

Safety and efficacy of the combined use of a facial cleanser and moisturizers containing pseudo-ceramide and a eucalyptus extract for Thai non-oily sensitive skin

Panomporn Tongchalaem BS,

Tiyachat Tongpaen MS,

Tsuyoshi Seki MS,

Yutaka Takagi PhD,

Hideyuki Hanazawa MS,

Atsushi Uzu MS,

Koichi Ishida MS,

Suwirakorn Ophaswongse MD.

ABSTRACT:

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From: Skin Care Products Research Laboratories, Kao Corporation, Tokyo, Japan

Corresponding Author: Tsuyoshi Seki, email: seki.tsuyoshi@kao.com

**ASIA RESEARCH LABORATORIES (THAILAND), KAO CONSUMER PRODUCTS (SOUTHEAST ASIA) CO., LTD., BANGKOK, THAILAND.*

***SKIN CARE PRODUCTS RESEARCH LABORATORIES, KAO CORPORATION, TOKYO, JAPAN.*

****DEPARTMENT OF SKIN CENTER, FACULTY OF MEDICINE, SRINAKHARINWIROT UNIVERSITY, BANGKOK, THAILAND.*

Background: In Thailand, many people feel irritation or itching in the sunshine and when they sweat, making them feel that their skin is sensitive.

Objective: To confirm the safety and the efficacy of a combination facial skincare regimen with a weakly acidic well foamed mild facial skin cleanser and moisturizers (lotion and cream) containing pseudo-ceramide and a eucalyptus extract on reducing skin symptoms of Thai non-oily sensitive facial skin.

Methods: We performed a 4-week clinical trial of facial care on 27 Thai females who have sensitive skin with normal or decreased levels of facial sebum. Each subject washed her face with a well foamed cleanser followed by application of an aqueous lotion with a eucalyptus extract and a moisturizing cream containing pseudo-ceramide and a eucalyptus extract twice a day for a total of 4 weeks. Prior to and following the 4 weeks of usage, the skin conditions of each subject were evaluated.

Results: Following 4 weeks of the combination skincare, redness, scaling, and acne were significantly improved. Accompanying those improvements, both skin hydration and cutaneous barrier function improved significantly. A lactic acid sting test indicated a significant decrease in skin sensitivity. No adverse events due to the test samples were observed. The subjects recognized the changes in their skin conditions.

Conclusion: The combination usage of a mild foaming cleanser and an aqueous lotion and moisturizing cream containing pseudo-ceramide and a eucalyptus extract is safe and may be effective for the care of sensitive skin in Thai subjects.

Key words: lactic acid stinging test, barrier function, ceramide, sensitive skin, Thailand

Introduction

Sensitive skin is a condition of self-perceived cutaneous hyper-sensitivity to environmental factors. Although no sign of irritation is commonly detected, itching, burning, stinging and/or a tight sensation are constantly present^{1,2}. Multiple other

factors, such as environmental factors (UV, dryness, cold, heat and wind) and lifestyle factors (usage of cosmetics and skin cleansing) may affect these skin symptoms³. In Thailand, many people recognize their skin as sensitive because they feel irritation or itching from their sweat.

There are many reports that sensitive skin has a lower cutaneous barrier function^{4,6}. Intercellular lipids in the stratum corneum play a crucial role in the barrier functions⁷ and water holding property of the skin⁸, and ceramides are major components of those lipids⁹. The decreased ceramide level in the stratum corneum induces a lower barrier function and less water holding capacity as seen in the skin of atopic dermatitis patients^{10,11}, and topically applied pseudo-ceramide, synthesized to compensate for natural ceramide, improves these cutaneous functions¹²⁻¹⁴. Ishikawa et al. found that a topically applied eucalyptus extract increases ceramide levels in the epidermis accompanied by improvements of stratum corneum function¹⁵. Nojiri et al confirmed the efficacy of a topically applied pseudo-ceramide and eucalyptus on improving sensitive skin in China⁵.

There are various factors that induce sensitive skin, and cleansing with high performance detergents may be one of the major factors. These detergents, which penetrate the stratum corneum, induce skin irritation and also extract natural moisturizing factors (NMF)¹⁶ and intercellular lipids¹⁷. Therefore, the usage of milder facial cleansers may help to improve sensitive skin conditions.

