Nagase Viita

PERSONAL CARE INGREDIENTS

A reviving solution for anti-aging; an upcycled ingredient Glucosyl Naringin

2024 October | Technical Whitepaper

INTRODUCTION

The global market for anti-aging reached $62.6 billion (USD) in 2021 and is projected to grow to $93.1 billion (USD) by 2027.[1] The market is expected to continue growing as disposable incomes increase, people become more aware of healthier lifestyles, life expectancy increases, and the aging population grows. From this perspective, "wellbeing" can be considered as a desire of all people to become healthy in mind and body, while aesthetically viewed, it is a concept that leads to "well aging", the idea that people become more attractive and graceful as they age.

Furthermore, the concept of "holistic beauty" is gaining attention due to the growing need for natural and clean products with less environmental impact. For consumers who wish to stay youthful and attractive without harming the environment and society, "holistic well aging" may be the essential concept for today.

An upcycled glycosylated naringin for well aging

Responding to these market needs, the upcycled ingredient Glucosyl Naringin (INCI name: glucosyl naringin and naringin), scientifically proven to improve skin elasticity, was launched. The aglycon naringin is a type of polyphenol derived from citruses, such as grapefruits and bergamots, known to have anti-inflammatory and antioxidant effects.[2] However, extremely low water solubility was the obstacle to its application in personal care products.

Nagase Viita, a Japanese saccharide manufacturer with a 140-year history, has a fundamental policy of sustainable material procurement and production, developed glucosyl naringin and successfully increased its water solubility by more than 6,000 times over naringin. Naringin and glucose are combined by the company's proprietary enzyme technology, resulting in a readily biodegradable compound. Moreover, the raw material of naringin is plant-derived waste, such as thinned or naturally fallen fruit.

The breakthrough of increasing water solubility also revealed biological activity to the skin and the effect on skin elasticity. This efficacy is suggested to be essential for a youthful appearance, since the negative correlation between wrinkle depth and skin elasticity is reported.[3]

COMPONENTS RELATED TO SKIN ELASTICITY

In the three layers of skin: epidermis, dermis, and hypodermis, the dermis is mainly responsible for skin elasticity. The dermis consists of extracellular matrix (ECM) and fibroblast, which provides a flexible and elastic structure providing the strength to withstand mechanical stimulation.

The ECM is composed of fibrous components, such as collagen and elastin fibres, and a matrix including glycoproteins and proteoglycans. Collagen fibres provide tensile strength, while elastin fibres afford extensibility and reversible recoil.

The crucial role of elastin fibres

Collagen fibres are indeed important, as we see various active ingredients in the market, while elastin fibres seem little known to consumers, despite their crucial role in skin elasticity.

Elastin fibres are principally composed of elastin and elastin-associated microfibrils.[4] Elastin is an insoluble polymer of 60-70 kDa tropoelastin monomers. Tropoelastin is an extremely extensible molecule, which self-assembles into elastin.[5] It is cross-linked through the activity of lysyl oxidase (LOX), which is a copper-requiring enzyme and combined with microfibrils to form elastin fibres. Microfibrils serve as a scaffold to aid the correct alignment of elastin fibres (Figure 1).[4] The elastin fibres intricately bundle collagen fibres, providing elasticity and resilience to the skin (Figure 2).

However, elastin fibres are known to decrease and degenerate with aging and photo-aging, breaking down the network structure of collagen fibres, and resulting in loss of firmness and elasticity.

Although injectable fillers, such as collagen and hyaluronic acid injections, have been developed to rejuvenate the skin, elastin fillers are currently little known since the formation of elastin fibres is complex and involves in multiple processes. Therefore, glucosyl naringin, which promotes the formation of elastin fibres, could be a reviving solution for consumers seeking a youthful appearance.

