EFFECT OF EMOLLIENT ESTERS ON SOLUBILIZING AND PREVENTING RECRYSTALLIZATION OF ORGANIC UV ABSORBERS, AND DISPERSING INORGANIC UV FILTERS IN SUNSCREEN FORMULATIONS

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Abstract

Background: With the rising awareness and demand towards sun protection, the need for highly efficient UV filter systems is growing. Organic UV absorbers of high efficiency are crystalline substances that can recrystallize in formulations if not well solubilized. Inorganic UV filters with better safety profiles require sufficient dispersion to prevent agglomeration. Therefore, it is crucial to find emollients to ensure the stability of organic UV absorbers and the dispersion of UV particulates to maximize the performance of UV filter systems.

Methods: The solubility of crystalline UV filters in selected emollients and the recrystallization of UV filters were determined by polarized microscope analysis. In vitro SPF and/or UVAPF values of oil-in-water emulsions containing organic UV filters and emollients were assessed. Dispersions of inorganic particulate UV filters in emollients were evaluated by fineness gauge for particle size and viscometer for viscosity change. The microstructure of the dispersions was determined by microscope analysis.

Results: Emollients exhibited different solubilization power for crystalline UV filters and dispersing capability for inorganic UV particulates. DIA, DIS, and LL are good solubilizers and performance enhancers for organic UV filters. CATC and GMIS are good dispersing emollients for Titanium Dioxide and Zinc Oxide particles.

Conclusion: Effective UV filter solubilizers and dispersants are proposed respectively, and sample sunscreen formulations are given as references with *in vitro* SPF/UVAPF indications. Proposed tools to study solubility, recrystallization, dispersion, and impact on UV filters can be used to assess the performance of emollient esters when developing effective and stable products for sun protection.

Keywords: Sun Protection; UV filters; Emollients; Ester; *In vitro* SPF; Dispersion

Introduction.

Ultraviolet (UV) filters, as the heart of sunscreen technology, are the key ingredients in sunscreen formulations protecting the skin. There are two types of UV filters available on the market: organic UV absorbers and particulate UV filters. Organic UV absorbers enjoy a long history of use and have higher efficiency with recent new development such as Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (BEMT), Diethylamino Hydroxybenzoyl Hexyl Benzoate (DHHB), and Ethylhexyl Triazone (EHT), which are high molecular weight hydrophobic compounds with improved photostability and safety profiles, as well as reduced environmental impact [1-3]. However, such high molecular weight organic UV absorbers, usually crystalline solids at ambient temperature, require proper solvents to facilitate the formulation process. In addition, crystalline substances tend to recrystallize if not properly solubilized and stabilized in the formulation, exerting a negative effect on the effectiveness of sunscreen products [4]. Although traditional liquid state organic UV absorbers, namely Ethylhexyl Methoxycinnamate (EHMC), Octocrylene (OCR), and Homosalate (HMS), can work as solvents for crystalline organic UV absorbers, studies have revealed their endocrine disrupting properties as well as potential adverse impacts on ecosystems [5-7]. Therefore, it is crucial to find emollients that exhibit excellent solubilization for crystalline organic UV absorbers while preventing them from recrystallizing in the formulation to maximize the performance of organic UV absorbers in commercial products.

On the other hand, there is a major boom in the use of inorganic particulate UV filters such as Titanium Dioxide (TiO2) and Zinc Oxide (ZnO) in sunscreen products because of their relatively low impact on the environment and skin sensitivity [8-9]. Nevertheless, these insoluble particulates are difficult to handle and tend to agglomerate in formulations, posing a major formulation challenge for effective sunscreen development. Finding emollients to efficiently disperse the UV filter particles and ensure the incorporation of adequate inorganic particulates into the formulation has always been a challenge.

The objectives of the present study were first to investigate the performance of emollients in solubilizing crystalline UV absorbers and preventing their recrystallization in the formulation, secondly to evaluate the dispersing properties of emollients for inorganic UV particulates, and finally to assess the effect of emollients on the performance of UV filters in vitro.