Thus, a combination skincare regimen with mild cleansing followed by intensive moisturizing with ceramide (combination skincare) may be

effective for the care of sensitive skin. Isoda et al. have previously shown that the combined use of a mild facial cleanser and moisturizers containing pseudo-ceramide and a eucalyptus extract is effective for the care of mild acne patients with sensitive skin in Japan¹⁸. However, the stratum corneum function and skin sensitivity may be affected by the temperature and humidity. Oh et al. reported that people in North China have a higher sensitivity against lactic acid compared to people in South China in the winter time¹⁹. Also, there is a report that a higher efficacy of a moisturizing cream was observed in the winter compared to the late spring²⁰. Therefore, consensus guidelines for the management of atopic dermatitis in Asia-Pacific subjects were published recently,²¹ which recommends the use of a moisturizer not only depending on skin type and degree of dryness, but also on the humidity of the climate.

In the present study, we evaluated the safety and the efficacy of a combination skincare regimen consisting of a mild facial skin cleanser and moisturizers containing pseudo-ceramide and a eucalyptus extract on reducing skin symptoms of Thai female non-oily sensitive skin.

MATERIALS and METHODS

Subjects

Thai female volunteers with self-diagnosed sensitive skin were recruited. The subjects with sensitive skin and normal or less sebum secretion

level were screened with sebum secretion level using Sebutape® (CuDerm Corporation, Dallas, TX, USA) and a lactic acid stinging test (LAST). Sebutape® was attached on the forehead and cheek for 30 minutes immediately after facial washing with a facial cleanser²². Referring to the standard scale paper from the CuDerm Corporation, sebum levels were visually graded on a scale from 1 (least) to 5 (most). The details in LAST are indicated below.

Twenty-seven subjects aged 20 to 39 years old (31.9 ± 6.0 , mean \pm SD) were selected and enrolled in the present study. Sebum secretion rates evaluated by Sebutape® were scored 3 (medium) or less both on the forehead and the cheek (average score was 1.6 on the forehead and 1.3 on the cheek). LAST score was higher than 2.

This study adhered to the tenets of the Declaration of Helsinki. A formal written informed consent was obtained from each subject before the study.

Test materials

All test materials used in this study, including the facial skin cleanser, the aqueous lotion and the moisturizing cream were provided by the Kao Corporation (Tokyo, Japan).

The foaming facial skin cleanser (pH 5.5) was based on alkylether phosphate²³ (Curél Foaming Wash (in 2011, Kao Corporation, Tokyo, Japan), the full ingredients list is shown in Table 1a). The fine foam was obtained using the dispenser and

there was no need to generate foam manually. Ingredients in the aqueous lotion (pH 4.5) containing the eucalyptus extract and in the moisturizing cream (pH 4.8) containing synthetic pseudo-ceramide and the eucalyptus extract (Curél Lotion (Kao Corporation, Tokyo, Japan) and Curél Moisture Cream (Kao Corporation, Tokyo, Japan), are listed in Table 1b and 1c, respectively). Each subject washed her face with the test facial skin cleanser followed by the use of the aqueous lotion and the moisturizing cream twice a day for 4 weeks after discontinuing their current skin cleanser and moisturizer. The amounts applied for all test materials were instructed prior to the start of usage as follows, foaming facial skin cleanser: 2mL controlled by the pumping containers, aqueous lotion: approximately 0.5mL, and moisturizing cream: approximately 0.5g. The steps of the combination skincare were performed as follows; 1st: facial wash with the foaming facial skin cleanser, 2nd: applying the aqueous lotion, and 3rd: applying the moisturizing cream. No specific instructions for use of the test materials were given except for information about the sequential use of the facial skin cleanser and moisturizers. Changing the current facial skincare products and cosmetics except for the test materials was prohibited during the study. All subjects recorded their usage of samples, their skin symptoms and health conditions daily in their diary.

Observation and trial period

Assessment of efficacy was conducted prior to the start of the study (week 0) and at the end of week 4 (week 4). The investigation was performed in Bangkok, Thailand from December, 2011 to January, 2012. All instrumental measurements and visual assessments were performed following washing the face with the weakly acidic facial skin cleanser and acclimatization in the room at $21 \pm 1^\circ\text{C}$, $45 \pm 5\%$ relative humidity for 15 minutes.

Visual assessments

Well trained specialist performed visual assessments of the scaling, redness and acne on the forehead, the cheek and around the mouth skin throughout this study. For redness and scaling evaluation, the visual scoring was determined from 1 to 4 based on the severity of scaly skin on the entire face as follows; 1: none, 2: mild, 3: moderate, 4: severe. The maximum score of redness and scaling on the forehead and cheek and around the mouth was used for the total facial score. For acne evaluation, the visual scoring was determined from 1 to 4 based on the number of acne lesions on the half face as follows; 1: no acne lesion, 2: 1-5 acne lesions, 3: 6-10 acne lesions, 4: more than 11 acne lesions¹⁸. Scores of 1 and 2 were comparable to “mild” and scores of 3 and 4 were comparable to “moderate”, which is modified the grading criteria for acne severity in the guidelines of the Japanese Dermatological Association²⁴.