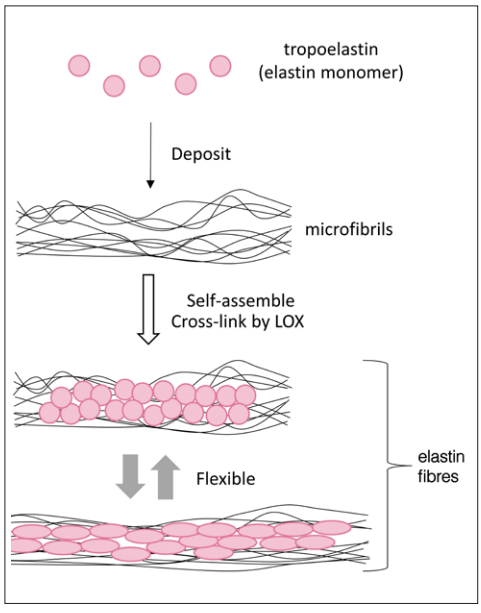
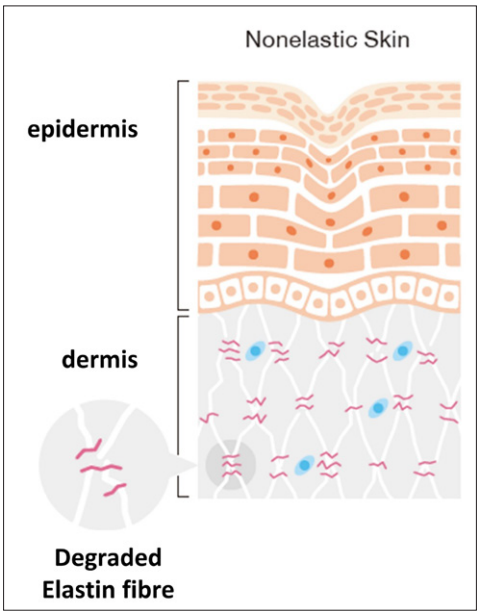


FIGURE 1: Process of elastin fibre formation.



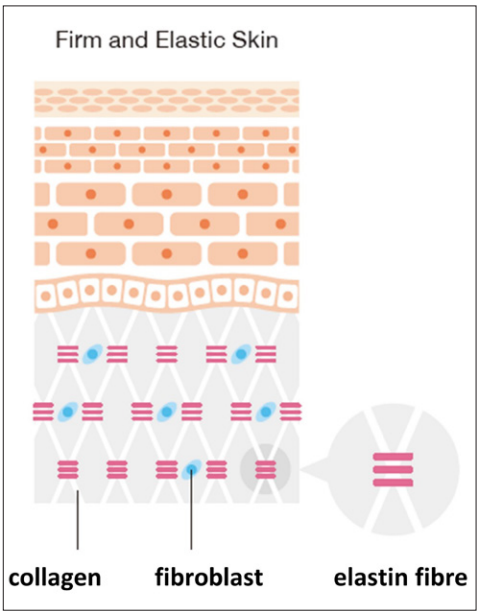


FIGURE 2: Elastin function for skin elasticity

RESULTS

Effects on quantity: enhancement of elastin production

Tropoelastin is a major component of elastin, and its expression decreases by aging.[4] Firstly, the effect on tropoelastin mRNA expression in normal human dermal fibroblasts (NHDF) were investigated. NHDF were incubated with or without 2.0, 5.0, 10.0 mg/mL of Glucosyl Naringin. After 48h incubation, it significantly upregulated the tropoelastin mRNA expression in a dose-dependent manner (Figure 3). Then, to investigate the effects on elastin protein production, NHDF were incubated for 5 days with or without 1.0, 10.0 mg/mL Glucosyl Naringin. The amount of elastin in NHDF was measured using the elastin assay kit. The elastin production in NHDF was significantly increased by the treatment (Figure 4).

