.

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