Evaluation of the sebum secretion rate, skin hydration and transepidermal water loss (TEWL)

Immediately after acclimatization, the sebum secretion rate on the forehead and on the cheek were estimated by measuring the sebum level with a Sebumeter[®] (Courage + Khazaka electronic GmbH, Cologne, Germany) within 15 minutes after the facial wash. Skin hydration was analyzed as cutaneous conductance on the cheek with a SKICON 200[®] (IBS Co. Ltd, Shizuoka, Japan) and TEWL on the cheek was analyzed with a Tewameter TM300[®] (Courage + Khazaka electronic GmbH, Cologne, Germany).

Lactic acid stinging test (LAST)

A filter paper ($\Phi 0.5\text{cm}$) soaked with $50\mu\text{L}$ of 10% aqueous solution of lactic acid was put on the cheek. Self-perceived unpleasant sensations (itching, burning, stinging and others) were recorded at 0, 2, 5 and 8 min using a 4-point scale (0 = none, 1 = slight, 2 = moderate, 3 = severe). The sum of each time clinical score was used as the LAST score⁵.

Subjective evaluation by the test subjects

The consumer's self-perception data obtained from the participant's recognition of improvement of skin conditions on week 4 were obtained as follows: agree, no change, and disagree.

Statistical analysis

Changes in data over the time course of the study were determined using the paired Student's t-test and the Wilcoxon signed rank test.

RESULTS

Subjects

There were no adverse events noted throughout the study and all subjects attended throughout the present study.

Redness was the major skin symptom of Thai sensitive skin subjects with normal or decreased

sebum secretion. Twenty-four of the 27 subjects had redness on their cheeks and most of them were mild redness (18 subjects: score 2, 5 subjects: score 3 and 1 subject: score 4) (Figure 1A). This redness was observed at least on the cheek region and one-third of the subjects also had redness on the forehead and around the mouth. Scaling was observed on 17 subjects, mainly on the cheek and around the mouth (Figure 1B). Twenty-one subjects had acne on the face and there were no significant differences between the 3 facial regions (Figure 1C).

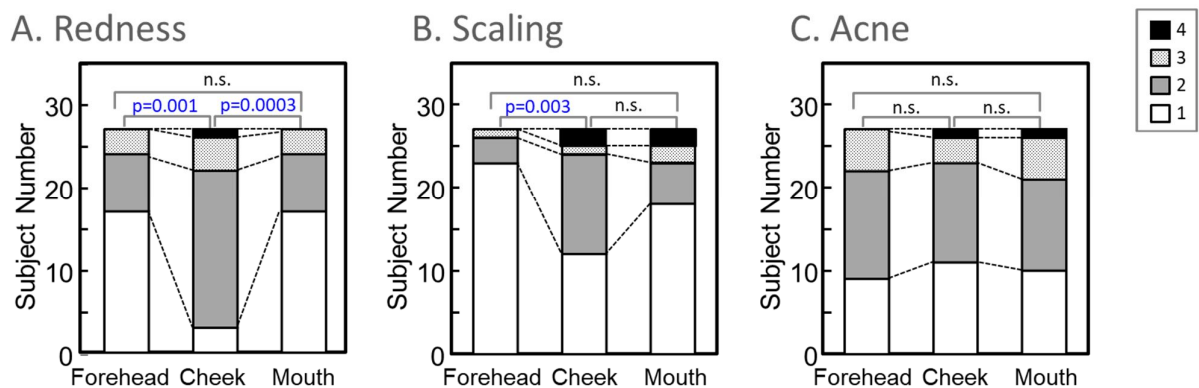


Figure 1 Differences in the severity of skin symptoms (Redness (A), Scaling (B) and Acne (C)) according to facial region. Open columns: none (1), gray columns: mild (2), dotted columns: moderate (3), closed columns: severe (4). P values were calculated using the Wilcoxon signed rank test; n.s. = no significant difference.