Additionally, 3D skin models were used to examine the effects on elastin production. The 3D skin models were reconstructed by building the epidermal layer on top of the constructed dermal layer. Immunostainings were performed on the tissue sections from the 3D skin models treated with or without 0.5, 5.0 mg/mL Glucosyl Naringin. Elastin positive surface area per dermal unit area was measured from its fluorescence staining image, which was considered equivalent to the

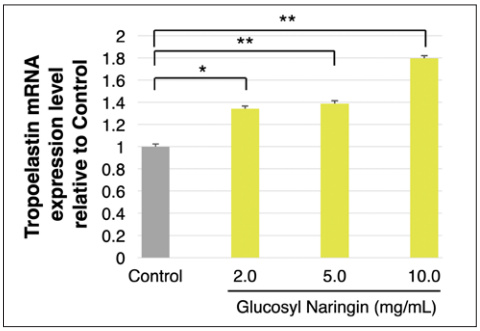


FIGURE 3: Tropoelastin mRNA expression level treated with or without Glucosyl Naringin relative to control. *N*=3, Mean + SD, *p<0.05, **p<0.01 vs control (Dunett's test).

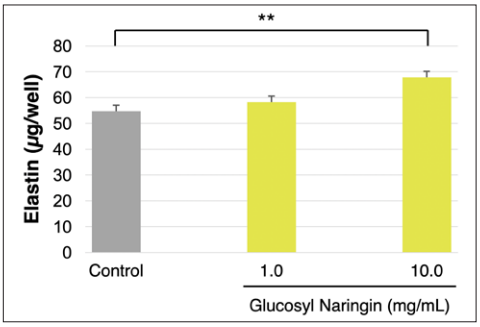


FIGURE 4: The amount of elastin in NHDF treated with or without Glucosyl Naringin. *N*=5, Mean + SD, **p<0.01 vs control (Dunett's test).

