Journal of Functional Foods 112 (2024) 105955

Contents lists available at ScienceDirect

Journal of Functional Foods

journal homepage: www.elsevier.com/locate/jff

Oral supplementation of vegan collagen biomimetic has beneficial effects on human skin physiology: A double-blind, placebo-controlled study

Yung-Kai Lin [a,b,c], Chia-Hua Liang [d], Yung-Hsiang Lin [e], Tai-Wen Lin [e], Josué Jiménez Vázquez [f], Anthony van Campen [f], Chi-Fu Chiang [e,*]

[a] Institute of Food Safety and Risk Management, National Taiwan Ocean University, Keelung, Taiwan
[b] Department of Food Science, National Taiwan Ocean University, Keelung, Taiwan
[c] Graduate Institute of Biomedical Engineering, National Chung Hsing University, Taichung, Taiwan
[d] Department of Cosmetic Science and Institute of Cosmetic Science, Chia Nan University of Pharmacy and Science, Tainan, Taiwan
[e] Research & Design Center, TCI CO., Ltd., Taipei, Taiwan
[f] Corpowell BV, Schilde, Belgium

A R T I C L E I N F O

Keywords:
Asiaticoside
Collagen biomimetic
Ginsenosides
Skin
Vegan collagen

A B S T R A C T

Background: Vegan collagen is an innovative plant-based collagen biomimetic that contains a variety of plant extracts, including asiaticoside, ginsenoside, and through fermented amino acids, which stimulates the natural process for type I collagen synthesis.
Methods: In this study, using vegan collagen (Corpowell BV, Schilde, Belgium) to explore the skin beautifying effects in the human body. 90 subjects were recruited and divided into a placebo group (n = 30), a vegan collagen group (n = 30), and a fish collagen group (n = 30). Subjects were informed to consume 1 sachet of the sample daily for 8 weeks. Skin conditions were measured at week 0, week 4 and week 8.
Results: The results showed that vegan collagen significantly increased collagen density and elasticity by 4.7% and 5.1% and decreased wrinkles, texture, and pores by 27.5%, 20.1%, and 12.3% compared to the placebo group. In addition, the hydration and lightness were increased by 4.3% and 2.3% compared to the placebo group.
Conclusion: Vegan collagen has the potential to improve skin collagen density, elasticity, texture, wrinkles, pores, hydration, and lightness.

1. Introduction

The demand of improving skin health has been increasing rapidly globally in recent years, highlighting the crucial roles of collagen in determining skin beauty. As one of the main proteins of skin structure, some studies have shown that collagen products have multiple benefits for beautiful skin (Bolke, Schlippe, Gerss, & Voss, 2019). First, supplementing exogenous collagen can improve skin elasticity and firmness (de Miranda, Weimer, & Rossi, 2021). Collagen, as the structural support substance of the skin, can strengthen the support structure of the dermis and slow down the aging phenomenon of the skin (Campos et al., 2023). Second, the amino acid composition in collagen products is critical to skin moisturizing and protective functions (Diaz, Namkoong, Wu, & Giancola, 2022).

Vegan collagen is alternative with the same amino acid structure as human type I collagen. Vegan collagen activates the natural type I collagen synthesis process containing a variety of plant extracts, including asiaticoside, and ginsenosides, which genetically induce collagen expression. In particular, asiaticoside and ginsenosides are well-known plant-derived bioactive ingredients that stimulate collagen secretion through TGF-β/Smad signaling pathways (Kwok, Yue, Mak, & Wong, 2012; J. Lee et al., 2006). TGF-β receptor-dependent Smad3 and Smad4 activation are responsible for conveying the signals to the nucleus and further activating the transcription activity of the collagen gene in fibroblast (Chen et al., 1999). Besides, vegan collagen also contains fermented amino acids that match the type I collagen's amino acids profile. These amino acids serve as readily available substrates during collagen synthesis within fibroblasts. Thus, the vegan collagen naturally utilizes collagen-producing machinery based on the central dogma of molecular biology, inducing the production of specific type I collagen through transcription of activated collagen gene to RNA and further translation to protein (Shoseyov, Posen, & Grynspan, 2014).

* Corresponding author.
E-mail address: Jimmy.Chiang@tci-bio.com (C.-F. Chiang).

https://doi.org/10.1016/j.jff.2023.105955
Received 12 September 2023; Received in revised form 8 December 2023; Accepted 10 December 2023

In the face of global challenges such as climate change, resource scarcity, and environmental pollution, it is urgently necessary to seek more sustainable methods of production to meet the increased demand for skin health and beauty. Fermentation technology, which exploits microorganisms for raw materials conversion processes in a more sustainable and transformative manner, has recently attracted considerable interest (Pérez-Rivero & López-Gómez, 2023). The fermented amino acids used in vegan collagen are obtained through fermentation technology from plant-based raw materials. In particular, these fermented amino acids are biosynthesized inside microorganisms, specifically by the Corynebacterium glutamicum. This bacterium is generally recognized as safe (GRAS) and was used widely in the food industry (Zahoor, Lindner, & Wendisch, 2012). Corynebacterium glutamicum is a glucose-utilizing bacterium that can convert glucose and ammonium sulfate into amino acids via a biosynthetic pathway (Hwang, Yeom, Kim, & Lee, 2002). The biosynthesis of amino acids involves a series of its enzymatic reactions, which convert the precursor molecules derived from glucose and ammonium sulfate into the desired amino acids (Ljungdahl & Daignan-Fornier, 2012). Plant-based amino acids are obtained through fermentation, while plant-based glucose is added as raw material and converted into amino acids (Zhao et al., 2021).