Materials and Methods.

Materials

UV filters: Butyl Methoxydibenzoylmethane (BMDBM), Ethylhexyl Triazone (EHT), Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (BEMT), and Diethylamino Hydroxybenzoyl Hexyl Benzoate (DHHB) were used as supply. Silicone-coated and Aluminium-coated Titanium Dioxide (TiO_2-TX and TiO_2-Z), silicone-coated Zinc Oxide (ZnO-ZX) and uncoated ZnO (nano-ZnO and micro-ZnO) were as supply.

Emollients: Diisopropyl Adipate (DIA), Diisopropyl Sebacate (DIS), Lauryl Lactate (LL), Neopentyl Glycol Diethylhexanoate (NGDO), Isopropyl Isostearate (318), Cocoyl Adipic Acid/Trimethylolpropane Copolymer (CATC), Glyceryl Isostearate (GMIS), Caprylic/Capric Triglyceride (CCT), and C12-15 Alkyl Benzoate (CAB) were used as supply.

Other ingredients: Acrylates/C10-30 Alkyl Acrylate Crosspolymer (EZ4U), PEG-20 Methyl Glucose Sesquistearate (SSE-20), Phenoxyethanol (and) Ethylhexyl Glycerin (PEHG), Glycerin, Methyl Gluceth-20 (E-20), and Disodium EDTA were used as supply. A basic neutralizer used was sodium hydroxide as 18% aqueous solution.

Methods

Preparation of emulsions

The water phase was first prepared using an over-head stirrer at 400 rpm until homogenous and the oil phase was added into the system under stirring. Both water and oil phases were heated at 60-80 °C and then mixed at the same temperature. The oil phase with inorganic UV particles was pre-dispersed and homogenized at 10 000 rpm for 3 min before added to the water phase. The mixture was then homogenized at 10 000 rpm for 3 min.

Solubility of organic UV absorbers in emollients

Crystalline UV filters were added to the emollient and the beaker was heated at 60 ± 1 °C for 2 h under stirring and then cooled down while mixing to room temperature. The solution was transferred to a glass bottle and kept in a temperature chamber at 6 ± 0.2 °C for 7 days. At the end of 7th day, the solution was examined by polarized light microscopy. The amount of each UV filter was added at 1 wt% interval. If crystals were detected, the amount of the emollient was insufficient to solubilize the corresponding UV filter. Such tests were conducted in triplicate to confirm the solubility of UV filters in emollients.