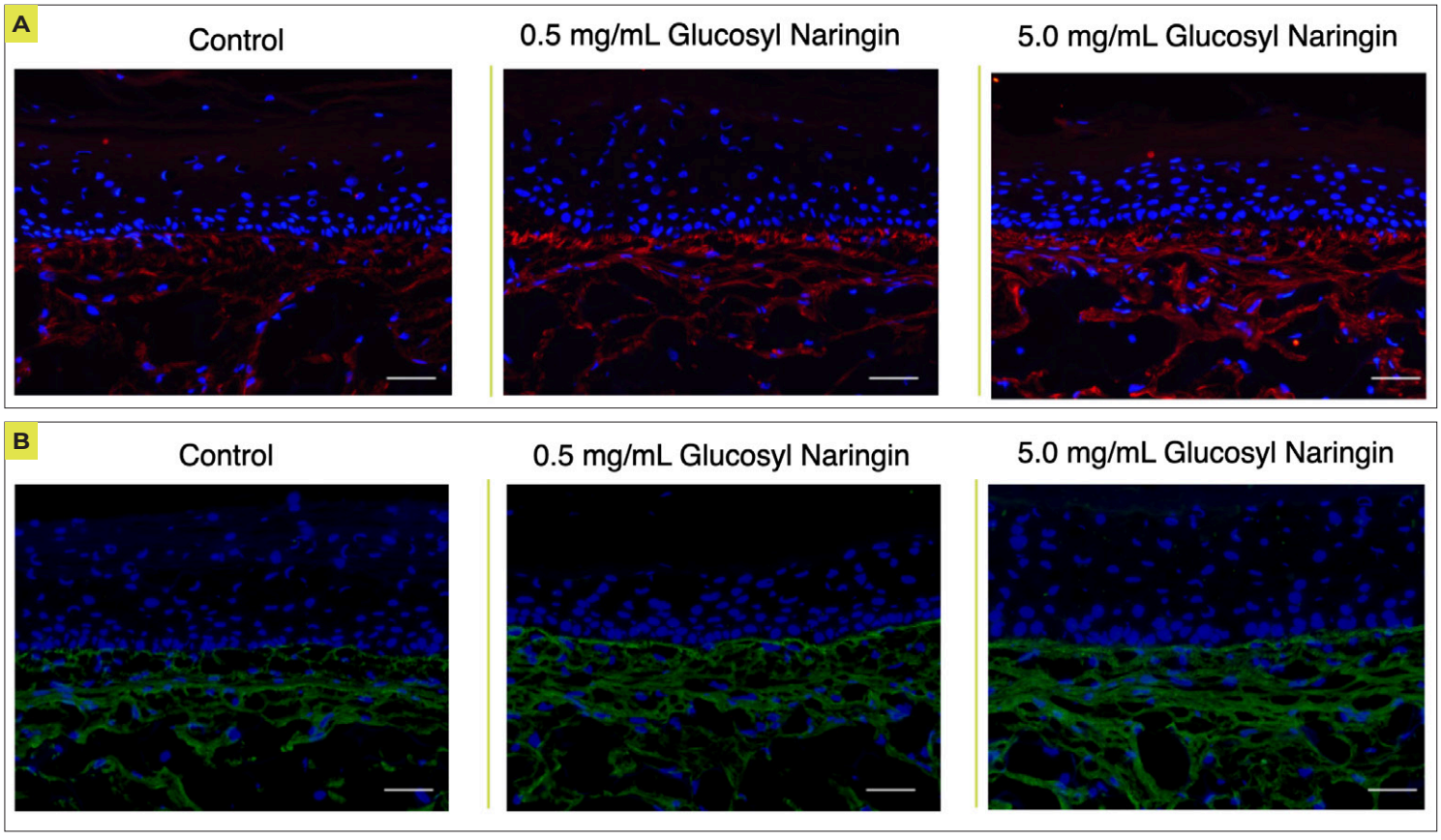
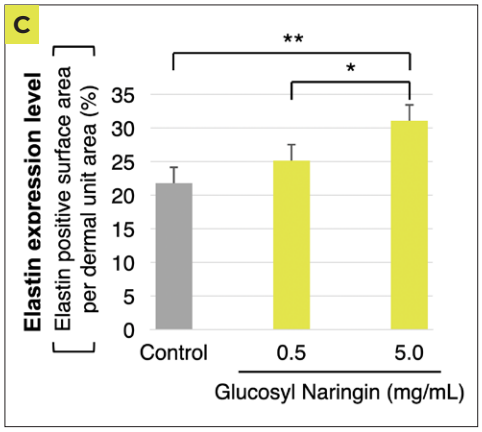


FIGURE 5: Elastin and fibrillin-1 expression in 3D construct treated with or without Glucosyl Naringin. A) Immunofluorescence images of elastin (red) and nucleus (blue). Scale bar: 50 μm. B) Immunofluorescence images of fibrillin-1 (green) and nucleus (blue). Scale bar: 50 μm.



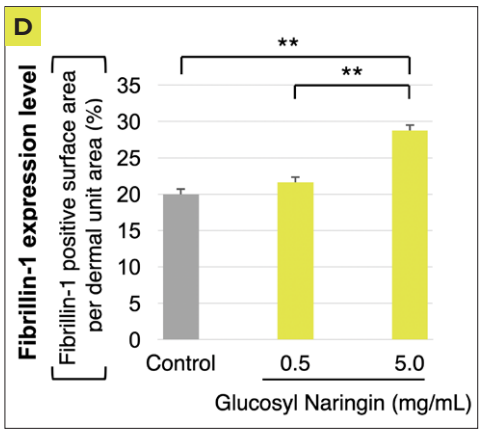


FIGURE 5 (continued): C, D) Elastin and fibrillin-1 expression level. *N*=3, Mean + SD, **p*<0.05, ***p*<0.01 (Tukey-Kramer test).

elastin expression level. The expression of elastin was significantly increased by the treatment (Figure 5A, C). Furthermore, it increased the expression of fibrillin-1, which is one of the microfibrillar components of elastin fibres (Figure 5B, D).[6] These data suggest that it plays an important role in both the elastin and its scaffold protein expression.

