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Method for screening sunscreen cream formulations by determination of *in vitro* SPF and PA values using UV transmission spectroscopy and texture profile analysis

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Synopsis

Formulation of sunscreen products to obtain high values of sun protection factor (SPF) and protection from ultraviolet A (PA) is challenging work for cosmetic chemists. This study aimed to study factors affecting SPF and PA values using ultraviolet transmission spectroscopy as well as texture profiles of sunscreen formulations using 2^3 factorial designs. Results demonstrate that the correlation coefficient between the labeled SPF values of counter-brand sunscreen products and the *in vitro* SPF values was 0.901. *In vitro* SPF determination showed that the combination effect of phase volume ratio (PVR) and xanthan gum caused a significant increase to the SPF values of the formulations, whereas the interaction effect between PVR and stearic acid significantly decreased the SPF value. In addition, there was the interaction effect between xanthan gum and stearic acid leading to significant reduction of hardness, compressibility, and pH, but significantly increasing the adhesiveness. All tested factors did not significantly affect the cohesiveness of tested formulations. In conclusion, apart from sunscreen agents, the other ingredients also affected the SPF and PA values. The calculated SPF values range from 21 to 60. However, a selected formulation needs to be confirmed by the standard method of testing. In addition, the physical, chemical, and biological stability; shelf life; and sensory evaluation of all formulations need to be evaluated.

INTRODUCTION

It is generally known that ideal sunscreen products should be able to protect skin from damage from ultraviolet (UV) radiation (290–400 nm). Long-term exposure to UVB (290–320 nm) and UVA (320–400 nm) may cause sunburn, immunosuppression, and skin cancer (1–3). The efficacy of sunscreen products may be indicated by numerical rating of sun protection factor (SPF) and UV-A protection (PA). Several attempts have been made to develop *in vitro* SPF testing methods (1,4–11), but there is no officially recognized

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method due to the limitation of measurement techniques (12). In 2011, Cosmetics Europe, formerly known as COLIPA, provided guidelines for an *in vitro* method for the determination of the UVA protection factor and critical wavelength values for sunscreen products using PMMA plates (polymethylmethacrylate) as a substrate for applying the tested sunscreen product (13,14). However, in the case of having limitation on the assessment of SPF and PA values using the standard guidelines, *in vitro* preliminary screening of processing variables in an earlier stage of sunscreen formulations such as sun protection efficacy using UV spectrophotometer appears to be practical. Moreover, the physical properties measurements, texture profiles, and stability studies should be simple, rapid, and reproducible, and provide important information before proceeding to the *in vivo* test, which is very expensive, time-consuming, and prone to having risks related to UV exposure of human volunteers. In addition, the relationship between the product texture measurement and sensory skin perception may be useful to predict consumer responses. In this study, although *in vitro* SPF testing methods demonstrated that the *in vitro* SPF values underestimated the *in vivo* SPF values, using a linear regression equation for the relationship between labeled SPF value and calculated SPF by UV transmission spectroscopy appears to be simple and directly proportional to the *in vivo* SPF values (15). Moreover, texture analysis may also be used for product characterization and stability evaluation. Many studies have demonstrated that there is a relationship between sensory and instrumental texture profiles in some aspects of food and cosmetic emulsions (16–20). As a result, a correlation between physical measurements and certain sensory attributes of the semi-solid products can be useful for a fast in-line screening study.

The aim of this study was to investigate factors affecting SPF and PA values of sunscreen formulations and their texture profiles. The SPF and PA values of the formulation were carried out using UV transmission spectroscopy.

MATERIALS AND METHODS

MATERIALS

Titanium dioxide (and) diethylhexyl carbonate (and) polyglyceryl-6 polyhydroxystearate was a gift from Evonic, Bangkok, Thailand. C12-15 Alkyl benzoate (and) dipropylene glycol dibenzoate (and) PPG-15 stearyl ether benzoate and other ingredients at cosmetic grade were purchased from Numsieng, Bangkok, Thailand. Two standard sunscreen products, which were the standard homosalate sunscreen (8%) with the mean SPF value of 4.47 and the high standard SPF value of 15, were prepared according to the recommendation of theUnited States Food and Drug Administration (FDA) (21) and COLIPA (22), respectively. The international counter-brand sunscreen products were purchased from a drug store.