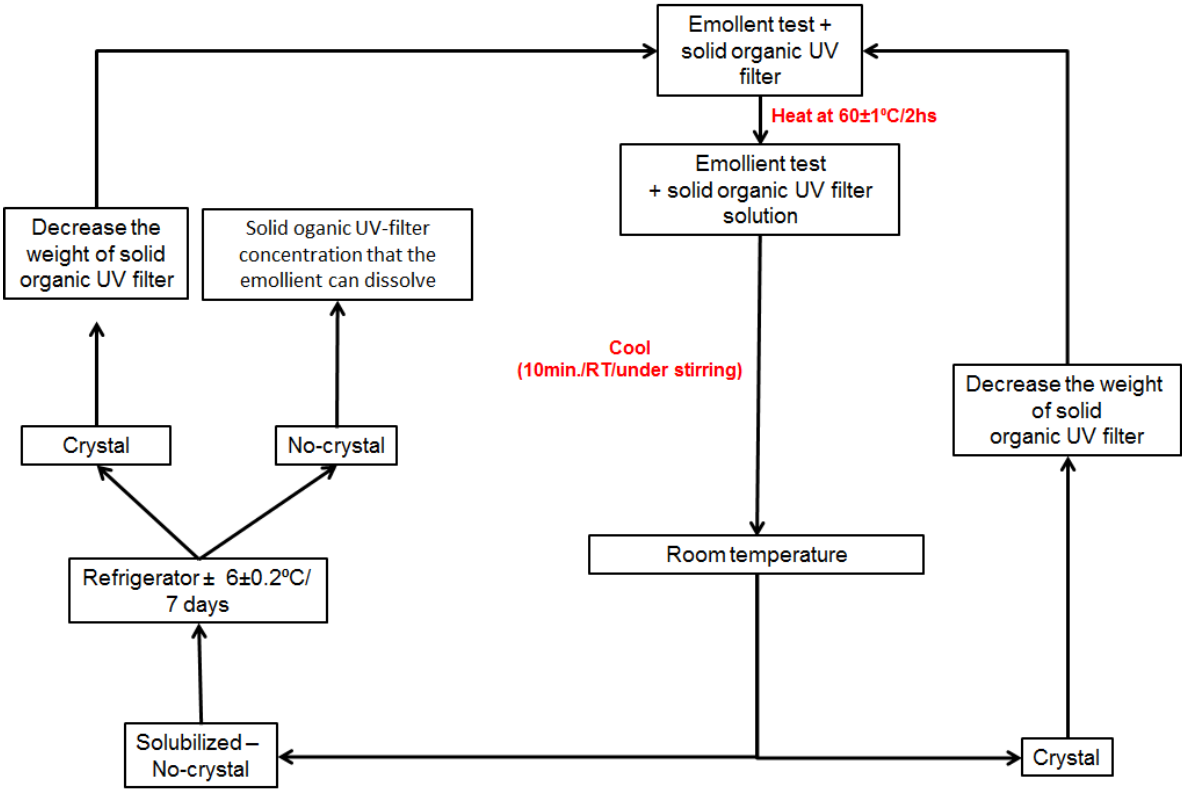


Figure 1. Schematic diagram of solubility test.

Recrystallization of organic UV absorbers in simple oil-in-water (O/W) emulsions

Simple oil-in-water emulsions were prepared, and the recrystallization of organic UV absorbers was accelerated by Freeze/Thaw (-18 °C to 25 °C) cycles. Samples were examined by polarized light microscopy after 5 Freeze/Thaw cycles.

Table 1. (A) Organic UV filter-based oil-in-water emulsion for recrystallization and *in vitro* UV performance analysis. (B) Inorganic UV particulate-based oil-in-water emulsion for *in vitro* UV performance analysis.

(A)	Ingredient	BMDBM	DHHB	EHT
		Weight %		
Water phase	Deionized water	To 100		
	EZ4U	0.3		
	SSE-20	1.0		
	Glycerin	5.0		
	PEHG	0.5		
Oil phase	Organic UV filter	3.0	5.0	5.0
	Emollient	10.00		
Additive phase	NaOH (18% solution)	pH 5.5		

(B)	Ingredient	TX	ZX	Micro-ZnO
		weight%		
Water phase	DI water	72.2		
	Glyceryl Stearate, PEG-100 Stearate	2.0		
	Xanthan Gum	0.3		
	Glycerin	5.0		
	PEHG	0.5		
Oil phase	Inorganic UV filter	5.0		
	Emollient	15.0		

Preparation and characterization of dispersion of inorganic UV particulates in emollients

UV particulates (18 g) were added in the emollient base (42 g) (30:70, w/w). Mixtures were homogenized at 10 000 rpm for 10 min and transferred to a glass bottle. The viscosity of the dispersions was evaluated by a viscometer. The particle size and the fineness of the dispersions were assessed by a fineness gauge.