Effects on Quality: Promotion of elastin fibre formation

It has been shown that the elastin fibres are formed in multi-steps, which indicates that an increase of elastin does not always promote elastin fibre formation.[4]

Therefore, the effects on elastin fibre formation in NHDF were investigated.

Firstly, the effect on LOX expression, which catalyses the cross-linking of elastin fibres, was investigated. NHDF were incubated for 24h with or without 2.0, 5.0 and 10.0 mg/mL Glucosyl Naringin. A significant increase of the LOX mRNA expression in a dose-dependent manner was confirmed (Figure 6).

Secondly, immunofluorescence staining of NHDF were performed to visually observe the elastin fibre formation. It has been reported that elastin fibres, which are thin and single-stranded in young skin, become gradually shrinking and sagging by aging.[7] The cells treated with or without 10.0 mg/mL Glucosyl Naringin for 9 days were fixed, dyed with elastin antibody, and then observed using a fluorescence microscope. The fibrous structure of elastin was clearly observed in the cells treated, suggesting the promotion of elastin fibre formation (Figure 7).

Skin elasticity

Elastin fibres play an important role in maintaining skin elasticity. With the objective of evaluating the impact on skin elasticity, a pre-clinical study was conducted where Japanese female subjects applied a toner containing 5.0 mg/g Glucosyl Naringin or a placebo toner to either the left or right half of

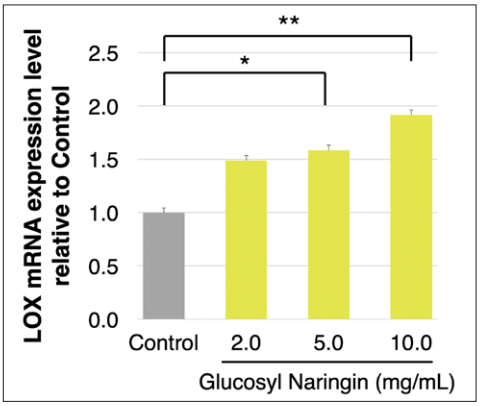


FIGURE 6: LOX mRNA expression level treated with or without Glucosyl Naringin relative to control. *N*=3, Mean + SD, **p*<0.05, ***p*<0.01 vs control (Dunett's test).

their faces twice a day for 8 weeks and evaluated their cheeks' viscoelasticity before and after application. The skin elongation value during skin suction was measured by a skin elasticity meter, and calculated R2 and R6 as the parameters of skin viscoelasticity. R2 refers to the recovery ratio of the skin length, while R6 represents the ratio of viscosity and elasticity part when elongated (Figure 8). An increase of R2 and a decrease of R6 suggest the improvement of skin elasticity.

The statistical analysis was performed by dividing the subjects into two groups: older and younger groups (Figure 9). In the younger group (age; 39.4±3.9), the values of R2 and R6 did not show significant changes by the application of either toners. In the older group (age; 49.2±2.9), the toner containing Glucosyl Naringin significantly

