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Relationship between skin redness and thymus and activation-regulated chemokine (TARC) in healthy people without atopic dermatitis, and suggestions for improving skin redness via TARC

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Introduction:

Skin redness is a straightforward clinical finding of facial erythema that is obvious even to the untrained eye. Interval flush or persistent facial erythema could be associated with multiple diseases, including rosacea, contact dermatitis, acne, corticosteroid-dependent dermatitis, and systemic lupus erythematosus. Although various factors are involved in skin redness, this study focused on thymus and activation-regulated chemokine (TARC; also known as CC chemokine ligand 17), a biomarker for atopic dermatitis (AD) [1]. TARC is a member of the CC chemokine family and is a potent and selective chemoattractant for T-helper 2 cells via CC chemokine receptor 4. Increasing evidence suggests that TARC is involved in the development of allergic diseases such as AD and bronchial asthma, and elevated blood levels of TARC have been observed in AD patients [2]. Serum levels of TARC have served as a reliable biomarker of AD progression [2]. However, the relationship between TARC and skin color in healthy individuals without AD has not been reported.

Materials & Methods:

[Experiment I]
Eleven blood components were analyzed in 101 Japanese women between 20 and 69 years old: including serum TARC levels; redness of facial images obtained using a VISIA Evolution system (Canfield Scientific, Fairfield, NJ, USA) for skin redness analysis; and skin color measurement with a spectrophotometer (Chromameter CM 600d; Konica Minolta, Osaka, Japan).

[Experiment II]
Since a relationship between skin redness and serum TARC levels was identified, we searched for materials that would inhibit serum TARC production to suppress skin redness. Using human peripheral blood mononuclear cells (PBMCs), we evaluated whether interleukin (IL)-13 could stimulate TARC production and whether certain food ingredients could inhibit this production [3].

[Experiment III]
We subsequently conducted a clinical trial with 30 Japanese women between 28 and 39 years old as subjects, to examine whether improvements in serum TARC levels or skin redness (by VISIA Evolution assessment) and skin color measurement (by Chromameter CM 600d spectrophotometer) were evident after ingesting a beverage containing artichoke leaf (Cynara scolymus) extract (1 bottle, 30 mL; artichoke leaf extract, 0.15 mg/mL). Subjects drank one bottle of the beverage containing artichoke leaf extract each day for 10 consecutive days. Serum TARC levels and VISIA Evolution analysis were performed before and after ingesting the beverage containing artichoke leaf extract after each day for a total of 10 days.

[Ethical considerations]
At the beginning of the study, written informed consent (reviewed by the ethics committee) was obtained from all individual participants included in the study, which was performed in accordance with the Declaration of Helsinki, and the regulatory and legal requirements of Japan.

Results & Discussion:

[Relationship between serum TARC levels and skin redness]
Serum TARC levels are known to be a biomarker for atopic dermatitis, but the relationship with skin redness in healthy subjects has been unclear. In Japanese women aged 20–49 years (61 subjects; mean age, 34.56 ± 9.48 years), a significant relationship was identified between higher serum TARC levels and greater skin redness (correlation coefficient, 0.3261; p=0.0103) (Figure 1). We found a relationship between serum TARC levels and skin redness, but no relationship was apparent between serum TARC levels and age (correlation coefficient, -0.0733; p=0.5744) (Figure 2). This interesting finding suggests that serum TARC is not an aging-related factor. No previous reports have clarified the relationship between serum TARC levels and skin brightness, but as serum TARC levels increased, skin lightness decreased (correlation coefficient, -0.2617; p=0.0416) (Figure 3). The study also examined the relationship between skin redness and age, finding no relationship (correlation coefficient, 0.2338; p=0.0698) (Figure 4), and no increase in skin redness with age. While melanin and glycation have been reported to contribute to skin brightness [4], so does skin redness (correlation coefficient, -0.3411; p=0.0071) (Figure 5).

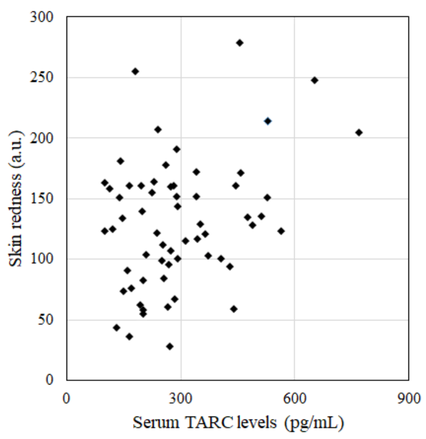


Figure 1. Scatterplot of serum TARC levels and skin redness
Japanese women aged 20–49 years (61 subjects; mean age, 34.56 ± 9.48 years) underwent measurement of serum TARC levels and redness of facial images taken by VISIA Evolution for skin redness analysis.