In vitro SPF/UVAPF analysis

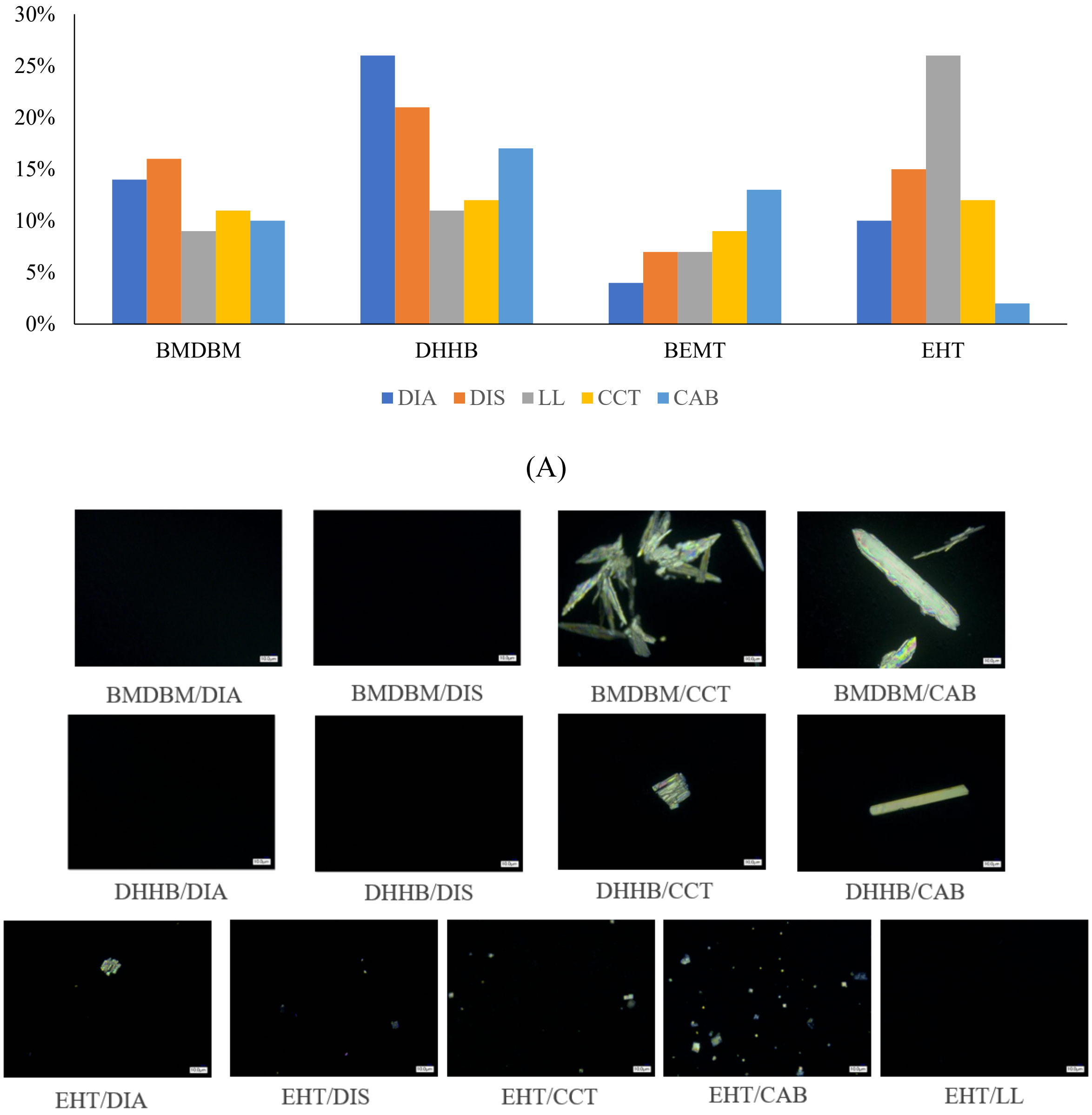
In vitro SPF and UVAPF values of O/W emulsions containing UV filters were determined by UV-2000S. A 0.0325 ± 0.0005 g portion of sample was applied on a moulded PMMA plate using an automatic robot arm and transmission of light was measured before and after solar simulation following the Colipa test method. Each sample was repeated at least three times.