In this study, we aimed to explore the roles of vegan collagen (Corpowell BV, Schilde, Belgium) in the skin-beautifying effects on the human body. The present work is based on the double-blinded, placebo-controlled, randomized study. 90 subjects were recruited and divided into a placebo group (n = 30), vegan collagen group (n = 30), and a fish collagen group (n = 30). Subjects were informed to consume 1 sachet (powder) of the sample daily for 8 weeks. Skin conditions were measured at week 0, week 4 and week 8.

2. Material and methods

2.1. Clinical trial design

The study was registered in clinicaltrials.gov (No. NCT05789368), and was performed under a protocol approved by the Antai Medical Care Cooperation Antai- Tian-Sheng Memorial Hospital Institutional Review Board (Approval Number: 22–112-A), and was conducted according to the code of ethics on human experimentation established by the Declaration of Helsinki (1964) and its amendments. Written informed consent was obtained from all participants after a full explanation of the study. A double-blinded, placebo-controlled, randomized study was conducted. The subjects were randomly assigned to three groups, with 30 subjects in each group. The subjects were informed to consume one sachet (powder) every day for 8 weeks. Before measurements, subjects were instructed to wash and wipe their face and acclimatize for at least 30 min to the standardized laboratory conditions (room temperature 25 °C, RH 55 ± 5 %). Skin conditions and self-assessment questionnaires of the subjects were collected at week 0, week 4, and week 8 of the study. The fasting blood samples were collected at week 0 and week 8 of the study and examined BUN, Creatinine, AST, and ALT. Inclusion criteria: Healthy adults aged above 20 years old. The exclusion criteria included: i) skin disease, liver cirrhosis, or chronic renal failure; ii) allergy to cosmetics, drugs, or foods; iii) pregnant and breastfeeding; iv) taking chronic drugs; v) people who had any cosmetic procedures (intense pulse light, medical peelings, or laser therapy) before 4 weeks of the study.

2.2. Supplement formulation

Vegan collagen sachet: containing VeCollal® 5 g (Corpowell BV, Schilde, Belgium), sucralose, citric acid, silicon dioxide, maltodextrin. Collagen sachet: containing fish collagen 5 g, sucralose, citric acid, silicon dioxide, maltodextrin. Placebo sachet: containing sucralose, citric acid, silicon dioxide, maltodextrin. Subjects were required to consume 1 sachet (powder) of the sample daily for 8 weeks. Skin conditions were measured at weeks 0,4 and 8. The placebo, vegan collagen, and collagen sachet were packaged in the same appearance, shape, and size.

2.3. Clinical skin efficacy assessment

DermaLab® Series SkinLab Combo was utilized to scan and analyze skin collagen density. The color scale indicates collagen density; white reflects the highest collagen density, and black reflects the lowest. Cutometer® dual MPA580 was utilized to measure skin elasticity, and the higher the relative value, the more significant the improvement. Corneometer® CM825 was utilized to measure skin moisture content, and the higher the relative value, the more significant the improvement. Chroma Meter MM500 was utilized to measure skin lightness, and the higher the relative value, the whiter the skin tone. Mexameter® MX18 was utilized to measure skin melanin index, and the lower the relative value, the more significant the improvement. VISIA Complexion Analysis System was utilized to measure skin texture, wrinkle, pores. The VISIA System ensured consistent positioning of each subject's head with a configurable head support. The photographic images were captured with standard and ultraviolet light at 0 degree head positioning. The results were presented as the mean value and the relative percentage (%) to the baseline.

2.4. Statistical analysis

The comparison of measurement results for skin parameters among groups and between groups was analyzed by Paired *t*-test or one-way ANOVA followed by GraphPad Prism, as $p < 0.05$ was considered statistical significance.

3. Results

3.1. Safety assessment

Fig. 1 showed the enrollment process of a clinical trial. All the subjects had no evidence of skin irritation, gastrointestinal discomfort, and any other discomforts. Table 1 shows the results of the biochemical analysis. In addition, the values of aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), creatinine (CRE) and glucose were not significantly changed. There was no significant difference between the three groups.

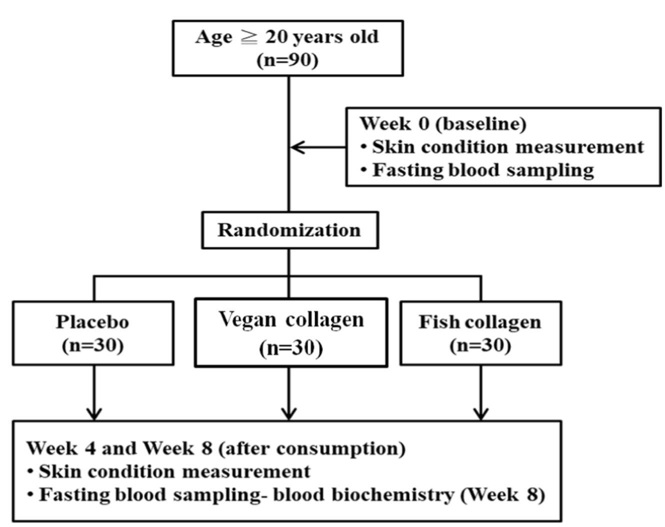

Fig. 1. Clinical trial flowchart.