Visual evaluation of the efficacy of the combination skincare

Following 4 weeks of skincare, there was no statistically significant decrease in the redness

score on the forehead, around the mouth or the whole face, but the that on the cheek was significantly decreased and the number of subjects with redness on the cheek were

decreased from 24 subjects (week 0) to 13 subjects (week 4) (Figure 2A). Scaling was significantly decreased on the whole face and on the cheek (Figure 2B). Scaling on the forehead disappeared at week 4 but this decrease was not statistically significant. There were no statistically significant changes in acne, but the total number of subjects with acne on the forehead, on the cheek, and around the mouth was decreased (Figure 2C).

Figure 3 shows the remarkable effective example of photographs showing the clinical improvement of redness and dry skin on the cheek through the present study. A: a 34 year old Thai female at week 0 and at week 4: scaling score (4 to 1), redness score (4 to 4) and acne score (4 to 3), respectively. B: a 36 year old Thai female at week 0 and at week 4: scaling score (4 to 1), redness score (2 to 1) and acne score (2 to 1), respectively.

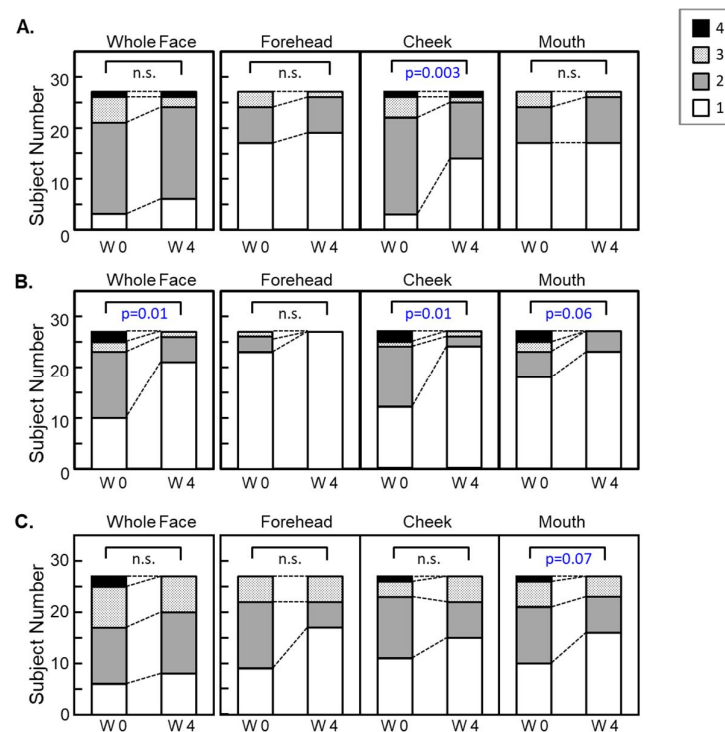


Figure 2 Changes of skin Redness (A), Scaling (B) and Acne (C) before and after usage of the combination skincare regimen for 4 weeks on the whole face, the forehead, the cheek and around the mouth. Open columns: none (1), gray columns: mild (2), dotted columns: moderate (3), closed columns: severe (4). P values were calculated using the Wilcoxon signed rank test.

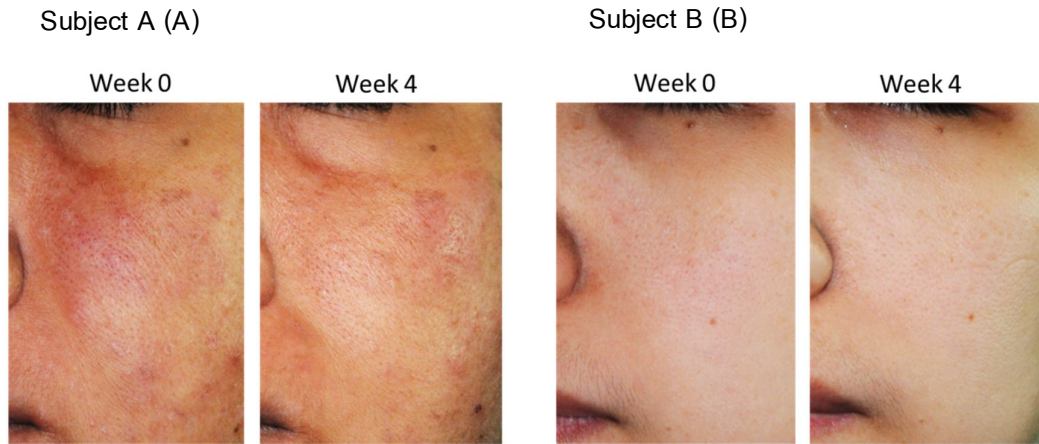


Figure 3 Remarkable effective example of clinical features at week 0 and at week 4 in the skincare regimen. (A) subject A: 34 year old Thai female. (B) subject B: 36 year old Thai female. Each of left photograph is week 0 and right side photograph is week 4 (right).