Stability measurement

Emulsion samples were subjected to stability evaluation at room temperature (RT), elevated temperature (50 °C) for 1 month, and centrifugation test at 3 000 rpm for 30 minutes. pH and viscosity were measured at 24 h RT, 1 month RT, and 1 month 50 °C. pH was measured by a pH meter and viscosity by a viscometer at 20 rpm at room temperature. Visual inspection was used to assess the apparent stability of emulsion samples.

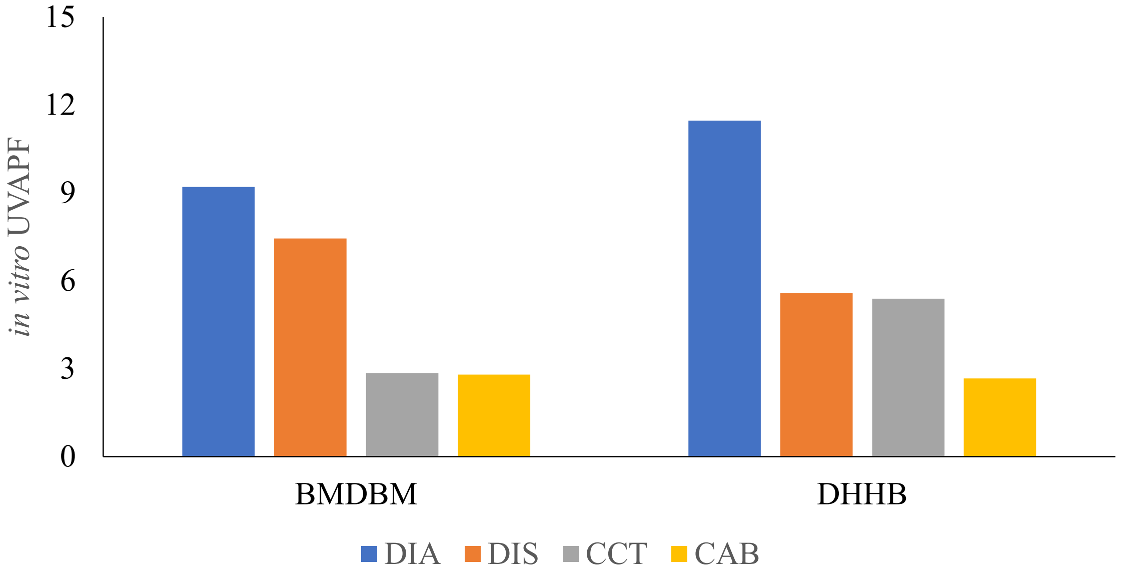
Results.

From the solubility test results (**Figure 2**), DIS exhibited the highest solubilization power for BMDBM (16%), followed by DIA, CCT, CAB, and LL. Regarding DHHB, DIA provided the greatest solubilization (26%), followed by DIS, CAB, CCT, and LL. For EHT, LL showed the highest solubility (26%), much greater than that of DIS, CCT, DIA, and CAB (only 2%). However, tested emollients did not give remarkable solubility data for BEMT, just 13% with CAB as the most, and the rest of the emollients provided less than 10%.


30%
25%
20%
15%
10%
5%
0%
BMDBM
DHHB
BEMT
EHT
■ DIA ■ DIS ■ LL ■ CCT ■ CAB
BMDBM/DIA
BMDBM/DIS
BMDBM/CCT
BMDBM/CAB
DHHB/DIA
DHHB/DIS
DHHB/CCT
DHHB/CAB
EHT/DIA
EHT/DIS
EHT/CCT
EHT/CAB
EHT/LL

(A)

(B)



(C)

Figure 2. (A) Solubility chart of crystalline organic UV filters in emollients. (B) Polarized light microscopic photo (×500 magnification) of organic UV filter-based O/W emulsions at 25 °C after 5 Freeze/Thaw cycles (-18 °C /25 °C). Recrystallization of crystalline UV filter molecules. (C) *in vitro* UVAPF analysis of crystalline UVA absorbers in O/W emulsions prepared by different emollients.