METHODS

Factorial design experiments. Sunscreen formulations were prepared based on 2^3 factorial designs. The following three factors were investigated: (i) oil to water phase volume ratio (PVR), concentrations of (ii) Xanthan gum, and (iii) stearic acid. Their levels are shown

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Table I
Factorial Design Parameters and Experimental Conditions

Factors	Levels	
	Low (−)	High (+)
(A) Phase volume ratio (oil:water)	25:75	30:70
(B) Xanthan gum	0%	0.30%
(C) Stearic acid	3%	5%

in Table I. The response parameters are calculated SPF and PA values as well as texture profiles of the developed formulations.

Formulations and preparation of sunscreen products. The ingredients of sunscreen formulations (F1–F8) in Table II were prepared based on a 2^3 factorial design layout shown in Table III. The center point of each factor was presented in F9. The oil phase containing octylmethylcinnamate, titanium dioxide (and) diethylhexyl carbonate (and) polyglyceryl-6 polyhydroxystearate, light mineral oil, stearic acid, C12-15 alkyl benzoate (and) dipropylene glycol dibenzoate (and) PPG-15 stearyl ether benzoate, Span 80, and butylated hydroxy toluene were mixed and heated in a water bath to 70°C. The water phase containing

Table II
Ingredients of Sunscreen Formulations Based on 2^3 Factorial Design

	F1	F2	F3	F4	F5	F6	F7	F8	F9
Octylmethoxycinnamate	7	7	7	7	7	7	7	7	7
Titanium dioxide (and) diethylhexyl carbonate (and) polyglyceryl-6 polyhydroxystearate	10	10	10	10	10	10	10	10	10
Mineral oil	2.5	7.5	2.5	7.5	0.5	5.5	0.5	5.5	4
Stearic acid	3	3	3	3	5	5	5	5	4
C12-15 alkyl benzoate (and) dipropylene glycol dibenzoate (and) PPG-15 stearyl ether benzoate	2	2	2	2	2	2	2	2	2
Vitamin E acetate	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Span 80	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Propylene glycol	3	3	3	3	3	3	3	3	3
Cabopol 940	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Xanthan gum	—	—	0.3	0.3	—	—	0.3	0.3	0.15
Triethanolamine	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
BHT	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
EDTA	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Tween 80	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Propylene glycol (and) diazolidinyl urea (and) methylparaben (and) propylparaben	1	1	1	1	1	1	1	1	1
Purified Water qs to	100	100	100	100	100	100	100	100	100

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Table III
2^3 Factorial Design Layout

Combination	Formulation	Composition A	Composition B	Composition C
(1)	F1	−	−	−
A	F2	+	−	−
B	F3	−	+	−
AB	F4	+	+	−
C	F5	−	−	+
AC	F6	+	−	+
BC	F7	−	+	+
ABC	F8	+	+	+
	F9	0	0	0

propylene glycol, carbopol 940, xanthan gum, EDTA (tetra sodium), Tween 80, and deionized water were mixed well before adding triethanolamine. The water phase mixture was then heated in water bath to 75°C and poured into the oil phase mixture. After that, the emulsion mixture was continuously stirred until the temperature reached 45°C. Then, vitamin E acetate, propylene glycol, diazolidinyl urea, methylparaben, and propylparaben were added and homogenized for 5 min.

Determination of in vitro SPF and PA values. An opened window in thick plastic with a dimension of 0.8 × 2 cm^2 was made as a sample holder. Transpore® tape of size 1.2 × 3 cm^2, which was taped one-side with transparent tape, was used as a sample plate. Sunscreen products, 2 mg/cm^2, were applied evenly on the whole surface of the rough side of the sample plate. After weighing, the sample was spread using light circular strokes over the whole surface of the plate and allowed to dry for 15 min at room temperature. Seven plates were prepared for each tested sample. The transmittance of UV in a range of 290–400 nm through the sample plate was measured against a blank plate using UV-visible spectrophotometer UV-17000 PharmaSpec (Shimazu, Japan).

Determination of SPF according to the method of Diffey and Robson (6)

In vitro SPF was calculated as in equation (1):

$$\textit{In vitro}\ \mathrm{SPF} = \frac{\sum_{290}^{400} E(\lambda) \in (\lambda)}{\sum_{290}^{400} E(\lambda) \in (\lambda) / T(\lambda)} \quad (1),$$

where $E(\lambda)$ is the spectral irradiance of the used light spectrum at wavelength λ nm, $\in(\lambda)$ is the erythemal action spectrum at wavelength λ nm corresponding to the International Commission on Illumination (CIE) publication (23), and $T(\lambda)$ is the spectral transmittance of the sunscreen.