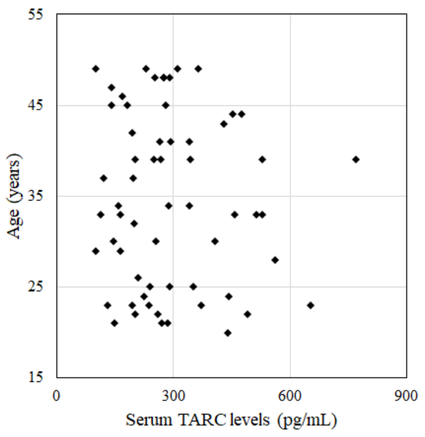
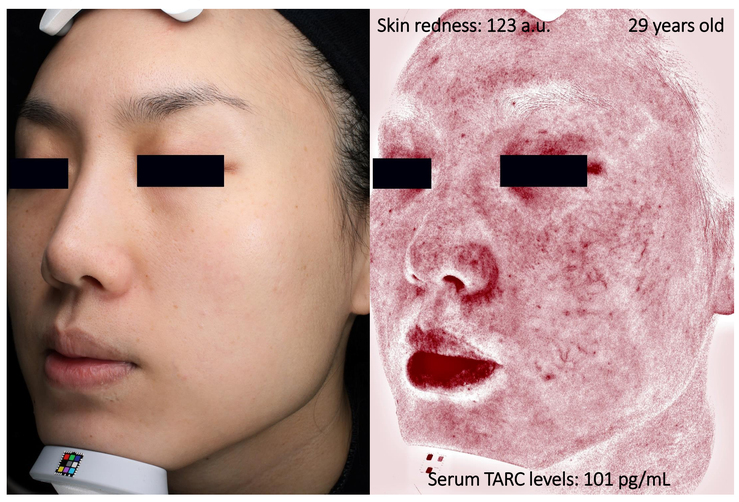


Figure 2. Scatterplot of serum TARC levels and age
Japanese women aged 20–49 years (61 subjects; mean age, 34.56 ± 9.48 years) underwent measurement of serum TARC levels.

Typical example of a woman with low serum TARC levels



Typical example of a woman with high serum TARC levels

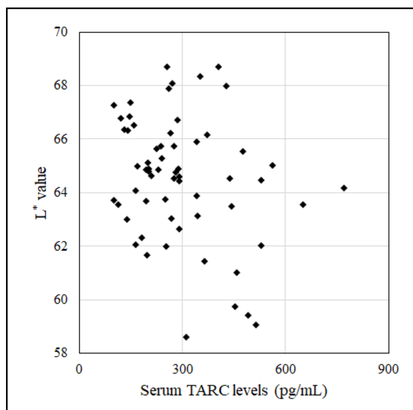


Figure 3. Scatterplot of serum TARC levels and L* value
Japanese women aged 20–49 years (61 subjects; mean age, 34.56 ± 9.48 years) underwent measurement of serum TARC levels and L* value of cheek by spectrophotometer.

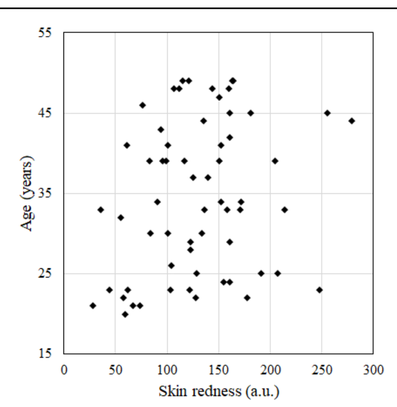


Figure 4. Scatterplot of skin redness and age
Japanese women aged 20–49 years (61 subjects; mean age, 34.56 ± 9.48 years) underwent measurement of redness of facial images taken by VISIA Evolution for skin redness analysis.

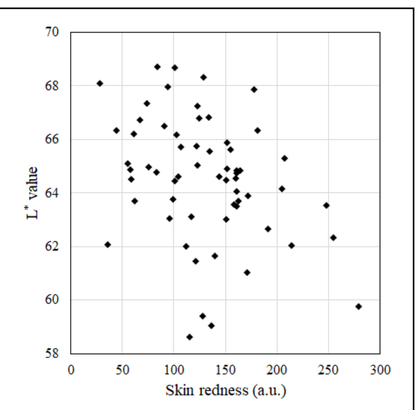


Figure 5. Scatterplot of skin redness and L* value
Japanese women aged 20–49 years (61 subjects; mean age, 34.56 ± 9.48 years) underwent measurement of redness of facial images taken by VISIA Evolution for skin redness analysis and L* value of cheek by spectrophotometer.

