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File: ■ Hydrangea (*Hydrangea serrata*, Hydrangeaceae)
■ Anti-aging
■ Skin

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RE: Oral Consumption of Hydrangea Leaf Extract May Have Anti-aging Effects on the Skin

Myung DB, Lee JH, Han HS, et al. Oral intake of *Hydrangea serrata* (Thunb.) Ser. leaves extract improves wrinkles, hydration, elasticity, texture, and roughness in human skin: A randomized, double-blind, placebo-controlled study. *Nutrients*. May 2020;12(6):1588. doi: 10.3390/nu12061588.

Photoaging results from exposure of the skin to ultraviolet (UV) rays from the sun and leads to wrinkles, dry skin, and reduced elasticity due to reduced collagen production. In severe cases, photoaging can cause pigmental disorders and skin tumors. Collagen in the outermost stratum corneum and dermal layers of the skin maintains elasticity and moisture. *Hydrangea* (*Hydrangea serrata*, Hydrangeaceae) contains bioactive compounds that have been shown to have protective effects on cell viability, prevention of degradation of pro-collagen type I, and suppression of the expression of metalloproteinase-1 (MMP-1) and pro-inflammatory cytokines. *Hydrangea* is also known to exhibit anti-inflammatory, antimicrobial, antidiabetic, antiallergic, antimalarial, and anti-cancer properties. Previous in vitro and animal studies have shown that a hot water extract of hydrangea leaves (WHS) protects mouse cells from ultraviolet B- (UVB) induced decreases in cell viability, protects pro-collagen type I by down-regulating MMPs, and induces hyaluronic acid (HA). This randomized, double-blind, placebo-controlled trial was designed to determine the efficacy and safety of hydrangea leaves (WHS) on skin wrinkle improvement and moisturization.

Healthy men and women between the ages of 35 and 60 years were recruited to participate. All participants had a global skin wrinkle grade higher than 3, as determined by dermatologists using the Guidance for Efficacy Evaluation of Functional Cosmetics (Korean Ministry of Food and Drug Safety [KMFDS]) and an average score of 49 points or less in water retention on both cheeks. Participants were excluded who received treatment on the face and used steroid-containing or other external skin agents, diet pills, contraceptives, hormone medications, or diuretics within one month of this study. Additionally, participants were excluded who suffered from skin diseases or sensitivities or allergies to pharmaceutical products; had unregulated hypertension, diabetes, or mental disorders; were pregnant, lactating, or planning to become pregnant within three

months of commencing this study; received hospitalization, medication, or rehabilitation for alcohol use, heart disease, or a central nervous system disorder. Smokers or those who had not smoked for less than one year, participated in another clinical trial within one month preceding this trial, or had participated in the same clinical trial within six months were also excluded. The trial was conducted between November 30, 2018 and May 31, 2019.

A total of 250 participants were recruited; 99 did not meet inclusion criteria. The remaining 151 participants were randomly assigned to the WHS 300 mg (n = 50), WHS 600 mg (n = 50), or placebo (n = 51) groups. Five participants dropped out for personal reasons or withdrew consent (WHS 300 mg, n = 2; WHS 600 mg, n = 1; placebo, n = 2).

Dried hydrangea leaves were extracted using distilled water followed by filtration and spray-drying to yield 23% per weight of dried WHS extract residue, containing 7.7 mg/g of hydrangenol as the bioactive compound. Capsules contained 300 mg or 600 mg of WHS. The placebo was identical to the test capsules (manufacturer not disclosed). Participants were instructed to take one capsule daily for 12 weeks [Note: The article describes this as consuming test I, II, or control food; however, the test foods and control were manufactured into 300 mg, 600 mg, and placebo capsules.].

There were no significant differences in demographics, blood pressure, pulse, or other study measurements within or among the groups at baseline. Skin wrinkles were assessed visually by expert dermatologists and instrumentally by analysis of silicone-based skin replicas with a Skin Visiometer SV 700. Grade changes in skin wrinkle visual evaluation of the left (Lt) and right (Rt) crow's feet were significantly lower in the WHS 300 mg and WHS 600 mg ($P < 0.001$ for both) compared to the placebo after the 12-week intervention. Five parameters for skin wrinkling were measured with the Visiometer including R1 (skin roughness), R2 (maximum roughness), R3 (average roughness), R4 (smoothness depth), and R5 (arithmetic average roughness). For both WHS groups, the changes from baseline were significantly lower than for the placebo for parameters R1-R3 ($P < 0.001$ for both) and R4 (WHS 300 mg, $P < 0.01$; WHS 600 mg, $P < 0.001$). R5 measurements were significantly lower in the WHS 600 mg ($P < 0.01$) compared to the placebo after the trial.

Skin hydration significantly improved over the 12-week trial in both WHS groups compared to the placebo ($P < 0.001$ for both) as measured by a Corneometer CM 825. No significant changes were observed via Tewameter TM 300 analysis within or among the groups in trans-epidermal water loss (TEWL) after 12 weeks. Using a Cutometer MPA 580, three parameters of skin elasticity were measured at the perpendicular intersection between the Lt or Rt eye pupil and nose tip including R2 (Ua/Uf; the overall elasticity of the skin, including creep and creep recovery), R5 (Ur/Ue; the net elasticity), and R7 (Ur/Uf; the ratio of elastic recovery to the total deformation). Changes in R2 for both WHS groups were significantly greater compared to the placebo ($P < 0.05$), except for the change in R2 value measured in the Rt area of WHS 300 mg group which was not significant. Significantly greater values were observed in the WHS 600 mg group in R5 measurements in the Lt area ($P < 0.05$) after eight weeks and in the Rt area ($P < 0.05$) after 12 weeks compared to the placebo. Changes in R5 value in both test areas of the WHS 300 mg group were not significantly greater than those observed in the placebo group. Changes in R7 values on the Lt side in the WHS 600 mg group were not significant compared to the placebo; however, in the Rt side, values were significantly greater ($P < 0.05$).

Changes in skin texture and roughness as measured using an Antera 3D camera for skin analysis were significantly lower for all measurements in both WHS groups compared to the placebo ($P < 0.001$) after the 12-week intervention. Changes in skin roughness (R5; arithmetic average roughness) were significantly lower on the Rt in WHS 300 mg ($P < 0.01$) and in WHS 600 mg ($P < 0.001$), and in both groups for the Lt side measurements compared to the placebo ($P < 0.001$).

No adverse events were reported.

The authors conclude that consumption of WHS has potential as a dietary supplement to protect against skin aging. The authors recommend nutricosmetic products be consumed over topical application to facilitate absorption of active compounds. Future studies should include an analysis of underlying mechanisms by which WHS improves skin wrinkles, hydration, elasticity, texture, and roughness.

The authors declare no conflict of interest.

—*Samaara Robbins*

Referenced article can be accessed at <https://www.mdpi.com/2072-6643/12/6/1588>.

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