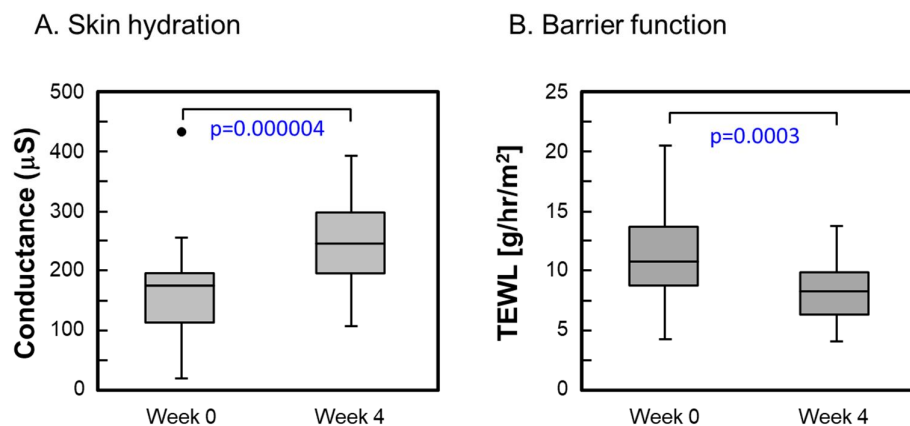


Figure 4 Change in skin hydration (A) and TEWL (B) in skin measurements on the cheek. P values were calculated using the paired Student's t-test.

Instrumental Analysis

Accompanied with the improvement of scaling, the skin hydration on the cheek increased significantly (Figure 4A). The median value

increased from $174 \mu\Omega^{-1}$ (week 0) to $245 \mu\Omega^{-1}$ (week 4), which was nearly the maximum value within subjects' value at week 0. The minimum value also dramatically increased from $20 \mu\Omega^{-1}$ to

109 $\mu\Omega^{-1}$. TEWL on the cheek significantly decreased (Figure 4B). There were no changes in the minimum value but the median value decreased from 10.8 g/m²/hr (week 0) to 8.3 g/m²/hr (week 4) and the maximum value

decreased from 20.5 g/m²/hr to 13.7 g/m²/hr.

There were no significant changes in the sebum secretion rate both on the forehead (from 18.0 $\mu\text{g}/\text{cm}^2$ to 16.8 $\mu\text{g}/\text{cm}^2$) and on the cheek (from 8.0 $\mu\text{g}/\text{cm}^2$ to 9.8 $\mu\text{g}/\text{cm}^2$).

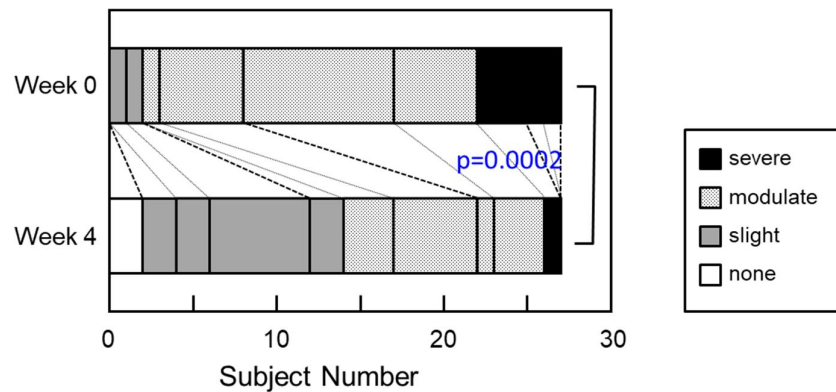


Figure 5 Changes in LAST score (total) on the cheek. Open columns: 0 'none', gray columns: 1 to 4 (mild), dotted columns: 5 to 8 (moderate), and closed columns: 9 to 12 (severe). P value was calculated using the Wilcoxon signed rank test.

