

## Title:

**Washing with a body cleanser and topical application of a moisturizer containing a pseudo-ceramide and a eucalyptus extract are effective to improve mild atopic dermatitis in Thailand**

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## **IRB**

This study adhered to the tenets of the Declaration of Helsinki and was reviewed and approved by the Ethics Committee of the Kao Corporation.

## **AUTHORSHIP**

NH, KK and TY were involved in the clinical trial design, data interpretation and manuscript preparation. PP, PK, PN, LK and KW were involved in clinical evaluation, assessment of patient outcomes and data collection. NT was involved in the clinical trial design, clinical trial management, data interpretation, manuscript preparation and final approval.

**To the Editor,**

Atopic dermatitis (AD) is a common chronic pruritic inflammatory skin disorder. The treatment paradigm for mild-to-moderate AD in South and East Asia is based on skincare, including the use of moisturizers,<sup>1</sup> but those are often ineffective. Here we confirmed the efficacy of a moisturizing skin lotion containing P-Cer<sup>2</sup> and a eucalyptus extract<sup>3</sup> (Table S1) on Thai AD patients. Body cleansers might also be a factor that affects AD skin symptoms. Thus, half of the patients in this study used a mild body cleanser<sup>4</sup> (Table S1) in addition to using a skin moisturizer. This study adhered to the tenets of the Declaration of Helsinki and was reviewed and approved by the Ethics Committee of the Kao Corporation. A formal informed consent was obtained from each subject before the study. This controlled usage test was performed in Bangkok, Thailand from February to March in 2017 when the average daily temperature and humidity were 29.6°C (range = 23 to 34°C) and 67.% (range = 32 to 96%), respectively. There were no major changes in climate during this test period. Thirty-eight Thai patients with mild AD who did not need medical treatment were enrolled in this study. Information about the subjects in this study is summarized in Table S2. All patients used the test lotion twice a day for 4 weeks. Half of them also used a test body cleanser (Group WL) while the rest of them kept using their own cleanser (Group L).

The results show that the test skin lotion significantly improved their skin symptoms both objectively (SCORAD score, Figure 1) and subjectively (POEM score, Figure 2) within 2 weeks. Two-thirds of the AD subjects had a habit of daily use of a skin moisturizer, with the main ingredients being petrolatum or glycerin, but that did not affect the improvement of SCORAD scores (Figure S1). Petrolatum and glycerin are effective moisturizing materials for AD care, however abundant amounts are needed on the skin

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surface and they are relatively easily removed. Thus, it is presumed that insufficient amounts of moisturizers remained on most subjects for the entire day. On the other hand, it has been confirmed that sufficient amounts of P-Cer remain on the skin more than 23 hours following the last application.<sup>5</sup>

In addition to the significant improvement of skin symptoms by application of the test lotion, the use of the test body cleanser induced an improvement of the SCORAD score and the POEM score and there were statistically significant differences between Group WL and Group L in both scores at week 4 (Figures 1 and 2). This result suggested that some body-washing habits of Thai AD patients might worsen their skin symptoms. Interestingly, evaluation of each parameter of the SCORAD indicated that intensity, itchiness and erythema in Group WL improved significantly better than Group L, and there were no statistically significant differences in the other parameters between these two groups (Figures S1 and S2). It is important to remove skin irritants such as oxidized sebum and air pollutants. However, the cleansing detergent may also be an irritant and also tends to remove natural moisturizing factors and intercellular lipids. The test cleanser has a high cleansing ability and is mild to the skin with less absorbance to the stratum corneum, which might reduce skin inflammation.

These results suggest that usage of a mild cleanser and a moisturizer containing ceramide is effective for the skincare of AD patients in Thailand. This evaluation has limitations in that no instrumental analyses were used to objectively measure the improvement of skin dryness or data of individual factors that may affect the efficacy, such as outdoor exposure, thus further evaluations are needed.

## CONFLICT OF INTEREST

The authors have no conflicts of interest.

## REFERENCES

1. Luk D, Hon KLE, Dizon MVC, et al. Practical recommendations for the topical treatment of atopic dermatitis in South and East Asia. *Dermatol Ther (Heidelb)*. 2021;11:275-291.
2. Imokawa G, Akasaki S, Kawamata A, et al. Water retaining function in the stratum corneum and its recovery properties by synthetic pseudoceramides. *J Soc Cosmet Chem*. 1989;40:273-285.
3. 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.
4. Takagi Y, Shimizu M, Morokuma Y, et al. A new formula for a mild body cleanser: sodium laureth sulphate supplemented with sodium laureth carboxylate and lauryl glucoside. *Int J Cosmet Sci*. 2014;36:305-311.
5. Ishida K, Takahashi A, Bito K, et al. Treatment with synthetic pseudoceramide improves atopic skin, switching the ceramide profile to a healthy skin phenotype. *J Invest Dermatol*. 2020;140:1762-1770.

## FIGURE LEGENDS

**FIGURE 1** Decreases in SCORAD scores following use of the test lotion only (Group L) or the lotion and body wash (Group WL). Horizontal lines inside the boxes indicate medians, and the lower and upper ends of the boxes are the first and third quartiles. The whiskers indicate values within 1.5x the interquartile range from the upper or lower quartile (or the minimum and maximum if within 1.5x the interquartile range of the quartiles), and data more extreme than the whiskers are plotted individually as outliers (open circles). The crosses in the boxes indicate mean values. \* indicates  $p < 0.05$  vs. week 0, \*\* indicates  $p < 0.01$  and \*\*\* indicates  $p < 0.005$ .