[Inhibitory effects of artichoke leaf extract on TARC production]
Since a relationship between skin redness and serum TARC levels was identified, we searched for materials that would inhibit serum TARC production to suppress skin redness. Given that TARC is present in blood, we thought that materials that inhibit TARC production would be more effective if consumed in foods, rather than if applied as cosmetics. Using human PBMCs, we evaluated whether IL-13 could enhance TARC production as a stimulus and whether food ingredients could inhibit this production. Results for cell viability of PBMCs are shown in Figure 6A. A significant increase in cell viability was seen with the addition of IL-13 (10 ng/mL), confirming that human PBMCs are stimulated by IL-13. On the other hand, comparing IL-13 without artichoke leaf extract (0 mg/mL) with IL-13 plus artichoke leaf extract (0.009 mg/mL), cell viability was observed to have decreased significantly. Artichoke leaf extract (0.009 mg/mL) was found to inhibit IL-13-induced cell counts in human PBMCs. The inhibitory effect of artichoke leaf extract (0.009 mg/mL) was compared with that without IL-13, suggesting that the effect was not cytotoxic, as the number of cells remained unchanged. The results of a TARC production study using PBMCs are shown in Figure 6B. Comparison of no IL-13 with IL-13 without artichoke leaf extract (0 mg/mL) showed that IL-13 treatment significantly increased TARC production, confirming IL-13 stimulation induction of TARC. IL-13 without artichoke leaf extract (0 mg/mL) as compared to IL-13 + artichoke leaf extract (0.003 mg/mL) showed no change in TARC production. In contrast, comparison of IL-13 without artichoke leaf extract (0 mg/mL) and IL-13 + artichoke leaf extract (0.009 mg/mL) showed significantly reduced TARC production, indicating that artichoke leaf extract (0.009 mg/mL) significantly inhibited IL-13-induced TARC production in human PBMCs.

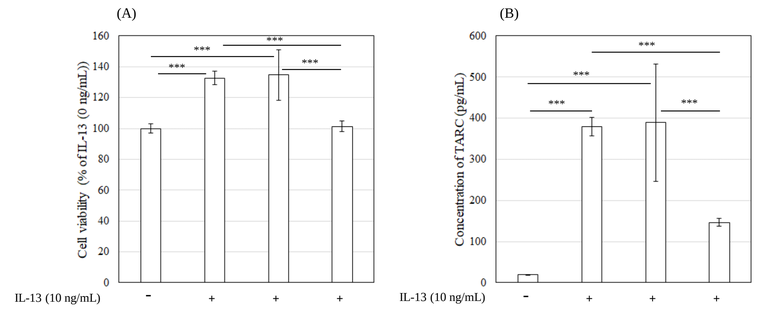


Figure 6. Effects of artichoke leaf extract (ALE) on the IL-13-induced production of TARC in peripheral blood mononuclear cells (PBMCs).
PBMCs were treated with or without IL-13 (10 ng/mL) and with various treatment concentration of ALE for 24 h. (A) Cell viability was determind by the 3-(4,5-dimethylthiazol-2yl)-2,5-diphenyl-2H-tetrazolium bromide assay. (B) TARC production was measured by an ELISA for TARC (Human TARC Quantikine ELISA Kit, R&D Systems). Results are expressed as means ± standard deviation (n=5). Statistical comparisons of different treatments were performed using JMP15 with Tukey's multiple comparison test. ***p<0.001.

[Inhibition of serum TARC production and reduction of skin redness with beverages containing artichoke leaf extract in human subjects]
We subsequently conducted a clinical trial in Japanese women aged 28–39 years (30 subjects; mean age, 32.80 ± 3.01 years) as subjects, to examine whether improvements in serum TARC levels and skin redness would be achieved after ingesting a beverage containing artichoke leaf extract. Subjects ingested the beverage for 10 days. Serum TARC levels were 268.6 ± 121.07 pg/mL before and 243.2 ± 112.50 pg/mL after consuming the beverage for 10 consecutive days, showing a significant reduction (Figure 7). Measuring skin brightness on the back, L* value was 66.80 ± 3.24 before and 67.32 ± 3.19 after consuming the beverage for 10 consecutive days, showing a significant increase (Figure 8).
No change in skin redness was identified from images obtained by VISIA Evolution analysis before and after drinking the beverage with artichoke leaf extract (data not shown). An example of significant skin redness is shown in Figure 9, serum TARC levels were 290 pg/mL before and 245 pg/mL after consuming the beverage for 10 consecutive days. Ingestion of the beverage resulted in significantly decreased serum TARC levels, significantly increased L* values, and reduced skin redness compared to before ingestion. Overall, these results indicated that ingestion of a beverage containing artichoke leaf extract decreased serum TARC levels, resulting in decreased skin redness. These results also showed that reducing skin redness results in brighter skin.