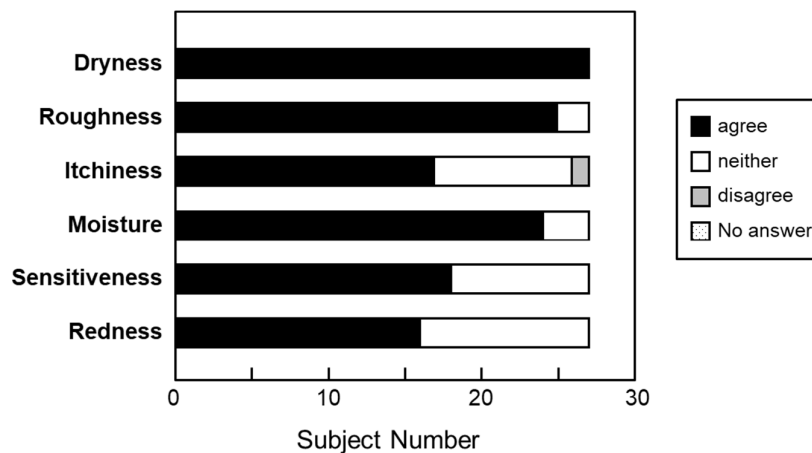


Figure 6 Recognition of improvement of skin conditions by subjective evaluation. Closed columns: agree,

open columns: neither agree nor disagree, gray columns: disagree.

LAST

Prior to using the test products, 3 subjects had a LAST score of 1 to 4 (slight), and 19 subjects had a LAST score of 5 to 8 (moderate) (Figure 5). Five subjects had a LAST score of 9 to 12 (severe), one was a score 10 and another was a score of 11. Following usage of the combination skincare products, the sensitivity was significantly decreased accompanied by an improvement of cheek skin conditions evaluated visually and by instrumental analysis. The number of subjects who had a LAST score of 9 to 12 (severe) was decreased to only one, who had a LAST score of 9. The number of subjects with a LAST score 5 to 8 (moderate) was also decreased to 12. The number of subjects who had a LAST score of 1 to 4 (slight) was increased to 12 and 2 subjects had no stinging at all

Subjective evaluation

All 27 subjects recognized that their skin had less dryness following usage of the test materials (Figure 6). Furthermore, decreased roughness and increased skin moisture were recognized by most subjects (roughness: 25 subjects (92%), moisture: 24 subjects (89%)). Decreases in redness, sensitivity and itchiness were also recognized by nearly two-thirds of the subjects and only one subject claimed an increase in itchiness. In the interviews, the subjects recognized those changes

according to the decrease in skin roughness and dryness in air conditioned environments and itchy skin induced by sunshine and sweat.

Discussion

The sensitive skins such as in atopic dermatitis have decreased cutaneous barrier function, which allows easy penetration of stimuli such as sweat and air pollution resulting in inducing skin redness, scaling and irritation. The treatment with an adequate moisturizer is beneficial for the dry skin of patients with that disease. The use of moisturizers containing pseudo-ceramide and a eucalyptus extract is effective for the care of sensitive skin in the dry season of China and Japan^{5,13,18}. However Kikuchi et al. reported that moisturizer does not influence the impaired stratum corneum barrier function as effectively in the less arid season in Japan²⁰. The present study was done from December, 2011 to January, 2012 in Bangkok and the average temperature was about 25 to 28°C and the average humidity was 60 to 70%. However, the usage of the combination of skincare improved their sensitive skin with significant decreases in skin symptoms on the face. The subjects had lower cutaneous functions with a high LAST score but following the combination of skincare, improvements of sensitive skin were observed accompanied by the improvement of stratum corneum function. This

improvement agrees with the data obtained in the previous study^{5,13,18}. On Chinese study, accompanied with improvement of skin sensitivity evaluated by LAST, significant increase in ceramides level was observed⁵. Thus we presume that the enhancement of stratum corneum function in present evaluation might also be caused by the increase in ceramide following application of the pseudo-ceramide and eucalyptus extract.

Skin cleansing is the major factor that induces dryness or irritation of the skin. However alkylether phosphate which used for facial cleanser was a mild detergent²³. The pH of skin cleansers affects skin conditions but a weakly acidic base for cleansers has less of an effect on the skin²⁵. Furthermore, The cleanser used in this study automatically foamed well when dispensed, which reduces friction and surfactant penetration into the skin²⁶. Thus, this facial cleanser might have less of an effect to induce sensitive skin.

Sebum is one of the major factors that induce sensitive skin because oxidized sebum or free fatty acids derived from sebum may irritate the skin and cause cutaneous problems such as seborrheic dermatitis and acne^{27,28}. However, in this study, the subjects did not have excess sebum on their face, and there were no significant changes in sebum secretion level. On the evaluation of skin cleanser consisted of different surfactants in Thailand, sebum secretion rate on

the forehead, which evaluated by Sebutape[®], was significantly decreased²⁹. This decrease in sebum secretion rate was particularly observed in the subjects with high sebum secretion rate (scored 4 or more) both on forehead and cheek. However in present evaluation only subjects with low sebum secretion (scored 3 or less evaluated by Sebutape[®]) enrolled, thus no change in sebum secretion rate might be made.

