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**File: ■ Green Satsuma Mandarin Oranges (*Citrus unshiu*, Rutaceae)
■ Skin Wrinkles
■ Aging**

HC 052234-704

Date: January 13, 2023

RE: Extract of Green Mandarins (Unripe Satsuma Mandarin Oranges) Improves Skin Wrinkles Caused by Ultraviolet Radiation

Ham YM, Yoon SA, Hyeon H, et al. Clinical evidence of effects of green mandarin (Putgyul) extract on skin aging: a randomized, double blind, placebo-controlled study. *Nutrients*. March 24, 2022;14(7):1352. doi: 10.3390/nu14071352.

Skin aging can be caused by various environmental factors, including ultraviolet radiation (UV). UV is classified according to wavelength as follows: UVA (315-400 nm), UVB (280-315 nm), and UVC (100-280 nm). UVC is mostly absorbed in the ozone layer in the atmosphere, UVB reaches the skin surface and penetrates to the epidermis, and UVA penetrates the skin more deeply to the dermis. UV exposure can cause DNA damage, oxidative damage to proteins and lipids, and inflammation. Green mandarins, eaten as unripe Satsuma mandarin oranges (*Citrus unshiu*, Rutaceae), exhibit anti-inflammatory and anti-wrinkle effects. In this randomized, double-blind, placebo-controlled, clinical study, the authors aimed to confirm the skin improvement efficacy and safety of the green mandarin extract Putgyul (PTE).

The authors hypothesized that a standardized dose of PTE administered for 12 weeks to patients with UV-induced periorbital wrinkles would improve the wrinkle depth, volume, length, and roughness. Secondary outcome measures included a survey on skin moisture content, transdermal water loss (TEWL), skin elasticity and gloss, and product efficacy.

In August 2020, one ton of green mandarins bought from a farmer in Jeju, Korea, were washed, pulverized and freeze-dried (11.4% yield). Green mandarin lyophilisate (50 kg) was extracted with ethanol, filtered, and concentrated under reduced pressure. The concentrate was lyophilized to obtain 50% ethanol extract powders of green mandarins (10 kg, 20% yield). High-performance liquid chromatography detected narirutin, a marker compound of PTE, in the extract at 50.2 minutes, with the narirutin content determined to be 40.07 ± 0.46 mg/g.

Participants were recruited through a website notice posted by the study institution, the Biodiversity Research Institute in Jeju, and by posters inside and outside the institute. Eligibility criteria included the following: female, age between 40 and 60 years, dry skin with less than 48 A.U. (skin capacitance as measured by corneometer), and periorbital

wrinkles (grade 3 or higher according to the Guideline for Efficacy Evaluation of Functional Cosmetics published by the Korean Ministry of Food and Drug Safety).

The 80 participants enrolled in the study were randomly and equally assigned to the PTE group or the placebo group. During the 12-week study, the participants took two tablets daily of the assigned study product. Each green mandarin tablet contained 150 mg of PTE, dextrin, and cellulose. The placebo tablets contained dextrin, cellulose, food coloring, and citrus flavoring. Four participants from the placebo group withdrew from the study because of personal reasons. The average age of the participants was 47.18 ± 4.402 in the PTE group and 46.23 ± 3.977 years in the placebo group.

Study outcomes were measured at baseline and at 4, 8, and 12 weeks after the beginning of the study intervention. No significant between-group differences were observed in changes in vital signs, complete blood count, serum biochemistry examination, or urinalysis during the study.

Significant improvements were observed in eye wrinkles ($P = 0.011$), volume of periorbital wrinkles ($P = 0.009$), and skin surface roughness ($P = 0.004$) in the PTE group compared with the placebo group after 12 weeks. Changes in the mean depth biggest wrinkle, maximum depth biggest wrinkle, wrinkle area, and length of wrinkle were not significant.

Survey results indicated no significant between-group differences in skin moisture content, TEWL, skin elasticity, or skin gloss. A significant difference between the time points was observed in increased skin moisture, gloss, elasticity, and overall improvement ($P = 0.001$ for all). Significant differences were observed between time points ($P = 0.001$) and between time points and groups ($P = 0.025$) in the reduction of periorbital wrinkles. Overall, the subjective survey results confirmed that the periorbital wrinkles decreased and the skin condition improved more in the PTE group than in the placebo group at week 12 compared with week 4 and week 8.

No adverse effects were reported. It should be noted that the product tested was an extract of green mandarin. Green mandarin essential oil can be phototoxic and should not be conflated with this extract.

Although the mechanism responsible for the improvements in wrinkles and skin roughness seen in the PTE group was not elucidated, "we speculate that green mandarin intake affects the reduction in collagen degradation" and that the polyphenols of the extract "helped improve the skin damage caused by UV," write the authors. They conclude that "PTE effectively improves UV-induced skin wrinkles" and that "PTE has sufficient value as a functional food ingredient that can prevent skin aging."

The authors declare no conflicts of interest.

—*Shari Henson*

Peer Reviewer's Comment

The clinical study was preceded by a paper by the same authors studying the same extract in which specific, relevant mechanisms were demonstrated in human dermal fibroblasts, namely MMP inhibition and increased collagen synthesis.¹ The same paper also documented decreases in cytokine expression and transepidermal water loss along with increases in collagen fibers and epidermal thickness in hairless mice exposed to UV.

Reference

¹Choi SH, Choi S, Jung TD, et al. Anti-photoaging effect of jeju putgyul (unripe citrus) extracts on human dermal fibroblasts and ultraviolet B-induced hairless mouse skin. *Int J Mol Sci.* September 2017;18(10):2052. doi: 10.3390/ijms18102052.

Referenced article can be accessed at <https://www.mdpi.com/2072-6643/14/7/1352>.

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