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Formulation and characterization of sunscreen creams with synergistic efficacy on SPF by combination of UV filters

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ABSTRACT

The objective of this study was to develop sunscreen cream formulations with high sun protection factor (SPF) and satisfied characteristics. The actives were anisotriazine (an organic UV filter) and titanium dioxide (an inorganic UV filter). Two optimal cream bases selected from several preliminary formulations were prepared and incorporated with both actives in the legislated concentrations via emulsification process. The samples were determined for *in vitro* SPF, physical appearance, pH, and viscosity. Moreover, the sunscreen creams were compared for SPF with those of their counterparts containing either anisotriazine or titanium dioxide at the identical concentrations. The stability was studied under freeze-thaw condition. The results indicated that synergistic efficacy on SPF of sunscreen combination was confirmed. The intrinsic properties of cream bases, especially viscosity, affected the SPF of the final products.

INTRODUCTION

An electromagnetic radiation in sunlight called ultraviolet (UV) has been lengthy been renowned as a main factor causing the skin damage. Three categories of UV based on wavelength include UVC (270 to 290 nm), UVB (290 to 320 nm) and UVA (320 to 400 nm). UVC is absorbed by ozone layer while UVB and UVA can arrive at the earth's surface. Hence, both UVA and UVB can injure the human skin, resulting in sunburns, solar keratosis, photoageing, and severe harms such as skin cancers. Therefore, the sunlight exposure protection by applying effective sunscreen products is necessary (Benson, 2007). Moreover, UV has been known that it probably relates to the skin color since UV can motivate the activity of α-melanin stimulating hormone (α-MSH) (Miller & Tsao, 2009). It can be seen that skin-lightening products have become very popular, especially in Asia (Boonme et al., 2009). Therefore, formulation of sunscreen products with highly efficient is interesting in order to respond the demand of consumers. The efficacy of sunscreen products has been usually measured in form of sun protection factor (SPF) which can be evaluated via either *in vivo* or *in vitro* techniques.

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In general definition, SPF is the ratio of the time duration of UV radiation required to produce erythema in the protected skin (with sunscreen) to that required to produce erythema in the unprotected skin (without sunscreen). Hence, SPF values can inform UVB protection efficacy of the sunscreen products. There are two main types of active ingredients used in sunscreen products to control the amount of UV radiation penetrating the skin, i.e. organic and inorganic UV filters. The organic or chemical sunscreens can chemically absorb UV light while the inorganic or physical sunscreens can reflect and scatter UV light (Serpone et al., 2007).

Many strategies are proposed for preparation of sunscreen products with high SPF such as nanotechnology formulations (Linn et al., 1990; Xia et al., 2007) and UV filter combinations (El-Boury et al., 2007; Couteau et al., 2008). The last method has high tendency in industries since it requires the identical preparation process to the conventional one; only ingredients in the formulations are adjusted. However, it was reported that the effectiveness of sunscreen products has been influenced by their solvents or vehicles (Agrapidis-Paloympis et al., 1987).Thus, the aims of this study were to investigate effects of cream formulations on SPF values of sunscreen creams containing the blends of organic and inorganic UV filters as the actives and to verify the synergistic efficacy on SPF by combination of the UV filters.

Anisotriazine and titanium dioxide were used as organic and inorganic UV filters, respectively. Anisotriazine is a broad-spectrum UV absorber since it has two absorption peaks at 310 and 340 nm while titanium dioxide blocks UV light through reflection and scattering properties. They are lipophilic and their maximum concentration authorized are 10% and 25%, respectively (Couteau, et al., 2007; El-Boury, et al., 2007).

MATERIALS AND METHODS

Materials

Anisotriazine was given as a gift from The Sun Chemical, Thailand. Titanium dioxide was purchased from S. Tong Chemicals, Thailand, respectively. All chemicals used in cream formulations (i.e., Amerchol L 101, butylhydroxytoluene (BHT), Carbopol Ultrez 21, Cetiol HE, cetyl alcohol, dimethicone, Eumulgin B1, Eumulgin B2, glycerin, glycerylmonostearate self-emulsifying (GMS SE), isopropyl palmitate, methylparaben, mineral oil, propylene glycol, propylparaben, sorbitan monostearate, stearic acid, triethanolamine**,** xanthan gum) were cosmetic or pharmaceutical grade, purchased from local distributors in Thailand and used without further modification. Paraben concentrate containing 10% methylparaben and 2% propylparaben in propylene glycol was prepared in-house for using as a preservative in the cream formulation. Distilled water was used throughout the experiments.

Table. 1: Formulations of the investigated sunscreen creams.