Table 1
Demographic and results of biochemical analyses.

Test Group	Placebo		Vegan collagen		Fish collagen	
Subject number	30		30		30	
Female	26		26		28	
Male	4		4		2	
Age (years)	36.8		40.8		35.5	
Test timepoint	Week 0	Week 8	Week 0	Week 8	Week 0	Week 8
AST (U/L)	16.3 ± 5.2	16.0 ± 4.1	19.2 ± 4.6	18.1 ± 4.2	16.8 ± 4.1	16.3 ± 3.7
ALT (U/L)	15.1 ± 7.4	15.1 ± 5.8	18.9 ± 7.5	16.7 ± 7.7	16.4 ± 8.2	15.0 ± 6.4
BUN (mg/dL)	12.2 ± 3.7	11.7 ± 4.3	13.2 ± 3.2	12.2 ± 3.2	12.0 ± 3.3	11.9 ± 3.2
CRE (mg/dL)	0.67 ± 0.13	0.66 ± 0.13	0.67 ± 0.11	0.67 ± 0.10	0.66 ± 0.12	0.64 ± 0.11
Glucose AC (mg/dL)	83.8 ± 15.5	83.4 ± 21.8	87.5 ± 13.2	83.1 ± 8.7	81.7 ± 9.3	78.5 ± 6.7

Data were expressed as the mean ± S.D.; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen; CRE, creatinine. Statistical significances were assessed by using one-way ANOVA followed by Tukey's Multiple Comparison Test.

3.2 Effect on skin collagen density and elasticity improvement

The skin collagen density and elasticity was significantly increased by 7.7 % (***, $p < 0.001$) and 6.0 % (***, $p < 0.001$) compared to baseline; the collagen density and elasticity was significantly increased by 4.7 % (#, $p < 0.05$) and 5.1 % (###, $p < 0.001$) compared to placebo group (Fig. 2).

3.3. Effect on skin wrinkles, texture, and pores improvement

The wrinkles value was significantly reduced by 32.9 % compared to baseline (***, $p < 0.001$); the wrinkles were reduced by 27.5 % compared to the placebo group (##, $p < 0.01$) (Fig. 3). After the subjects took the vegan collagen sachet for 8 weeks, the skin texture and pores were significantly reduced by 13.1 % (**, $p < 0.01$) and 5.6 % (*, $p < 0.05$) compared to baseline; the skin texture and pores were reduced by 20.1 % (##, $p < 0.01$) and 12.3 % compared to the placebo group (Fig. 3).

3.4. Effect on skin hydration and lightness improvement

The skin hydration and lightness was significantly increased by 6.0 % (***, $p < 0.001$) and 2.6 % (***, $p < 0.001$) compared to baseline; the