The calculated SPF values were obtained from equation (1). A corrected SPF value for samples was determined using a linear regression equation plotted between the label SPF values of SPF 4.47 and SPF 15 as well as the labeled SPF and PA values of the international

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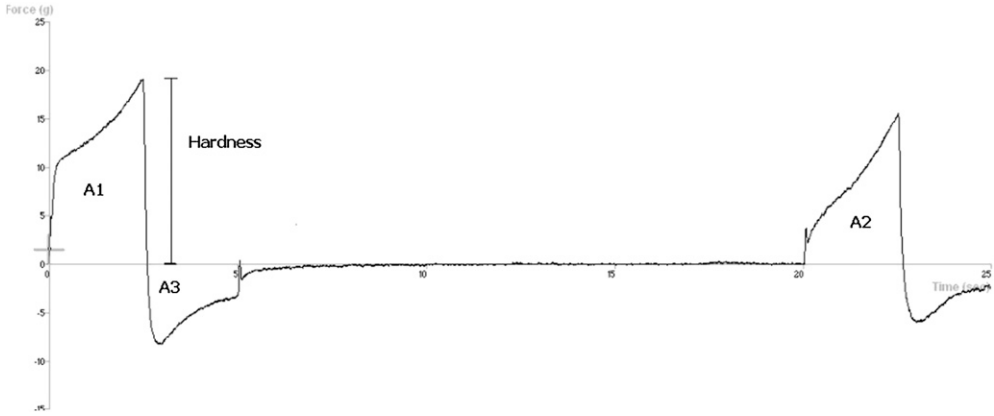

Figure 1. Correlation between labeled SPF and calculated SPF of tested counter-brand sunscreen products.

counter-brand sunscreen products in Figure 1, which were found to have a good correlation with a determination of coefficient (r^2) of 0.901.

Determination of UVA-PF according to the method of Ferrero *et al.* (8)

In vitro UVA-PF was calculated with spectral range of 320–400 nm as in equation (2):

$$\textit{Invitro}\ \mathrm{UVA-PF} = \frac{\sum_{320}^{400} \Delta\lambda}{\sum_{320}^{400} T_\lambda \cdot \Delta\lambda} = \frac{1}{T_m} \qquad (2),$$

where T_m is the arithmetic mean of the transmittance data in the UVA range. UVA-PF was classified according to the Japan Cosmetic Industry Association into four categories as follows: UVA-PF < 2: no protection against UVA; 2–4 (PA+): protection against UVA; 4–8 (PA++): considerable protection against UVA; and ≥8 (PA+++): the greatest protection against UVA (2).

Instrumental texture analysis of sunscreen formulations. Each sample was packed with a height of 7 cm in a 28-ml McCartney bottles (S Murray & Co., Surrey, UK) and kept at 25 ± 1°C for 48 h before performing texture profile analysis. The texture profiles of each formulation were determined according to Jones *et al.* (17) with some modification using a texture analyzer (Model TA.XT Plus, Stable Micro Systems, Surrey, UK). A stainless steel probe of 1 cm in diameter (P/0.5R) was compressed twice into the sample at a defined rate of 6 mm·s^{-1} to a depth of 1.5 cm, with a delay period of 15 s between the two compressions. Data collection and calculation were performed using the XTRA Dimension software package of the instrument. The texture profile analysis values of hardness, compressibility, adhesiveness, and cohesiveness of sunscreen samples were calculated by determining the load and displacement at predetermined points on the texture profile analysis curve (Figure 2). Hardness was the maximum force required to attain a given deformation of the sample during the first compression. Compressibility was the work required to deform the sample during the first compression (A_1). Adhesiveness (A_3) was the work required to overcome the attractive force