F1		F2	
Oil Phase		**Oil Phase**	
Amerchol L 101	3.0g	Mineral oil	6.0g
Dimethicone	0.5g	Cetiol HE	2.5g
Stearic acid	1.5g	BHT	0.005g
Cetyl alcohol	0.5g	Stearic acid	2.0g
Isopropyl palmitate	2.5g	Eumulgin B1	0.75g
GMS SE	1.5g	Eumulgin B2	0.75g
Anisotriazine	Qs	Anisotriazine	Qs
Titanium dioxide	Qs	Titanium dioxide	Qs
Aqueous Phase		**Aqueous Phase**	
Triethanolamine	0.5g	Glycerin	2.0g
Propylene glycol	2.0g	Propylparaben	0.025g
Paraben concentrate	0.5g	Methylparaben	0.05g
Water to	50.0g	Xanthan gum	0.45g
		Triethanolamine	0.15g
		Water to	50.0g

Preparation of sunscreen creams

Several cream bases were formulated in the preliminary study. The components used were in a generally recognized as safe (GRAS) status. The cream bases were prepared via emulsification process. Briefly, an oil phase containing lipophilic substances and an aqueous phase containing hydrophilic substances were separately heated in a water bath to 80±2°C. Afterwards, the aqueous phase was gradually added into the oil phase with constantly stirring until the mixture was congealed at the room temperature.

The resulted cream bases were optically observed for appearance, texture and spreadability. It was found that three cream bases had desirable properties; however, only two bases provided good characteristics after incorporated with anisotriazine and titanium dioxide (Boonme & Amnuaikit, 2013). Thus, they were adapted for using in this study as exhibited in Table 1 and then incorporated with pure active or combination of the actives. Anisotriazine was investigated at the concentrations of 4, 6, or 8% while titanium dioxide was investigated at the concentrations of 8 or 12%. All studied concentrations were in the legislated range. Both actives were incorporated in an oil phase in order to prepare the sunscreen creams by emulsification process as previously described.

SPF measurement of sunscreen creams

The monochromatic protection factor (MPF) values of the creams were *in vitro* evaluated by a SPF-290S analyzer (Optometrics Corporation, USA) based on spectral transmittance measurement which carried out between 290 and 400 nm. Each sample was applied and spread on Transpore tape which was placed on a frame of the analyzer, approximately 2 mg/cm^2. The sample was then exposed to light from xenon lamp. The measurement was performed at least six replicates for each sample. The obtained MPF values were finally used to calculate the *in vitro* SPF values of the samples with WinSPF software. The *in vitro* SPF values of the sunscreen creams containing both UV filters were also compared with those of their cream counterparts containing either anisotriazine or titanium dioxide at the identical concentrations.

Physical characterization and stability study of sunscreen creams

Appearance and texture of the creams was optically observed. Viscosity values at 25°C of the creams were measured in triplicate using a Brookfield DV-III Ultra rheometer (Brookfield Engineering Laboratories Inc., USA) fitted with a LV spindle Number 4 at 10 rpm. Brookfield Rheocalc operating software (version 3.1-1) was used to control the rheometer. The samples were determined for pH values at 25°C by a pH meter (Mettler Toledo, Switzerland). The sample characteristics were evaluated after preparation and after storage in freeze and thaw condition (4 and 45 °C, 24 hours for each storage temperature) for 6 cycles. All measurements were carried out in triplicate.

RESULTS AND DISCUSSION

SPF values of the obtained sunscreen creams

The *in vitro* SPF values of the sunscreen creams containing both anisotriazine and titanium dioxide in various concentrations as the actives but incorporated in different cream formulations were shown in Table 2. It was noted that the SPF values were not directly depended on UV filter concentrations or cream formulations. For example, at the same cream base, the mean SPF values of F1 with 8% titanium dioxide but various concentrations of anisotriazine were in the range of F1-6A8T > F1-8A8T > F1-4A8T. The mean SPF values of F1 with 12% titanium dioxide but various concentrations of anisotriazine were