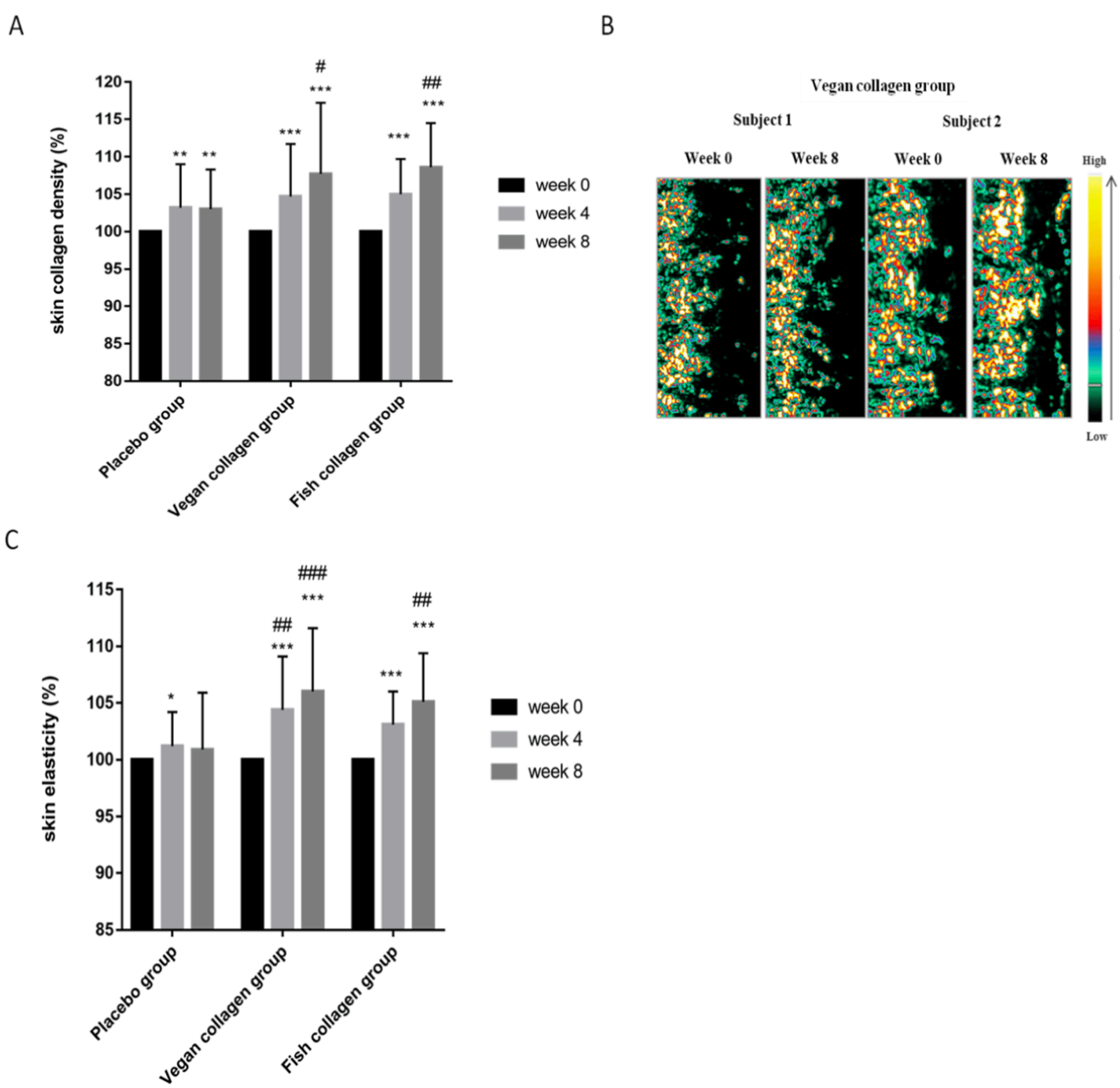

Fig. 2. The Vegan collagen improved skin collagen and elasticity. The (A) collagen density, (B) image of collagen, (C) elasticity, ($n = 30$; mean value ± SD.) *, compared with baseline (week 0) (*, $p < 0.05$, **, $p < 0.01$, ***, $p < 0.001$). $^{\#}$, compared with placebo group ($^{\#}$, $p < 0.05$, $^{\#\#}$, $p < 0.01$, $^{\#\#\#}$, $p < 0.001$).