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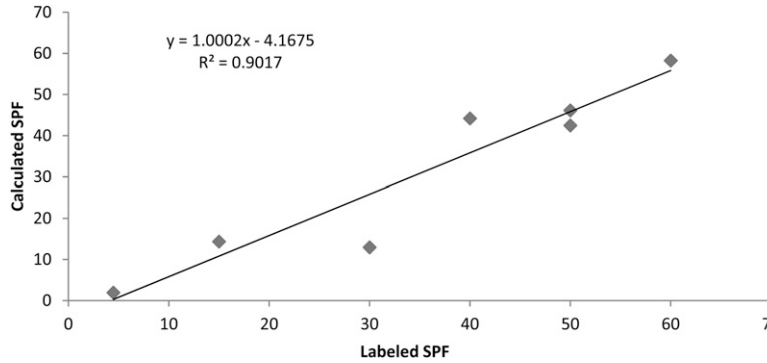

Figure 2. Texture profile curve of a sample.

between the surface of the sample and the surface of the probe. Cohesiveness (A_2/A_1) was the ratio of the area under curve for the second compression (A_2) to that under curve for the first compression (A_1). Four replicate analyses were performed for each formulation at 25 ± 1°C.

Physical stability study. Each sample underwent six cycles of freeze-thaw cycling. In each cycle, the sample was kept at 4 ± 1°C for 24 h following by keeping at 45 ± 1°C for 24 h. Before and after undergoing the freeze-thaw cycling, texture profiles, viscosity, and pH of each formulation using a flat electrode (Metler Toledo in Lab surface, Greifensce, Switzerland) were examined. The viscosity of each sample was measured at 25 ± 1°C using a digital Brookfield Viscometer (Model DV-III+ Programmable Rheometer, Stoughton, MA) mounted on the helipath stand fitted with a T-F spindle. The rheometer was set at 5 rpm. The apparent viscosity, expressed as centripoints (cPs), was an average of the data points collected for 30 s.

Statistical analysis. Unless otherwise stated, all experiments were performed in triplicate. The effects of PVR, xanthan gum, and stearic acid on SPF and PA values as well as texture profiles among formulations were evaluated using regression analysis. The differences between before and after freeze-thaw cycling of each formulation were analyzed using a paired-samples *t*-test. $p < 0.05$ denoted statistical significance. All statistical analyses were performed using SPSS software.

Mathematical models for 2^3 full factorial design were obtained, relating the responses with the experimental conditions as follows:

$$y = b_0 + b_1 A + b_2 B + b_3 C + b_{12} AB + b_{13} AC + b_{23} BC \quad (3),$$

where the coefficients estimations were b_1, b_2, and b_3 corresponding to the response obtained with the factors A, B, and C, respectively. The interaction coefficients were b_{12}, b_{13}, and b_{23} corresponding to the response obtained with interaction terms of AB, AC, and BC respectively.

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Table IV
SPF and PA Values Labeled on the Reference Products in Comparision with Their Corrected Values from Equation (1) and PA Grading Values from Equation (2)

Sample	SPF (cal) ± S.D.	SPF (labeled)	PPD ± S.D.	PA (cal)	PA (labeled)
SPF 4.47	1.92 ± 0.52	4.47	–	–	–
SPF 15	14.36 ± 2.61	15	3.53 ± 0.20	2+	–
S1	12.97 ± 2.07	30	5.29 ± 0.47	2+	2+
S2	44.19 ± 3.50	40	9.91 ± 1.02	3+	–
S3	42.48 ± 8.16	50	8.37 ± 1.83	2+	3+
S4	46.15 ± 10.23	50	15.45 ± 1.51	3+	3+
S5	58.25 ± 0.85	60	15.12 ± 1.36	3+	3+

S#: Sample number from a counter-brand sunscreen product.

Table V
Corrected SPF and PA Values of Test Samples

Sample	SPF (cal) ± S.D.	PPD ± S.D.	PA (cal)
F1	21.81 ± 4.28	4.45 ± 1.51	2+
F2	29.27 ± 2.75	6.59 ± 1.62	2+
F3	38.54 ± 3.11	6.57 ± 0.73	2+
F4	53.82 ± 5.41	9.78 ± 1.83	3+
F5	60.68 ± 10.89	11.99 ± 1.83	3+
F6	26.05 ± 4.35	6.72 ± 2.30	2+
F7	40.18 ± 5.73	7.17 ± 1.78	2+
F8	32.92 ± 2.3	6.05 ± 0.39	2+
F9	30.98 ± 2.43	6.83 ± 0.51	2+

RESULTS

As shown in Table V, SPF and PA values of F1, F5, and F4 were 21.81/2+, 60.68/3+, and 53.82/3+, respectively. F5 and F4 appeared to have good protection against UVB and UVA. The difference between F5 and F4 was the PVR and the presence of xanthan gum. When comparing the components in F1, F5, and F4 (Tables II and III), it was found that F1 contained a low level of PVA, had no xanthan gum, and a low level of stearic acid, whereas F5 contained a low level of PVR with an absence of xanthan gum and a high level of stearic acid and F4 contained a high level of PVR and xanthan gum with low stearic acid.