**FIGURE 2** Decreases in POEM scores following use of the test lotion only (Group L) or the lotion and body wash (Group WL). Horizontal lines inside the boxes indicate medians, and the lower and upper ends of the boxes are the first and third quartiles. The whiskers indicate values within 1.5x the interquartile range from the upper or lower quartile (or the minimum and maximum if within 1.5x the interquartile range of the quartiles), and data more extreme than the whiskers are plotted individually as outliers (open circles). The crosses in the boxes indicate mean values. \* indicates  $p < 0.05$  vs. week 0, \*\* indicates  $p < 0.01$  and \*\*\* indicates  $p < 0.005$ .

**FIGURE S1** The daily usage of a moisturizer did not affect SCORAD scores following use of the test lotion only (Group L, A) or the lotion and body wash (Group WL, B). Horizontal lines inside the boxes indicate medians, and the lower and upper ends of the boxes are the first and third quartiles. The whiskers indicate values within 1.5x the

interquartile range from the upper or lower quartile (or the minimum and maximum if within 1.5x the interquartile range of the quartiles), and data more extreme than the whiskers are plotted individually as outliers (open circles). The crosses in the boxes indicate mean values. \* indicates  $p<0.05$  vs. week 0, \*\* indicates  $p<0.01$  and \*\*\* indicates  $p<0.005$ .

**FIGURE S2** Changes in each parameter of the SCORAD score (Affected area (A), dryness (B)), Itchiness (C) and Sleeplessness (D)) following use of the test lotion only (Group L) or the lotion and body wash (Group WL). The whiskers indicate values within 1.5x the interquartile range from the upper or lower quartile (or the minimum and maximum if within 1.5x the interquartile range of the quartiles), and data more extreme than the whiskers are plotted individually as outliers (open circles). The crosses in the boxes indicate mean values. \* indicates  $p<0.05$  vs. week 0, \*\* indicates  $p<0.01$  and \*\*\* indicates  $p<0.005$ .

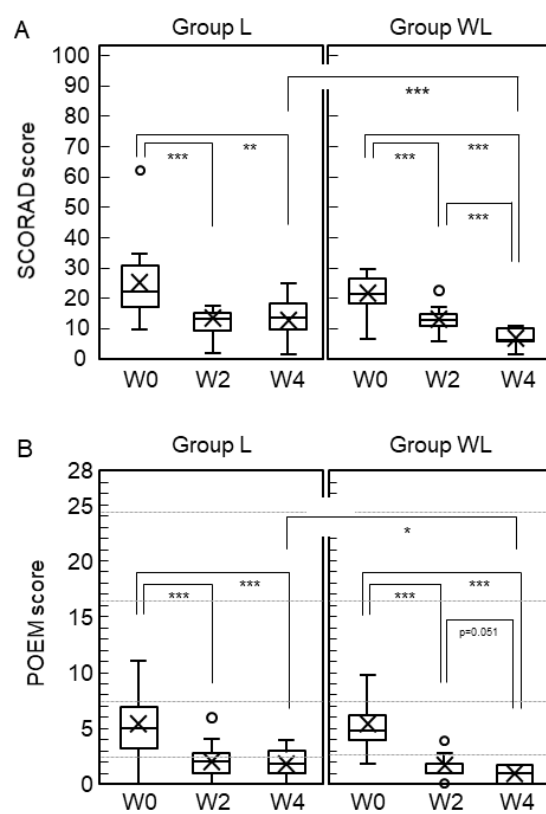


Figure 1



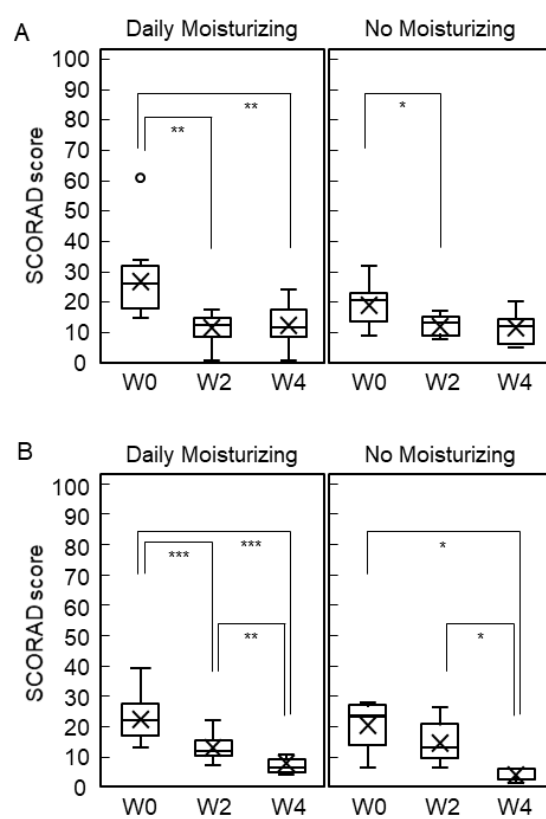


Figure 2