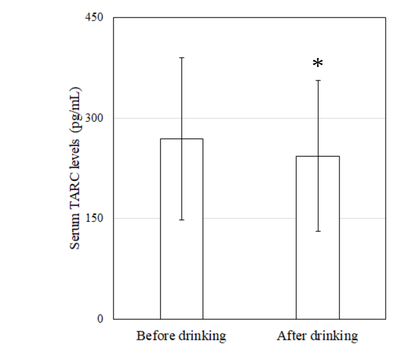


Figure 7. Effect of beverages containing artichoke leaf extract on serum TARC levels in human studies.
Japanese women aged 28–39 years (30 subjects; mean age, 32.80 ± 3.01 years) underwent measurement of serum TARC levels. Statistical analysis was performed using JMP15 with a corresponding t-test. *p<0.05

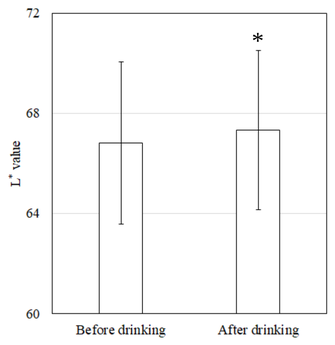


Figure 8. Effect of beverages containing artichoke leaf extract on skin brightness in human studies.
Japanese women aged 28–39 years (30 subjects; mean age, 32.80 ± 3.01 years) underwent measurement of L* value of the back by spectrophotometer. Statistical analysis was performed using JMP15 with a corresponding t-test. *p<0.05

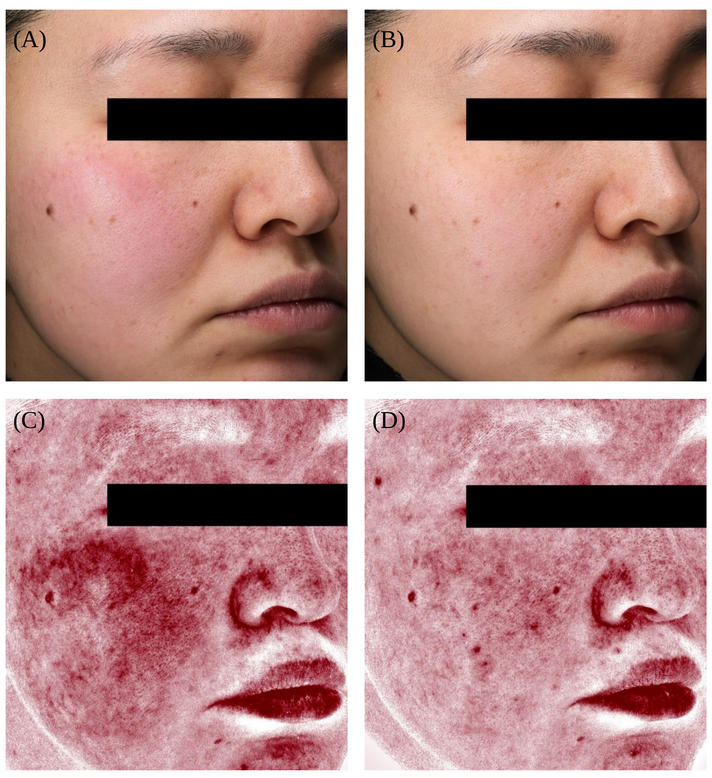


Figure 9. Photographs of an example of significant skin redness.
(A) Photograph taken in normal light before drinking. (B) Photograph taken in normal light after drinking. (C) Skin redness photograph taken before drinking. (D) Skin redness photograph taken after drinking.

Conclusions:

Ingestion of a beverage containing artichoke leaf extract decreased serum TARC levels, resulting in brighter skin and decreased skin redness. By elucidating the relationship between skin redness and TARC, and proposing a method to improve skin redness via TARC, we have found a potential method to obtain healthier, brighter skin using artichoke leaf extract.

References:
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