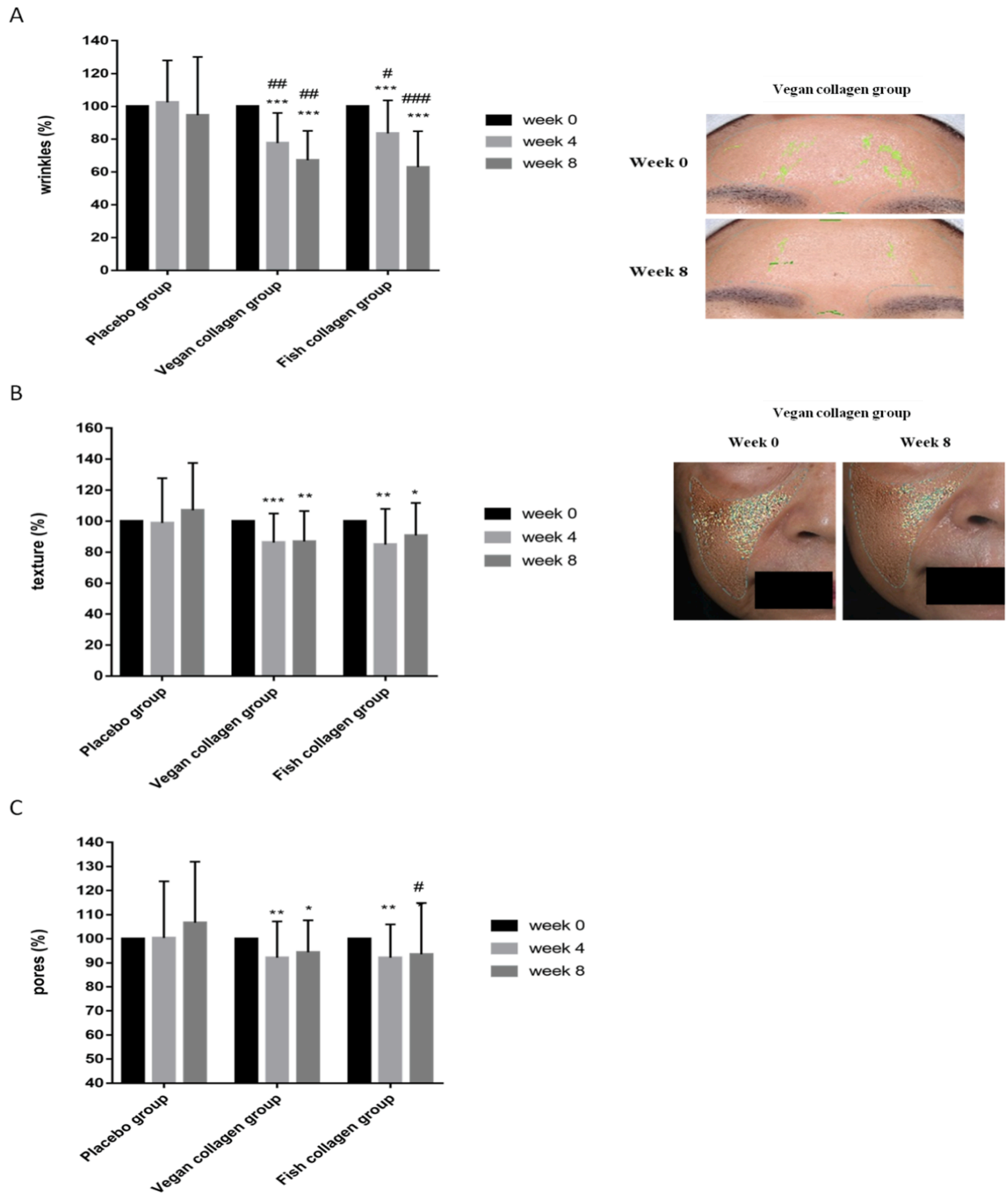

Fig. 3. The Vegan collagen improved skin wrinkles, texture and pores. The (A) wrinkles, (B) texture, (C) pores ($n = 30$; mean value ± SD.) *, compared with baseline (week 0) (*, $p < 0.05$, **, $p < 0.01$, ***, $p < 0.001$). $^{\#}$, compared with placebo group ($^{\#}$, $p < 0.05$, $^{\#\#}$, $p < 0.01$, $^{\#\#\#}$, $p < 0.001$).

skin hydration and lightness was increased by 4.3 % and 2.3 % (###, $p < 0.001$) compared to placebo group (Fig. 4). The results are summarized in Table 2.

4. Discussion

The results revealed that vegan collagen can potentially improve skin collagen density, elasticity, texture, wrinkles, pores, hydration and lightness. In addition, there was no skin irritation or any other discomforts for subjects during the study. Interestingly, the overall effect is almost similar to taking fish collagen. Collagen is primarily sourced from animal tissues; however, animal-derived collagen poses risks of virus transmission, non-uniform molecular weight, and difficulties in quality control, significantly limiting its clinical applications (Meyer, 2019; Varma, Orgel, & Schieber, 2016). Peptides, on the other hand, offer several advantages, including virus-free characteristics, low immunogenicity, uniform molecular weight, and ease of quality control. Biomimetic collagen, an innovative biomaterial, is prepared by mimicking natural collagen's complex structure and properties (Varanko, Saha, & Chilkoti, 2020). The manufacturing process typically involves biotechnological techniques and cell culture, using natural collagen as a prototype. This allows biomimetic collagen to exhibit similar biological characteristics to natural collagen, including biocompatibility, biodegradability, and bioactivity (Dong & Lv, 2016). The advantages of biomimetic collagen lie in its applications in tissue engineering and regenerative medicine. It can serve as a scaffold or structural carrier for

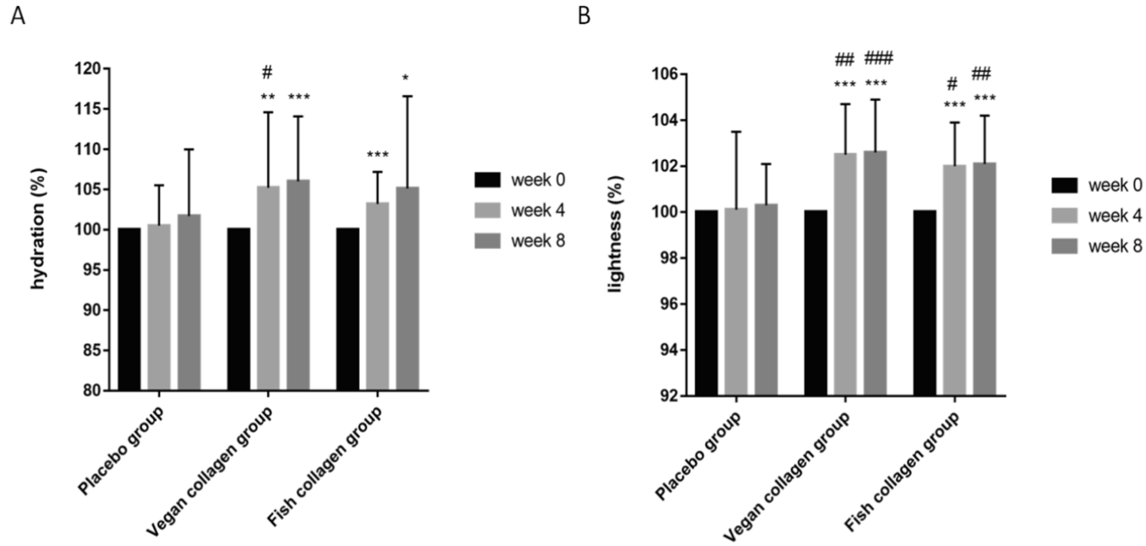

Fig. 4. The Vegan collagen improved skin hydration and lightness. The (A) hydration, (B) lightness (n = 30; mean value ± SD.) *, compared with baseline (week 0) (*, $p < 0.05$, **, $p < 0.01$, ***, $p < 0.001$). #, compared with placebo group (#, $p < 0.05$, ##, $p < 0.01$, ###, $p < 0.001$).