The formulations having high levels of PVR and xanthan gum with low levels of stearic acid (F4) appeared to possess SPF values of 53.82, which was greater than the formulation containing low levels of PVR and stearic acid with high levels of xanthan gum (F3) having an SPF value of 38.54. This indicates that formulations having a higher level of PVR and xanthan gum can improve the SPF values. In contrast, if the level of xanthan gum was low and stearic acid was high, the formulation that contains a low level of PVR (F5) was found to have an SPF value of 60.68, which was much greater than the formulation containing a high level of PVR (F5), which had the SPF value of only 26.05. This indicates that there is an interaction between PVR and the amount of stearic acid.

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F5 and F4 appear to have good protection against UVB and UVA. Even though a high level of PVR could significantly increase the SPF value, the high level of stearic acid significantly affected the SPF value more than the PVR did. However, due to the interaction between PVR and stearic acid, the high level of PVR and stearic acid (F6) caused a significant lowering of the SPF value, while a low level of PVR and a high level of stearic acid (F5) resulted in an increase in the SPF value (Tables II and V). In addition, adding xanthan gum to F5 could improve the SPF value (F7), but not as effectively as that of F5.

Regression analysis revealed that all three factors which were PVR and the concentrations of xanthan gum and stearic acid significantly affected the calculated SPF values. It should be noted that interaction between PVR and xanthan gum possessed a positively significant effect on the SPF value. In contrast, interaction between PVR and stearic acid, and xanthan gum and stearic acid caused a negatively significant effect on the SPF values.

All three factors affected the texture profiles of the tested products (Table VI). Although PVR caused a positively significant effect on the product hardness, it had a negatively significant effect on their adhesiveness. In addition, the amount of stearic acid in the formulations caused a negatively significant effect on the product hardness and compressibility but it caused a positively significant effect on the product adhesiveness. Nevertheless, the interaction effect between xanthan gum and stearic acid caused a negative effect on the hardness and compressibility of the formulations, while it caused a positive effect on their adhesiveness. Except for interaction between PVR and xanthan gum, it was found that all factors significantly increased the pH of the formulation, whereas the interaction between the main factors significantly decreased pH of the products.

Figure 3 shows the stability of tested formulations after undergoing freeze-thaw cycling. Except for cohesiveness, the texture profiles of F6–F9 were unstable. The pH of F1–F3 and F6 were significantly decreased, whereas the viscosity of F3, F6, F8, and F9 were significantly increased.

DISCUSSION

The variability of COLIPA SPF values depends on the skin type variations of the volunteers. Therefore, 20% deviation of SPF values is acceptable for the requirements of the international standard of SPF test methods (24). Bendova *et al.* (1) demonstrated that methods of SPF *in vitro* testing showed great differences from SPF determination by the COLIPA method of *in vivo* testing because the high variability of *in vitro* SPF values depends on substrate selection and product application technique. Kelley *et al.* (9) found that there was limitation to using Transpore® tape due to its perforation. In this study, the Transpore® tape was modified by sticking transparent tape on one side and applying the sample on the rough side. With this modification, the variation of obtained SPF values appears to be less than 20% deviation, and the test sample was quite uniformly distributed over the plate. In this study, the SPF values, calculated according to a study of Diffey and Robson (6), were less than the labeled SPFs of the majority of counter-brand sunscreen products and the standard sunscreen products, SPF 4.47 and SPF 15. The results of this finding were similar to a study of Sheu *et al.* (15). However, linear regression analysis showed that there was a good correlation between calculated SPF values and labeled SPF values at a coefficient of determination of 0.901. As a result, the calculated SPF

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Table VI
Coefficient Estimation of Tested Factors on Responses

	Coefficient estimation					
Factor	SPF	Hardness	Compressibility	Cohesiveness	Adhesiveness	pH
A: Phase volume ratio (PVR)	7.26*	1.587**	3.893	−0.027	−2.961**	0.140**
B: Xanthan gum	−6.869*	2.181	6.097	−0.067	−2.746	0.322**
C: stearic acid	20.897*	−11.437**	−4.196**	−0.347	11.098*	0.132**
AB: PVR × Xanthan	27.367**	2.62	−0.468	0.067	−2.491	−0.300
AC: PVR × Stearic acid	−22.538**	3.301	−9.568	0.347	−3.693	−0.177**
BC: Xanthan gum × Stearic acid	−17.683**	−2.788**	−20.272*	0.379	5.031**	−0.457**

*$p < 0.05$.
**$p < 0.001$.