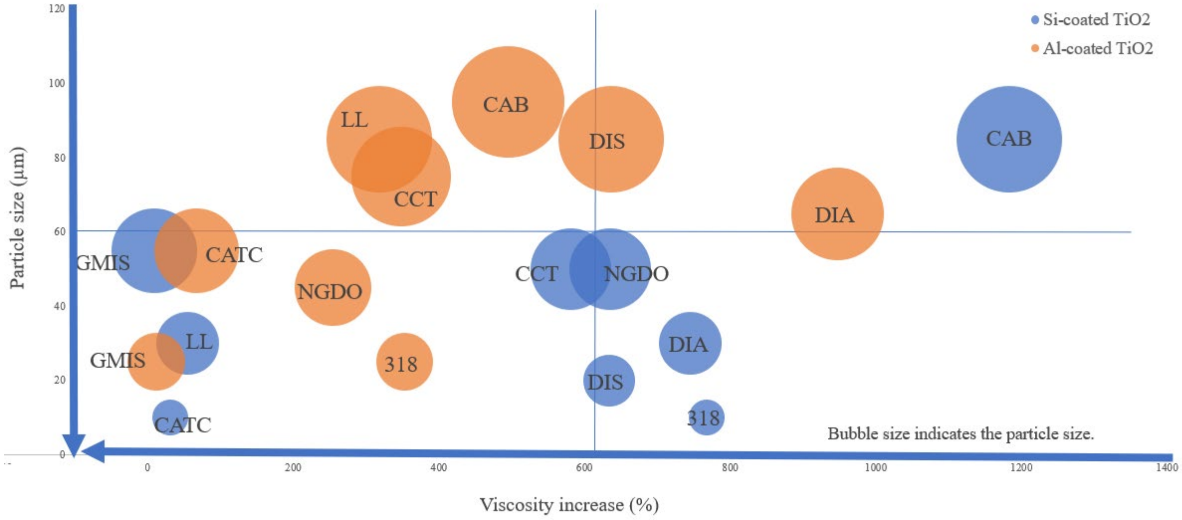
The stability concern of the recrystallization of organic UV filters is reflected in the present study. The polarizing microscopic images of BMDBM and DHHB with different esters in O/W emulsions clearly showed different stability profiles against recrystallization. With DIA and DIS, there was no crystal (a complete dark view) of BMDBM or DHHB observed after Freeze/Thaw cycles, while the UV filters with CCT and CAB displayed needle- and trapezoid-shaped crystals of BMDBM molecule and planar rectangles with rounded ends of DHHB.

Such observations align well with our solubility test results—DIA and DIS exhibited greater solubility capability for BMDBM and DHHB than CCT and CAB. In the case of LL, only LL, the one offering the highest solubility of EHT, passed the recrystallization test under all test conditions.

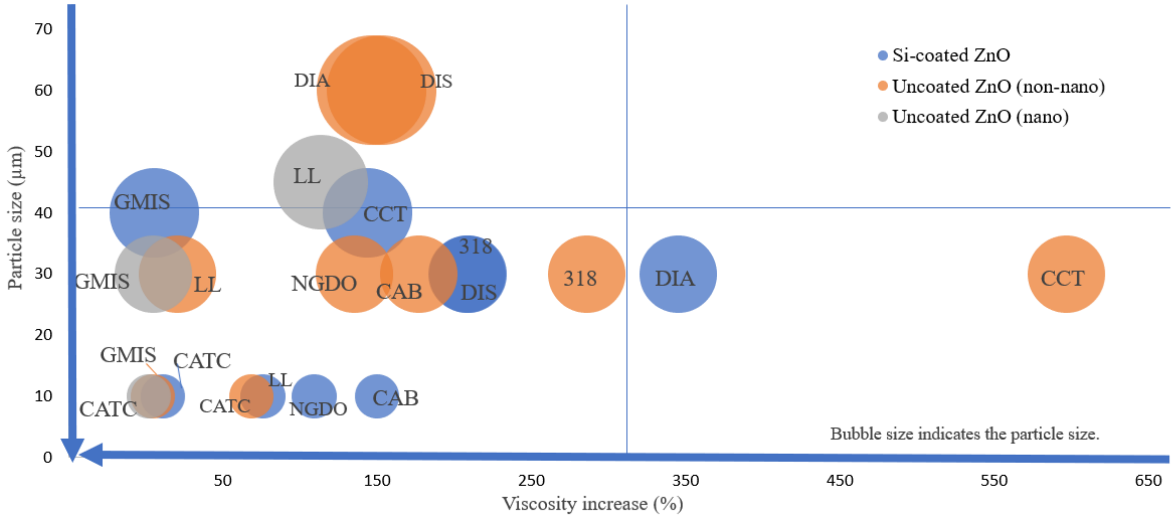
Furthermore, *in vitro* UVAPF analysis of the simple O/W emulsion samples was conducted to assess the performance of the UV filters with different emollients. DIA and DIS were effective in boosting the performance of BMDBM and DHHB against UVA.