It is known that the selection of materials for reference and usage during wash out period are quite important because these materials affect the decision of the efficacy. Thus we have aimed to clarify the efficacy of our combination skincare compared to the subjects' skincare regimen in Thai non-oily people with sensitive skin on this evaluation. Cleansing face and application of moisturizers are habitual behaviors of Thai women. No specific instructions for the use of the test materials were given and all the subjects might have kept performing the facial skincare in their own method. However, following switching the facial skin cleanser and moisturizers, their skin symptoms were improved, which may indicate our skincare regimen is more suitable for Thai people with non-oily sensitive skin.

Neither test cleanser nor moisturizer contained any anti-inflammatory materials, so they may not prevent the skin inflammation themselves. However, following using our skincare regimen, inflammatory symptoms were

decreased significantly accompanied with a decrease in skin dryness. It is reported that moisturizers have the ability to prevent irritation³⁰. Thus, it is suggested that the improvement of skin redness and decrease in LAST in this study may be caused by the improvement of their skin dryness, in addition to, prevent the invasion of stimuli by enhancing cutaneous barrier function.

This study was carried out on Thai dry season thus the further study in deferent season such as hot and rainy season might be required. Moreover, the efficacy of these skincare regimen on sensitive skin with normal barrier function or high sebum secretion are still not clarified on this evaluation.

Based on these findings, the combination skincare with a mild acidic foamed cleanser and moisturizers containing pseudo-ceramide and the eucalyptus extract is safe for Thai non-oily sensitive skin, furthermore could help reduce redness and dryness and improve sensitiveness on the cheeks accompanied with enhancing their cutaneous functions. We conclude this combination of skincare may be effective on Thai non-oily sensitive skin.

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Conflict of interest

Panomporn Tongchalaem, Tiyachat Tongpaen, Tsuyoshi Seki, Yutaka Takagi, Hideyuki Hanazawa, Atsushi Uzu, and Koichi Ishida are employees of Kao Corporation (Tokyo, Japan). These studies were funded in full by Kao Corporation. Suwirakorn Ophaswongse received honoraria for participation in advisory boards for Kao Corporation.

The authors have no other conflicts of interest.

References

1. Richters R, Falcone D, Uzunbajakava N, Verkruysse W, van Erp P, van de Kerkhof P. What is sensitive skin? A systematic literature review of objective measurements. *Skin Pharmacol Physiol* 2015; 28: 75-83.
2. Farage MA, Katsarou A, Maibach HI. Sensory, clinical and physiological factors in sensitive skin: a review. *Contact Dermatitis* 2006; 55: 1-14.
3. Marriott M, Holmes J, Peters L, Cooper K, Rowson M, Basketter DA. The complex problem of sensitive skin. *Contact Dermatitis* 2005; 53: 93-99.
4. Draeos ZD. Sensitive skin: perceptions, evaluation, and treatment. *Am J Contact Dermatol* 1997; 8: 67-78.
5. Nojiri H, Ishida K, Yao X, Liu W, Imokawa G. Amelioration of lactic acid sensations in sensitive skin by stimulating the barrier function and improving the ceramide profile. *Arch Dermatol*