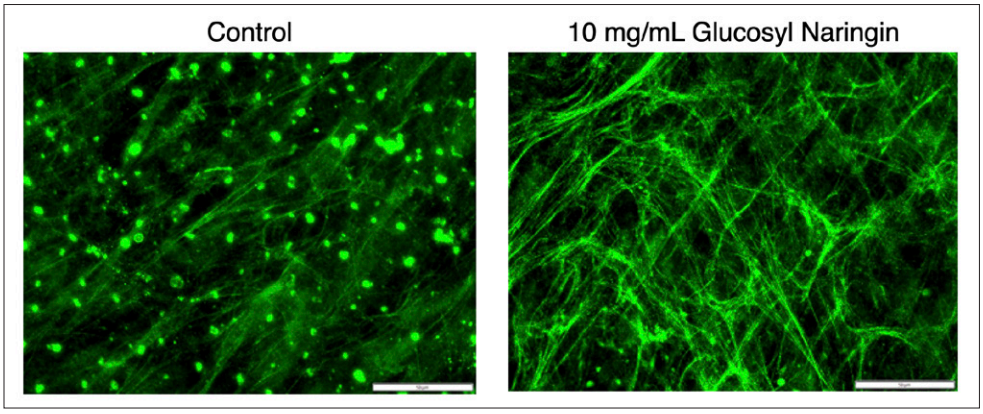


FIGURE 7: Elastin fibre formation in NHDF treated with or without Glucosyl Naringin. Scale bar: 50 μm

increased the value of R2 and significantly decreased the value of R6, while the placebo toner did not have significant changes in either value. Also, after 8 weeks of application, there was a significant difference in the R2 value between the toners with and without Glucosyl Naringin. These results indicate the improvement of skin elasticity in the older group. It has been reported that skin elasticity decreases age-dependently, thus it can be assumed that Glucosyl Naringin improves the skin elasticity loss caused by aging.[8] Therefore, it is expected to be more effective for elderly people facing the age-related changes: loss of skin elasticity leading to wrinkles and sagging.

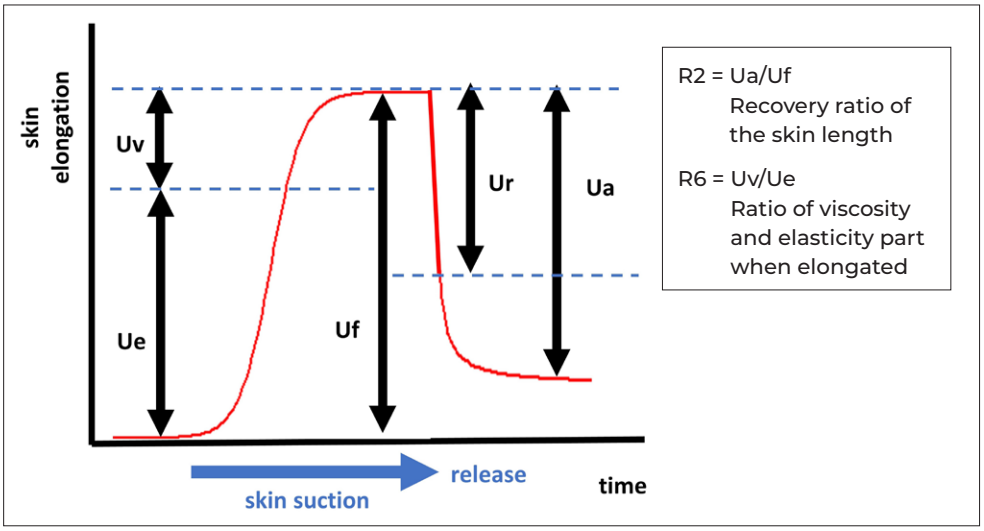


FIGURE 8: Skin elasticity parameter using a skin elasticity meter.