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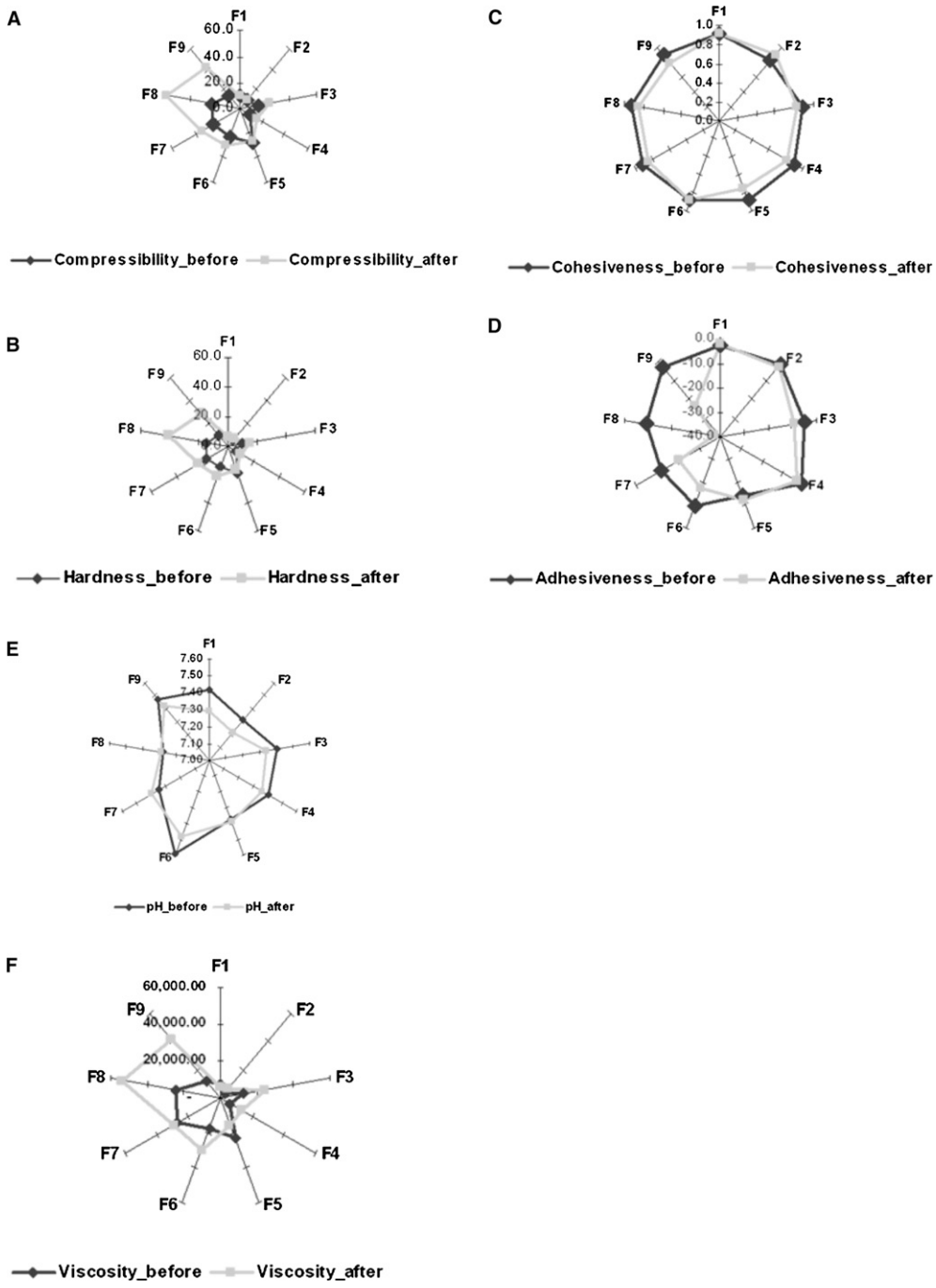

Figure 3. Texture profiles, pH, and viscosity of sunscreen products before and after undergoing freeze-thaw cycling.