Table 2
Summary of the change rate on each test items after 8-week intervention.

Test Group	Placebo		Vegan collagen		Fish collagen	
Test timepoint	Week 4	Week 8	Week 4	Week 8	Week 4	Week 8
Collagen density (%)	3.2 ± 5.8**	3.0 ± 5.3**	4.7 ± 7.0***	7.7 ± 9.5***, #	5.0 ± 4.7***	8.6 ± 5.9***, ##
Elasticity (%)	1.2 ± 3.0*	0.9 ± 5.0	4.4 ± 4.7***, ##	6.0 ± 5.6***, ###	3.1 ± 2.9***	5.1 ± 4.3***, ##
Wrinkles (%)	2.5 ± 25.5	−5.4 ± 35.5	–22.4 ± 18.4***, ##	–32.9 ± 18.0***, ##	−16.5 ± 20.2***, #	−37.1 ± 22.0***, ###
Texture (%)	−1.1 ± 28.9	7.0 ± 30.6	−13.8 ± 18.7***	−13.1 ± 19.6**	−15.1 ± 23.0**	−9.2 ± 21.0*
Pores (%)	0.4 ± 23.5	6.7 ± 25.3	−7.8 ± 15.0**	−5.6 ± 13.3*	−7.8 ± 13.8**	−6.4 ± 21.3#
Hydration (%)	0.5 ± 5.0	1.7 ± 8.3	5.2 ± 9.4**, #	6.0 ± 8.1***	3.2 ± 4.0***	5.1 ± 11.5*
Lightness (%)	0.1 ± 3.4	0.3 ± 1.8	2.5 ± 2.2***, ##	2.6 ± 2.3***, ###	2.0 ± 1.9***, #	2.1 ± 2.1***, ##

Data were expressed as the mean ± S.D.
Significantly different from the baseline (Paired *t*-test): *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$;
Significantly different from the placebo (One-way ANOVA): #, $p < 0.05$; ##, $p < 0.01$; ###, $p < 0.001$.

repairing damaged tissues and organs, promoting tissue regeneration and repair, accelerating wound healing, and enhancing tissue functionality and performance (Krishani, Shin, Suhaimi, & Sambudi, 2023). In addition to its medical applications, biomimetic collagen has garnered attention in beauty and skincare. Many cosmetic products utilize their moisturizing and anti-aging properties to improve skin texture and reduce wrinkles (Carlomagno, Roveda, Michelotti, Ruggeri, & Tursi, 2022).

Vegan collagen is mainly composed of amino acids (90 %), and plant extracts, including asiaticoside, and ginsenosides. Asiaticosides are active constituents found in the Centella asiatica plant (Gray et al., 2018). Some studies suggest that asiaticosides can promote wound healing. They can stimulate collagen synthesis and skin cell proliferation, accelerating wound recovery and reducing scar formation (Arribas-Lopez, Zand, Ojo, Snowden, & Kochhar, 2022). Asiaticosides possess anti-inflammatory properties, potentially aiding in alleviating skin inflammation and sensitivity. This renders them potentially valuable in treating inflammatory skin conditions such as eczema and dermatitis (Park et al., 2017). Asiaticosides can support skin barrier maintenance. They are believed to enhance skin hydration and elasticity, improving skin texture (Bylka, Znajdek-Awizen, Studzinska-Sroka, & Brzezinska, 2013). Asiaticosides also exhibit antioxidant characteristics, helping to mitigate damage caused by free radicals (Pittella, Dutra, Junior, Lopes, & Barbosa, 2009). Ginsenosides are the active ingredients in the ginseng plant. Some research suggests that ginsenosides can stimulate or boost collagen production. Ginsenosides have antioxidant properties that help prevent hyperpigmentation and blemish formation and can also lessen cellular damage caused by free radicals (Kim, 2015). Collagen degradation and aging are partly related to oxidative stress, so antioxidant effects may help maintain collagen health. Ginsenosides inhibit the activity of tyrosinase and inhibit the production of pigment; ginsenosides help to lighten dark spots and hyperpigmentation (C. S. Lee, Nam, Bae, & Park, 2019). Study indicated MMP1 degradation enhances collagen production in human dermal fibroblasts (Chou et al., 2016). Consistent with our results, subjects can improve skin collagen density, elasticity, texture, wrinkles, pores, hydration and lightness after taking vegan collagen.

The fermented amino acids used in vegan collagen are obtained through fermentation technology from plant-based ingredients. As early as 1958, Kinoshita et al. facilitated identifying glutamine-overproducing microorganisms through biological methods. As an essential tool for the biological production of amino acids, Corynebacterium glutamicum has been successfully applied to the production of amino acids to meet the global market's needs (Banerjee et al., 2021). Advances in whole-genome sequencing and mutagenesis will better understand how C. glutamicum produces and how it maintains high productivity at larger scales. These technologies enable Corynebacterium glutamicum to produce the required molecules more efficiently, providing more possibilities for further application of biotechnology and more sustainable and environmentally friendly industrial development (Wolf et al., 2021). Furthermore, this fermentation technique enables the precise formulation of vegan collagen with an amino acid profile that closely matches human type I collagen. By supplying fibroblasts with amino acids that harmonize with the body's natural collagen structure, vegan collagen optimizes its effectiveness in stimulating collagen production. This technique also serves as a key factor in reducing the variations and uncertainties frequently associated with skincare and beauty products that rely on animal-derived resources. It ensures that each application of vegan collagen consistently delivers dependable and reproducible results. And this study is also the first application of this technology in the skin health food.