The results of emollients' effectiveness in dispersing 30% inorganic UV filters are shown in scattered plots of viscosity increase against particle size (**Figure 3**). The bubble size represents the particle size of the dispersion. An ideal dispersion is small in particle size and viscosity increase—the area at the 3rd quadrant. Silicon-coated titanium dioxide and alumina-coated titanium dioxide are combined in one plane and all types of Zinc Oxide in another. CATC and GMIS stand out with both smaller particle size and less increase in viscosity. The droplet sizes of the TiO_2 particles in 318 are relatively small. LL is good for silicon-coated TiO_2 and NGDO for Al-coated TiO_2. Regarding Zinc Oxide, more emollients are showing a good dispersion for Si-coated ZnO. However, for uncoated nano-sized ZnO, there are not many dispersing candidate emollients. Overall, CATC, GMIS, LL, 318, and NGDO can be selected to disperse Zinc Oxide.

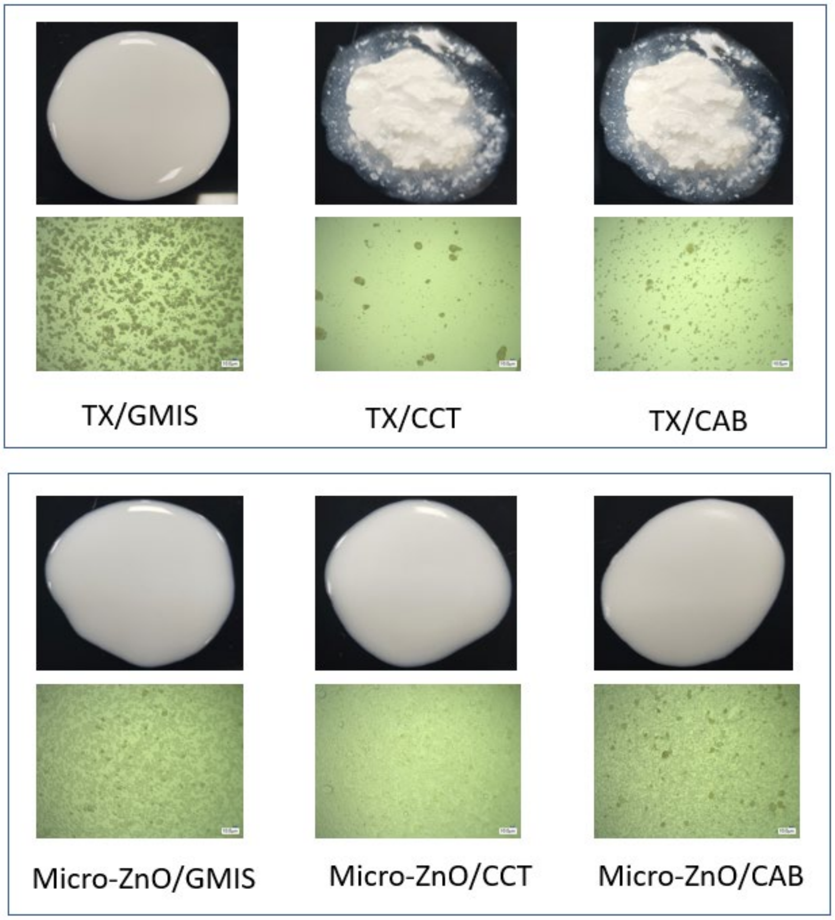
The O/W emulsions made with conventional emulsifiers (Glyceryl Stearate and PEG-100 Stearate) and a common stabilizer (Xanthan Gum) showed limitations in making a smooth and homogenous emulsion with inorganic UV particulates and emollients. Among the emollients tested, GMIS exhibited excellent performance for all types of particulates, and the textures were smooth and glossy. Only a well-dispersed emulsion can give meaningful *in vitro* SPF/UVAPF values.