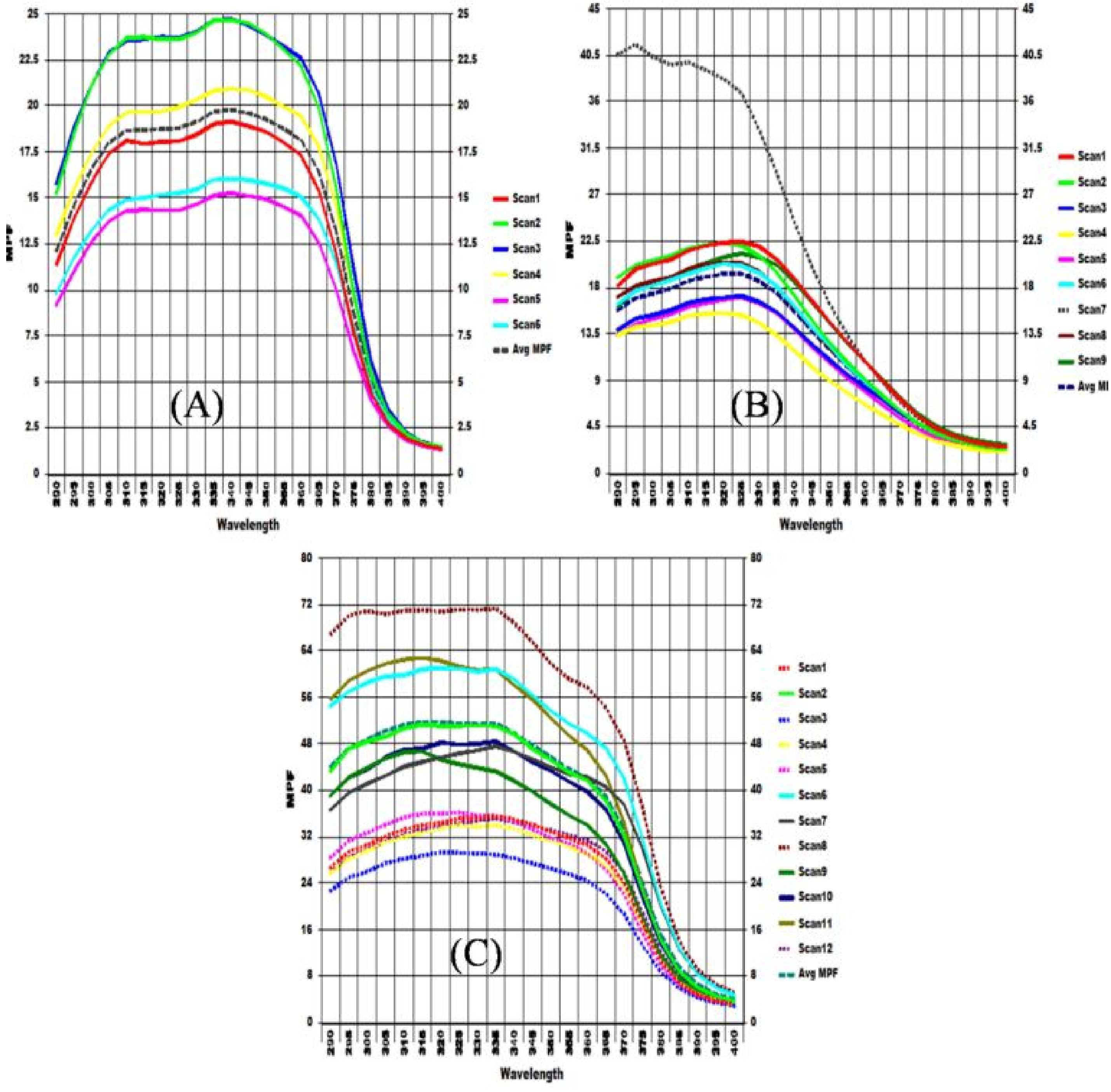

Fig. 1: SPF-290S graph reports of (A) F1-4A0T, (B) F1-0A12T, and (C) F1-4A12T.

in the range of F1-4A12T > F1-8A12T ≈ F1-6A12T. At the same concentrations of the actives, the mean SPF values of F1 sunscreen creams were higher than those of F2 sunscreen creams, except at 8% anisotriazine. The reasons were unclear; however, it was found that the intrinsic characteristics of sunscreens might relate to the measured SPF values as discussing in next topic.

Table. 2: SPF values of the sunscreen creams containing various concentrations of anisotriazine and titanium dioxide ($n \geq 6$).

Sunscreen %	SPF of F1 with various anisotriazine and titanium dioxide (TiO_2)		
	4% Anisotriazine	**6% Anisotriazine**	**8% Anisotriazine**
8% TiO_2	24.79±5.89 (F1-4A8T)	37.22±8.67 (F1-6A8T)	31.45±4.02 (F1-8A8T)
12% TiO_2	45.43±7.40 (F1-4A12T)	41.06±6.56 (F1-6A12T)	42.22±6.85 (F1-8A12T)
Sunscreen%	**SPF of F2 with various anisotriazine and titanium dioxide (TiO_2)**		
	4% Anisotriazine	**6% Anisotriazine**	**8% Anisotriazine**
8% TiO_2	22.81±3.14 (F2-4A8T)	35.51±9.47 (F2-6A8T)	41.58±5.63 (F2-8A8T)
12% TiO_2	25.19±4.29 (F2-4A12T)	25.62±2.95 (F2-6A12T)	42.94±3.43 (F2-8A12T)

Table 3 showed SPF comparison between F1 with UV filter combination (4%, 6% or 8% anisotriazine and 12% titanium dioxide) and F1 with either UV filter at the identical concentrations. It was found that the SPF values of the creams containing a combination of anisotriazine and titanium dioxide were higher than those containing an active, anisotriazine only or titanium dioxide only. A combination of UV filters could provide more SPF values due to synergistic effect (El-Boury et al., 2007; Couteau, et al., 2008). Moreover, sunscreen creams with a combination of UV filters could provide high MPF in wider wavelength range than those with a UV filter as illustrated in Fig1.