5. Conclusion

Vegan collagen is a new type of collagen biomimetic without animal sources, rich in asiaticoside, and ginsenosides; through clinical results, it was found that vegan collagen improves skin collagen density, elasticity, texture, wrinkles, pores, hydration, and lightness. Consumers are increasingly concerned about naturalness and sustainability, and future biomimetic collagen products may use environmentally friendly production methods and natural ingredients to meet the demand for sustainability.

Ethics statements

The clinical study had been approved by Antai Medical Care Cooperation Antai- Tian-Sheng Memorial Hospital Institutional Review Board (Approval Number: 22-112-A).

CRediT authorship contribution statement

Yung-Kai Lin: Resources. **Chia-Hua Liang:** Methodology, Investigation, Formal analysis, Data curation. **Yung-Hsiang Lin:** Project administration, Funding acquisition, Conceptualization. **Tai-Wen Lin:** Methodology, Investigation, Formal analysis, Data curation. **Josué Jiménez Vázquez:** Formal analysis, Software, Writing – review & editing. **Anthony van Campen:** Writing – review & editing, Software, Formal analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgements

Thanks to all the subjects and related assistants who participated in the trial.

References

Arribas-Lopez, E., Zand, N., Ojo, O., Snowden, M. J., & Kochhar, T. (2022). A Systematic Review of the Effect of Centella asiatica on Wound Healing. *International Journal of Environmental Research and Public Health, 19*(6). https://doi.org/10.3390/ijerph19063266

Banerjee, D., Eng, T., Sasaki, Y., Srinivasan, A., Oka, A., Herbert, R. A., … Mukhopadhyay, A. (2021). Genomics Characterization of an Engineered Corynebacterium glutamicum in Bioreactor Cultivation Under Ionic Liquid Stress. *Frontiers in Bioengineering and Biotechnology, 9*, Article 766674. https://doi.org/10.3389/fbioe.2021.766674

Bolke, L., Schlippe, G., Gerss, J., & Voss, W. (2019). A Collagen Supplement Improves Skin Hydration, Elasticity, Roughness, and Density: Results of a Randomized, Placebo-Controlled, Blind Study. *Nutrients, 11*(10). https://doi.org/10.3390/nu11102494

Bylka, W., Znajdek-Awizen, P., Studzinska-Sroka, E., & Brzezinska, M. (2013). Centella asiatica in cosmetology. *Postepy Dermatol Alergol, 30*(1), 46–49. https://doi.org/10.5114/pdia.2013.33378

Campos, L. D., Santos Junior, V. d. A., Pimentel, J. D., Carregã, G. L. F., & Cazarin, C. B. B. (2023). Collagen supplementation in skin and orthopedic diseases: A review of the literature. *Heliyon, 9*(4), e14961. 10.1016/j.heliyon.2023.e14961.

Carlomagno, F., Roveda, G., Michelotti, A., Ruggeri, F., & Tursi, F. (2022). *Anti-Skin-Aging Effect of a Treatment with a Cosmetic Product and a Food Supplement Based on a New Hyaluronan: A Randomized Clinical Study in Healthy Women., 9*(3), 54.

Chen, S. J., Yuan, W., Mori, Y., Levenson, A., Trojanowska, M., & Varga, J. (1999). Stimulation of type I collagen transcription in human skin fibroblasts by TGF-beta: Involvement of Smad 3. *Journal of Investigative Dermatology, 112*(1), 49–57. https://doi.org/10.1046/j.1523-1747.1999.00477.x

Chou, H. Y., Lee, C., Pan, J. L., Wen, Z. H., Huang, S. H., Lan, C. W., … Wang, H. M. (2016). Enriched Astaxanthin Extract from Haematococcus pluvialis Augments Growth Factor Secretions to Increase Cell Proliferation and Induces MMP1 Degradation to Enhance Collagen Production in Human Dermal Fibroblasts. *International Journal of Molecular Sciences, 17*(6). https://doi.org/10.3390/ijms17060955

de Miranda, R. B., Weimer, P., & Rossi, R. C. (2021). Effects of hydrolyzed collagen supplementation on skin aging: A systematic review and meta-analysis. *International Journal of Dermatology, 60*(12), 1449–1461. https://doi.org/10.1111/ijd.15518

Diaz, I., Namkoong, J., Wu, J. Q., & Giancola, G. (2022). Amino acid complex (AAComplex) benefits in cosmetic products: In vitro and in vivo clinical studies. *Journal of Cosmetic Dermatology, 21*(7), 3046–3052. https://doi.org/10.1111/jocd.14544

Dong, C., & Lv, Y. (2016). Application of Collagen Scaffold in Tissue Engineering: Recent Advances and New Perspectives. *Polymers (Basel), 8*(2). https://doi.org/10.3390/polym8020042