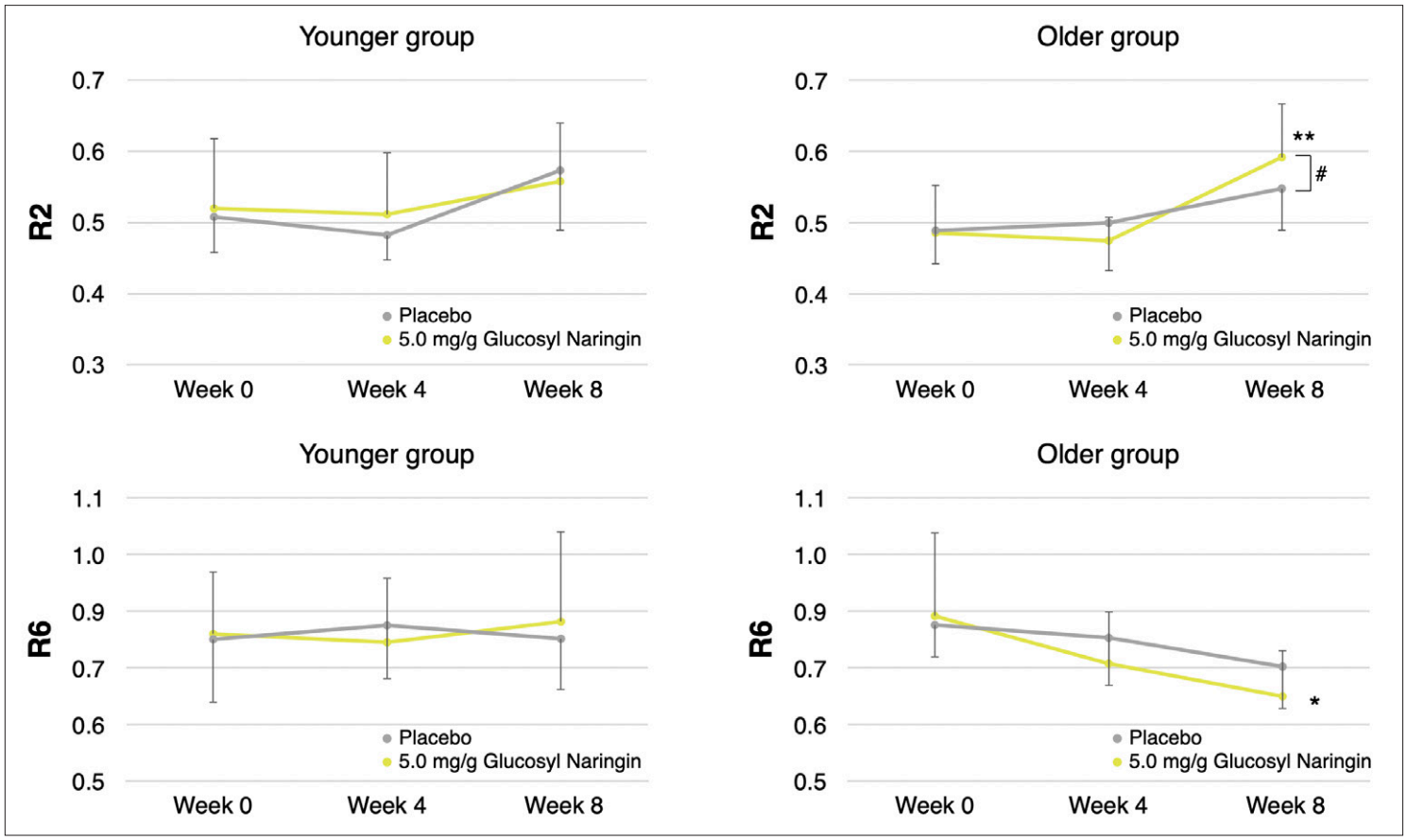


FIGURE 9: Change of the skin elasticity after treatment with or without Glucosyl Naringin. *N*=8 (younger group) or 9 (older group), Mean ± SD, **p*<0.05, ***p*<0.01 vs Week 0 (Dunett's test), #*p*<0.05 (paired t-test).

CONCLUSION

Glucosyl Naringin is an upcycled ingredient derived from inedible citrus fruit which is readily biodegradable and produced by sustainable manufacturing. In vitro studies confirmed the enhancement of elastin production and fibre formation, indicating the effects on both the quantity and the quality of elastin. Also, pre-clinical study showed that continuous treatment improved skin elasticity in the older group of subjects, suggesting that Glucosyl Naringin can improve skin elasticity loss caused by chronological aging.