- Res 2018; 310: 495-504.
6. Roussaki-Schulze AV, Zafiriou E, Nikoulis D, Klimi E, Rallis E, Zintzaras E. Objective biophysical findings in patients with sensitive skin. *Drugs Exp Clin Res* 2005; 31: 17-24.
 7. Elias PM, Brown BE. The mammalian cutaneous permeability barrier: defective barrier function is essential fatty acid deficiency correlates with abnormal intercellular lipid deposition. *Lab Invest* 1978; 39: 574-83.
 8. Imokawa G, Akasaki S, Hattori M, Yoshizuka N. Selective recovery of deranged water-holding properties by stratum corneum lipids *J Invest Dermatol* 1986; 87: 758-61.
 9. Lampe MA, Burlingame AL, Whitney J, et al. Human stratum corneum lipids: characterization and regional variations. *J Lipid Res* 1983; 24: 120-30.
 10. Melnik B, Hollmann J, Plewig G. Decreased stratum corneum ceramides in atopic individuals—a pathobiochemical factor in xerosis? *Br J Dermatol* 1988; 119: 547-9.
 11. Imokawa G, Abe A, Jin K, Higaki Y, Kawashima M, Hidano A. Decreased level of ceramides in stratum corneum of atopic dermatitis: an etiologic factor in atopic dry skin? *J Invest Dermatol* 1991; 96: 523-6.
 12. Imokawa G, Akasaki S, Kawamata A, Yano S, Takaishi N. Water retaining function in the stratum corneum and its recovery properties by synthetic pseudoceramides. *J Soc Cosmet Chem* 1989; 40: 273-285.
 13. Hata M, Tokura Y, Takigawa M, Tamura Y, Imokawa G. Efficacy of using pseudoceramide-containing cream for the treatment of atopic dry skin in comparison with urea cream. *Nishi Nihon Hifuka* 2002; 64: 606-1.
 14. Matsuki H, Kiyokane K, Matsuki T, Sato S, Imokawa G. Reevaluation of the importance of barrier dysfunction in the nonlesional dry skin of atopic dermatitis patients through the use of two barrier creams. *Exog Dermatol* 2004; 3: 293–302.
 15. Ishikawa J, Shimotoyodome Y, Chen S, et al. Eucalyptus increases ceramide levels in keratinocytes and improves stratum corneum function. *Int J Cosmet Sci* 2012; 34: 17-22.
 16. Prottey C, Ferguson T. Factors which determine the skin irritation potential of soaps and detergents. *J Soc Cosmet Chem* 1975; 26: 29–46.
 17. Takagi Y, Nakagawa H, Higuchi K, Imokawa G. Characterization of surfactant-induced skin damage through barrier recovery induced by pseudoacylceramides. *Dermatology* 2005; 211: 128–34.
 18. Isoda K, Seki T, Inoue Y, et al. Efficacy of the combined use of a facial cleanser and moisturizers for the care of mild acne patients with sensitive skin. *J Dermatol* 2015; 42:181-8.
 19. Oh M, Lee J, Kim S, et al. Regional and seasonal differences in skin irritation and neurosensitivity in Chinese and South Korean women. *J Eur Acad Dermatol Venereol* 2015; 29: 115-9.
 20. Kikuchi K, Tagami H; Japanese Cosmetic Scientist Task Force for Skin Care of Atopic Dermatitis. Noninvasive biophysical assessments of the efficacy of a moisturizing cosmetic cream base for patients with atopic dermatitis during different seasons. *Br J Dermatol* 2008; 158: 969-78.

21. Rubel D, Thirumoorthy T, Soebaryo RW, Weng SC, Gabriel TM, Villafuerte LL, Chu CY, Dhar S, Parikh D, Wong LC, Lo KK. Asia-Pacific Consensus Group for Atopic Dermatitis. Consensus guidelines for the management of atopic dermatitis: an Asia-Pacific perspective. *J Dermatol* 2013; 40: 160-171.
22. Kligman AM, Miller DL, McGinley KJ. Sebutape: A device for visualizing and measuring human sebaceous secretion. *J Soc Cosmet Chem* 1986; 37: 369-74.
23. Imokawa G, Tsutsumi H, Kurosaki T. Surface activity and cutaneous effects of monoalkyl phosphate surfactants. *J Am Oil Chem Soc* 1978; 55: 839-44.
24. Hayashi N, Akamatsu H, Kawashima M. Establishment of grading criteria for acne severity. *J Dermatol* 2008; 35: 255-260.
25. Grafter R, Hackl P, Braun F. Effects of soap and detergents on skin surface pH, stratum corneum hydration and fat content in infants. *Dermatology* 1997; 195: 258-62.
26. Sonoda J, Sakai T, Inomata Y. Liquid oil that flows in spaces of aqueous foam without deforming. *J Phys Chem B* 2014; 118: 9438-44.
27. Ekanayake Mudiyanse S, Hamburger M, Elsner P, Thiele JJ. Ultraviolet a induces generation of squalene monohydroperoxide isomers in human sebum and skin surface lipids in vitro and in vivo. *J Invest Dermatol*. 2003; 120: 915-22.
28. Smith KR, Thiboutot DM. Thematic review series: skin lipids. Sebaceous gland lipids: friend or foe? *J Lipid Res* 2008; 49: 271-81.
29. Jananya S, Praewpatoo B, Takagi Y, et al. An Alkyl Ether Carboxylate and Alkyl Carboxylate Formulated Cleanser Decreases Facial Sebum and Inflammatory Acne Without Inducing Dry Xerotic Skin in Thai Females. *Int J Clin Dermatol Res* 2015; 3: 60-64.
30. Simion FA, Abrutyn ES, Draelos ZD. Ability of moisturizers to reduce dry skin and irritation and to prevent their return. *J Cosmet Sci* 2005; 56: 427-44.