Gray, N. E., Alcazar Magana, A., Lak, P., Wright, K. M., Quinn, J., Stevens, J. F., … Soumyanath, A. (2018). Centella asiatica - Phytochemistry and mechanisms of neuroprotection and cognitive enhancement. *Phytochemistry Reviews, 17*(1), 161–194. https://doi.org/10.1007/s11101-017-9528-y

Hwang, B. J., Yeom, H. J., Kim, Y., & Lee, H. S. (2002). Corynebacterium glutamicum utilizes both transsulfuration and direct sulfhydrylation pathways for methionine biosynthesis. *Journal of Bacteriology, 184*(5), 1277–1286. https://doi.org/10.1128/JB.184.5.1277-1286.2002

Kim, K. (2015). Effect of ginseng and ginsenosides on melanogenesis and their mechanism of action. *Journal of Ginseng Research, 39*(1), 1–6. https://doi.org/10.1016/j.jgr.2014.10.006

Krishani, M., Shin, W. Y., Suhaimi, H., & Sambudi, N. S. (2023). Development of Scaffolds from Bio-Based Natural Materials for Tissue Regeneration Applications. *A Review. Gels, 9*(2). https://doi.org/10.3390/gels9020100

Kwok, H.-H., Yue, P.-Y.-K., Mak, N.-K., & Wong, R.-N.-S. (2012). Ginsenoside Rb1 induces type I collagen expression through peroxisome proliferator-activated receptor-delta. *Biochemical Pharmacology, 84*(4), 532–539. https://doi.org/10.1016/j.bcp.2012.05.023

Lee, C. S., Nam, G., Bae, I. H., & Park, J. (2019). Whitening efficacy of ginsenoside F1 through inhibition of melanin transfer in cocultured human melanocytes-keratinocytes and three-dimensional human skin equivalent. *Journal of Ginseng Research, 43*(2), 300–304. https://doi.org/10.1016/j.jgr.2017.12.005

Lee, J., Jung, E., Kim, Y., Park, J., Park, J., Hong, S., … Park, D. (2006). Asiaticoside induces human collagen I synthesis through TGFbeta receptor I kinase (TbetaRI kinase)-independent Smad signaling. *Planta Medica, 72*(4), 324–328. https://doi.org/10.1055/s-2005-916227

Ljungdahl, P. O., & Daignan-Fornier, B. (2012). Regulation of amino acid, nucleotide, and phosphate metabolism in Saccharomyces cerevisiae. *Genetics, 190*(3), 885–929. https://doi.org/10.1534/genetics.111.133306

Meyer, M. (2019). Processing of collagen based biomaterials and the resulting materials properties. *Biomedical Engineering Online, 18*(1), 24. https://doi.org/10.1186/s12938-019-0647-0

Pérez-Rivero, C., & López-Gómez, J. P. (2023). *Unlocking the Potential of Fermentation in Cosmetics: A Review., 9*(5), 463.

Park, J. H., Choi, J. Y., Son, D. J., Park, E. K., Song, M. J., Hellstrom, M., & Hong, J. T. (2017). Anti-Inflammatory Effect of Titrated Extract of Centella asiatica in Phthalic Anhydride-Induced Allergic Dermatitis Animal Model. *International Journal of Molecular Sciences, 18*(4). https://doi.org/10.3390/ijms18040738

Pittella, F., Dutra, R. C., Junior, D. D., Lopes, M. T. P., & Barbosa, N. R. (2009). Antioxidant and cytotoxic activities of Centella asiatica (L) Urb. *International Journal of Molecular Sciences, 10*(9), 3713–3721. https://doi.org/10.3390/ijms10093713

Shoseyov, O., Posen, Y., & Grynspan, F. (2014). Human collagen produced in plants: More than just another molecule. *Bioengineered, 5*(1), 49–52. https://doi.org/10.4161/bioe.26002

Varanko, A., Saha, S., & Chilkoti, A. (2020). Recent trends in protein and peptide-based biomaterials for advanced drug delivery. *Advanced Drug Delivery Reviews, 156*, 133–187. https://doi.org/10.1016/j.addr.2020.08.008

Varma, S., Orgel, J. P. R. O., & Schieber, J. D. (2016). Nanomechanics of Type I Collagen. *Biophysical Journal, 111*(1), 50–56. https://doi.org/10.1016/j.bpj.2016.05.038

Wolf, S., Becker, J., Tsuge, Y., Kawaguchi, H., Kondo, A., Marienhagen, J., … Wittmann, C. (2021). Advances in metabolic engineering of Corynebacterium glutamicum to produce high-value active ingredients for food, feed, human health, and well-being. *Essays in Biochemistry, 65*(2), 197–212. https://doi.org/10.1042/EBC20200134

Zahoor, A., Lindner, S. N., & Wendisch, V. F. (2012). Metabolic engineering of Corynebacterium glutamicum aimed at alternative carbon sources and new products. *Computational and Structural Biotechnology Journal, 3*, e201210004.

Zhao, Y. S., Eweys, A. S., Zhang, J. Y., Zhu, Y., Bai, J., Darwesh, O. M., … Xiao, X. (2021). Fermentation Affects the Antioxidant Activity of Plant-Based Food Material through the Release and Production of Bioactive Components. *Antioxidants (Basel), 10*(12). https://doi.org/10.3390/antiox10122004