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values of samples from equation (1) were corrected using a correlation linear equation in Figure 2 to make the calculated SPF value equivalent to the labeled SPF values of the samples.

Apart from sunscreen active agents, the other ingredients in cosmetic bases and application patterns also affect sunscreen efficacy and cosmetic acceptability (25). Schulz *et al.* (26) demonstrated that SPF values of micronized titanium dioxide in hydrodispersion were less than in o/w emulsion and w/o emulsion. It could increase the SPF value approximately 40% compared to o/w emulsion. This was due to the difference in remaining film thickness and irregularities on the skin. In this study, it was found that for o/w emulsion, the interaction between PVR and thickening agent, which was xanthan gum, led to a significant increase of SPF value. This might be due to the improvement of xanthan gum in the water phase resulting in uniformity and thickness of film after application to the substrate, while the interaction between PVR and the stiffening agent, which was stearic acid, significantly reduced the SPF value. This suggests that a sunscreen formulation which contains a high level of oil phase with low level of stearic acid might significantly reduce the SPF value. However, the formulation F5 contained a low level of oil phase with the absence of xanthan gum and a high level of stearic acid appeared to have the highest SPF, while the formulation with a high level of oil phase (F6) appeared to have the lowest SPF value. These findings indicate that the oil phase and the ratio of stearic acid to liquid oils containing C12-15 alkyl benzoate, dipropylene glycol dibenzoate, PPG-15 stearyl ether benzoate, and mineral oil may play an important role in forming a solid lipid nanostructure matrix that can act as a sunscreen by its light scattering properties (27,28).

Although the advantages of the Transpore® tape are inexpensive, readily available, and ease of use, it is not suitable for formulations containing alcohol or oil as a vehicle because the product would not absorb onto the tape. In addition, the pore size of the tape could vary from batch to batch. Therefore, the tape needs to be validated with standard sunscreen formulations of known SPF before screening any unknown SPF sunscreen product. Furthermore, any ingredient causing a swelling of tape's substrate or solvation of the tape's adhesive might be resulting in poor correlation between *in vitro* and *in vivo* SPF values (29). As a result, Transpore® tape for *in vitro* SPF and PA testing is not recommended by the FDA or COLIPA as a substrate for sunscreen *in vitro* studies. It is only suitable for screening of some categories of sunscreen products.

Jones *et al.* (17) demonstrated that texture profile analysis for the characteristics of semisolids could be used as a tool for development of topical formulations. The mechanical properties in terms of hardness and compressibility indicate the ease of removal of the product from the container, adhesiveness indicates the spreadability and feeling of the product on the skin, and cohesiveness indicates the structural reformation following subsequent applications of a shear stress. In addition, Lukic *et al.* (19) demonstrated that rheological and texture profiles could be used to determine preliminary sensory characteristics of cosmetic cream, and some rheology and texture profiles could be used to predict some sensory attributes. Sensory texture, the impression of the sample thickness when rubbed between thumb and forefinger, directly correlated with hardness and yield value. Slipperiness, the area covered by the sample after rubbing with a circular motion at the forearm, directly correlates with viscosity, elastic and viscous modulus, consistency, and cohesiveness. In this study, the compressibility and hardness of each formulation appeared to be correlated with the viscosity (Figures 3a, 3b, and 3f). Among all formulations, the

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compressibility and hardness of F8 was found to be the highest and F1 was the lowest. These might be due to an interaction between xanthan gum and stearic acid causing a significant lowering of the compressibility, hardness, and adhesiveness as well as the SPF value of the formulation (Table VI).

In conclusion, *in vitro* SPF testing using UV transmission spectroscopy shows a good correlation with the labeled SPF values of counter-brand sunscreen products. According to the sunscreen product development, the *in vitro* SPF testing of the formulation showed the calculated SPF values ranging from 21 to 60. However, care should be taken when using Transpore® tape as a substrate for sunscreen *in vitro* studies due to some limitations. However, a selected formulation needs to be confirmed by a standard method of testing. In addition, the physical, chemical, and biological stability; shelf life; and sensory evaluation of all formulations need to be evaluated.

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