Moreover, there is a report showing that it also has effects on collagen fibres, increasing type 1 collagen expression and enhancing the gene expression of cell adhesion related factors.[9] This provides an insight indicating that Glucosyl Naringin approaches both the tensile strength provided by collagen fibres and the elasticity provided by elastin fibres of skin dermis, which offers significant value for anti-aging active.

Today, as life expectancy increases, more and more consumers are seeking healthy lifestyles and well aging. Glucosyl Naringin satisfies those seeking self-esteem, a good feeling about themselves to age naturally, and sustainability for the planet. It revives healthy skin for an affluent and progressive generation, enabling them to engage in their proactive and comfortable lives which leads to “holistic well aging”.

REFERENCES

[1] Imarc. “Size of the anti-aging market worldwide from 2021 to 2027 (in billion U.S. dollars).” Chart. 28 March, 2022. Statista. Accessed 16 June, 2023. https://www.statista.com/statistics/509679/value-of-the-global-anti-aging-market/

[2] Sharma A, Bhardwaj P, and Arya SK. Naringin: A potential natural product in the field of biomedical applications. Carbohydrate Polymer Technologies and Applications. 2021;2(25):100068.

[3] Fujimura T, Haketa K, Hotta M, and Kitahara T. Loss of skin elasticity precedes to rapid increase of wrinkle levels. Journal of Dermatological Science. 2007;47(3):233-239.

[4] Baumann L, Bernstein EF, Weiss AS, Bates D, Humphrey S, Silberberg M et al. Clinical Relevance of Elastin in the Structure and Function of Skin. Aesthetic Surgery Journal. 2021;3(3):ojab019

[5] Ozsvar J, Yang C, Cain SA, Baldock C, Tarakanova A, and Weiss AS. Tropoelastin and Elastin Assembly. Frontiers in Bioengineering and Biotechnology. 2021;9:643110.

[6] Uitto J, Li Q, and Urban Z. The complexity of elastic fiber biogenesis in the skin – a perspective to the clinical heterogeneity of cutis laxa. Experimental Dermatology. 2013;22(2):88-92.

[7] Montagna W and Carlisle K. Structural Changes in Aging Human Skin. The Journal of Investigative Dermatology. 1979;73(1):47-53.

[8] Lynch B, Pageon H, Blay HL, Brizion S, Bastien P, Bornschlögl T et al. A mechanistic view on the aging human skin through ex vivo layer-by-layer analysis of mechanics and microstructure of facial and mammary dermis. Scientific Reports. 2022;12:849.

[9] Kawashima E, Kobayashi T, and Mizutani Y. Glycosylated naringin promotes fibrillin-1 formation and collagen synthesis. Fragrance Journal. 2020;8:16-21.

This white paper has been featured in PERSONAL CARE MAGAZINE (2023 September issue), published by Step Communications Ltd. (https://personalcaremagazine.com/)

Authors

Yui Sunada, Ami Chikatomo, Kohta Kanazawa, Yohsuke Matsumoto, Yuko Takai, Jiro Kishimoto (Nagase Viita)

Glucosyl Naringin

Awaken Your Skin's Natural Power

Strengthen, protect, rejuvenate your skin

An upcycled citrus polyphenol glucoside that strengthens your skin's resilience against stress and environmental disturbances while enhancing elasticity to rejuvenate your skin's natural beauty and promote overall well-being.

- Restores skin elasticity by improving quality and quantity of elastin
- Reduces UVB-induced stress
- Strengthens the skin's barrier function

Learn more about Glucosyl Naringin

Approved by ECOCERT RAW MATERIAL
COSMOS APPROVED

Where nature and glycoscience thrive

Nagase Viita

Learn more about our sustainability

PLATINUM Top 1%
ecovadis
Sustainability Rating
MAR 2024

Glucosyl Naringin is manufactured by Nagase Viita Co., Ltd. in Japan