Table. 3: SPF comparison between F1 with UV filter combination and F1 with either UV filter ($n \geq 6$).

Sunscreen %	SPF of F1 with various anisotriazine and titanium dioxide (TiO_2)			
	0% Anisotriazine	**4% Anisotriazine**	**6% Anisotriazine**	**8% Anisotriazine**
0% TiO_2	-	16.49±2.41 (F1-4A0T)	20.64±3.63 (F1-6A0T)	16.06±2.47 (F1-8A0T)
12% TiO_2	16.24±2.41 (F1-0A12T)	45.43±7.40 (F1-4A12T)	41.06±6.56 (F1-6A12T)	42.22±6.85 (F1-8A12T)

Table. 4: Viscosity and pH of the samples (n=3).

Sample	Viscosity (cps)		pH	
	After preparation	**After stability test**	**After preparation**	**After stability test**
F1-4A8T	$2.8\times10^5\pm100$	$3.0\times10^5\pm150$	7.71±0.03	8.00±0.02
F1-6A8T	$3.6\times10^5\pm95$	$2.8\times10^5\pm120$	7.79±0.01	7.97±0.02
F1-8A8T	$4.4\times10^5\pm116$	$8.0\times10^5\pm711$	7.83±0.05	8.04±0.01
F1-4A12T	$4.6\times10^5\pm500$	$6.8\times10^5\pm200$	7.91±0.08	7.90±0.03
F1-6A12T	$4.6\times10^5\pm100$	$6.4\times10^5\pm390$	8.01±0.08	8.03±0.02
F1-8A12T	$5.8\times10^5\pm870$	$6.4\times10^5\pm458$	8.02±0.09	8.10±0.10
F2-4A8T	$0.4\times10^5\pm70$	$3.2\times10^5\pm134$	6.62±0.05	6.64±0.01
F2-6A8T	$0.2\times10^5\pm870$	$5.0\times10^5\pm420$	6.52±0.02	6.35±0.08
F2-8A8T	$0.4\times10^5\pm0$	$0.5\times10^5\pm1775$	7.01±0.03	7.02±0.03
F2-4A12T	$0.8\times10^5\pm110$	$5.4\times10^5\pm343$	6.21±0.04	6.15±0.01
F2-6A12T	$0.8\times10^5\pm220$	$8.2\times10^5\pm1850$	6.41±0.02	6.37±0.05
F2-8A12T	$0.8\times10^5\pm190$	$15.8\times10^5\pm2840$	6.31±0.01	6.03±0.01

Characteristics of the samples before and after stability test

All samples were off-white creams as seen in Fig 2. The texture of the F1 samples seemed to be stickier than that of the F2 samples. No phase separation and changing in color as well as odor were observed in all samples after stability test; however, they seemed to be more viscous.

Fig. 2: Appearance of the prepared sunscreen creams.

As seen in Table 4, the viscosity values of the F1 samples were much higher than those of the F2 samples. Both F1 and F2 sample groups had increasing viscosity values after storage in freeze-thaw condition. All samples were oil-in-water creams; hence, their water content might lose at fluctuated temperatures. Therefore, the suggested storage condition for these products should be at constant temperature. Furthermore, it was obviously found that the viscosity values of the sunscreen creams were directly related to the obtained SPF values. The formulations with suitable viscosity could provide more adhesiveness and spreading efficacy. In previous report, SPF values measured by *in vivo* method in 30 volunteers of the sunscreen formulations were found to be depended on rheological behavior (Gaspar & Maia-Campos, 2003). The averaged pH values of all samples were around 6-8 as shown in Table 4, implying that they were safe for application on the skin. The pH values of the F1 samples were slightly higher than those of the F2 samples due to more amount of triethanolamine in F1 formulations. After stability test, no appreciable change in pH was observed in any sample. This result might imply to that there were no degradation or chemical change in all studied formulations. With respect to the obtained data of SPF values and physical characteristics, F1 samples, especially F1-4A12T, possessed high SPF value, desirable properties and good stability. Thus, F1-4A12T should be further investigated for consumer's satisfaction.

CONCLUSIONS

Combination of organic and inorganic UV filters could provide synergistic efficacy on SPF. Additionally, SPF of the sunscreen cream was depended on the intrinsic characteristics of cream bases, especially viscosity. In this current study, formulation of sunscreen creams with high SPF, aesthetic appearance and acceptable viscosity as well as pH on skin application could be obtained by combination of 4% anisotriazine and 12% titanium dioxide, and incorporation in suitable cream base formulation (F1).

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