Si-coated TiO2
Al-coated TiO2
Particle size (µm)
Viscosity increase (%)
120
100
80
60
40
20
0
0
200
400
600
800
1000
1200
1400
LL
CAB
DIS
CAB
CCT
DIA
GMIS
CATC
CCT
NGDO
NGDO
LL
DIA
GMIS
318
DIS
CATC
318
Bubble size indicates the particle size.

(A)


Si-coated ZnO
Uncoated ZnO (non-nano)
Uncoated ZnO (nano)
Particle size (µm)
Viscosity increase (%)
70
60
50
40
30
20
10
0
50
150
250
350
450
550
650
DIA
DIS
LL
GMIS
CCT
318
GMIS
LL
NGDO
CAB
DIS
318
DIA
CCT
GMIS
CATC
LL
CATC
CATC
NGDO
CAB
Bubble size indicates the particle size.

(B)



(C)

Figure 3. Bubble chart of dispersion of 30% TiO_2 (A) and 30% ZnO (B) in 70% emollient bases, respectively. Sample appearances and microscopic images of O/W emulsion containing 5% inorganic UV particulates (TX and Micro-ZnO) and 15% tested emollients.

Discussion.

Emollients provided different levels of solubilization based on the chemical nature of both emollients and UV filters. Good solubilization profiles can help prevent the recrystallization of organic UV absorbers. The recrystallization of UV filters may lead to loss of protection as well as skin irritation.

The *in vitro* UVAPF test results reveal certain boosting effects of emollients on organic UV filters, which maybe because of the participation of emollient molecules in the energy dissipation of UV filter molecules when excited by the UV rays. Emollients play a role not only in stabilizing the organic UV filters but also in their efficiency.

The challenges posed by inorganic UV filters to formulations are very different from organic UV filters. Although inorganic UV filters do have a lot of advantages over organic UV filters in terms of sustainability and safety profile, inorganic particulates require a good medium for them to function in a formulation matrix.

The dispersing property depends on the structure of metal oxides and coating technologies used to make the handling of particulates easier. Based on the dispersion study, uncoated nano-sized Zinc Oxide is one of the most difficult types to disperse. CATC and GMIS performed well regardless of the type of particulates. CATC and GMIS are emollients of medium polarity and relatively higher consistency compared with other emollients tested. They can effectively wet, disperse and stabilize the particles in the system. However, when formulated into an O/W emulsion, the selection of the emulsifier/stabilizer system will affect the overall compatibility and performance. In the system tested, GMIS displayed the best performance.

Conclusion.

Effective UV filter solubilizers and dispersants are proposed respectively, and sample sunscreen formulations are given as references with *in vitro* SPF/UVAPF indications. Proposed tools to study solubility, recrystallization stability, dispersion property, and *in vitro* SPF/UVAPF are provided for formulators who want to assess the performance of emollient esters when developing effective and stable products for sun protection.

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Conflict of Interest Statement.

NONE.

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