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Research Article

Anti-Aging Effects of Hydrolyzed Collagen Beverage with Herbal Extracts on Facial Skin: A Double-Blind, Randomized, Placebo-Controlled Trial

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Abstract

The anti-skin aging studies of hydrolyzed collagen combined with herbal extracts were currently based on cell or animal models, and few clinical studies have been reported. This clinical study investigated the combination of hydrolyzed collagen with goji berry, aloe vera, chamomile, and acerola cherry to improve skin parameters. Using combination of hydrolyzed fish collagen and herbal extracts to develop a new functional formula for skin improvement. Sixty subjects were randomly allocated (in a 1:1 ratio) to the placebo or a collagen beverage. Compared to placebo, the supplement significantly increased skin collagen content (6.1% vs. 3.3%, p<0.001), elasticity (8.2% vs. 0.0%, p<0.001), moisture (5.2% vs. 0.8%, p<0.05), whitening (4.1% vs. 0.3%, p<0.001), while reducing melanin content (-2.8% vs. 1.4%, p<0.05). There was a non-significant reduction in the appearance of wrinkles (-19.1% vs. -3.8%), visible spots (-6.3% vs. 3.8%), and UV spots (-4.4% vs. 1.0%). The improvement levels indicated competitive skin improvement effects in comparison with previous studies. This clinical study demonstrates the combination of hydrolyzed collagen and goji berry, aloe vera, chamomile, and acerola cherry for substantial improvements in facial skin's structural and functional appearance.

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Keywords: Herbal extracts; Hydrolyzed fish collagen; Skin aging

Introduction

Anti-aging skin care is an increasingly popular topic in the cosmetic and aesthetic fields. Skin aging includes thinning of the skin, loss of elasticity and moisture, the formation of pigmentation, and the development of wrinkles [1]. Associated with skin aging is a reduction of epithelial turnover rate and cellular recovery and a reduction of elastin and collagen content, collectively resulting in increased formation of wrinkles or folds in the skin [2]. The current skin anti-aging strategies include topical use of skin care products containing anti-aging ingredients, dermabrasion, laser, botulinum injections, filler injections, and facelifts [1]. Oral use of anti-aging skin care products was the most convenient and cheapest way to achieve skin anti-aging effects [3]. However, it was accompanied by high cost-effectiveness, a painful treatment process, and the necessity of repeated treatment. Thus, as functional foods and oral supplements, nutraceuticals are increasingly investigated to improve skin health.

Hydrolyzed collagen from different sources had been proposed for skin care, such as cow, pig, chicken, and fish collagen. Marine fish collagen and collagen peptides had a high degree of homology to human structure and bioavailability through the gastrointestinal barrier [3]. Some studies have shown that hydrolyzed fish collagen supplements can improve skin wrinkles, elasticity, and moisture and have been proven to reduce wrinkles and pores. In addition to fish collagen, natural plant extracts were recently added to skin care products [4]. Since the active ingredients come from natural herbs and do not contain heavy metals, hormones, and antibiotics, and has become a new trend for people to pursue natural beauty.

Goji berry had been used for centuries in traditional Chinese medicine for a wide range of medicinal and beauty purposes. Goji berry had excellent antioxidant and immunomodulatory potential [5]. The ingredients of Goji berry include flavonoids which may help reduce inflammation, thereby minimizing signs of aging [6]. Additionally, goji berry contains vitamins, minerals, and other nutrients, which may reduce wrinkles and promote collagen production [6]. Aloe vera was a cactus-like plant grown in desert areas worldwide. Its leaves produced a gel rich in vitamins A, C, E, and B12 [7]. Studies have shown that aloe vera can promote the production and release of collagen, accelerate wound healing time, and limit scar formation [8]. Aloe vera has an antioxidant effect, which can help repair sunburn and slow down skin aging [9]. In addition, aloe vera contained 98% water, which helped moisturize, soothe and moisturize the skin [10]. Chamomile has long been a chosen ingredient in soothing skin care regimens, contains the antioxidant apigenin, which aids in lowering inflammation by inhibiting the release of inflammation-causing chemicals [11]. In addition to its astringent and brightening properties, skin care creams containing chamomile also tighten pores and soften the skin, reducing acne scars and pigmentation [12]. Acerola cherries had a very high vitamin C content and increased collagen production [13]. Acerola cherries contain functional ingredients as carotenoids, γ-Aminobutyric Acid

(GABA), and polyphenols [14]. Oral intake of acerola cherries can effectively reduce UVB-induced hyperpigmentation [15]. Although several preclinical studies provided evidence for the beneficial effect of hydrolyzed collagen and herbal extracts on skin health, less information was known about the clinical benefits.

This study used a hydrolyzed collagen-containing beverage, which contained goji berry, aloe vera, chamomile, and acerola cherry, to explore whether the skin can be improved after consuming the collagen beverage. This study evaluated the clinical benefits of a 4-week supplementation of a collagen beverage on skin appearance.

Materials and Methods

Clinical trial design

The study was registered in clinicaltrials.gov (No. NCT04878536), was performed under a protocol approved by the Antai Medical Care Cooperation Antai- Tian-Sheng Memorial Hospital Institutional Review Board (Approval Number: 21-042-B), 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 two groups, with 30 subjects in each group. The subjects were informed to consume one bottle of the supplement daily for four weeks. Before measurements, subjects were instructed to wash and wipe their face and acclimate for at least 30 minutes. The skin conditions of the subjects were measured on week 0 and week 4 of the trial. 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 four weeks of the study.

Supplement formulation

The marine collagen beverage (Collagen Elixir™; Isagenix Worldwide, LLC) contains 10% hydrolyzed fish collagen, 0.4% ascorbic acid, 0.1% goji berry, 0.1% aloe vera, 0.1% acerola cherry, 0.02% chamomile, citric acid, and water. The placebo beverage contains primarily citric acid and water. Subjects were required to consume 50 mL of the collagen beverage or a placebo beverage daily for 4 weeks.

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 reflect the lowest. Cutometer® dual MPA580 was utilized to measure skin elasticity, and the higher the relative value, the more significant the improvement. VISIATM Complexion Analysis was utilized to measure skin wrinkles. Wrinkles are identified by their characteristic long, narrow shape. The green lines reflect the wrinkles that the computer used to analyze wrinkle presence and depth. 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 tone, 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 visible skin spots and UV spots, and the lower the relative value, the more significant the improvement.

Statistical analysis

The comparison of measurement results for skin parameters among groups and between groups was analyzed by one-way repeated measures ANOVA and one-way ANOVA, respectively, followed by Tukey's post hoc test through GraphPad Prism, as p < .05 was considered statistical significance.

Results

Combined with goji berry, aloe vera, chamomile, and acerola cherry increased skin collagen, elasticity, moisture, and decreased wrinkles

First, we want to know whether collagen beverages improve skin collagen, elasticity, wrinkles, and moisture. Subjects were required to consume 50 mL of the collagen beverage or a placebo beverage daily for 4 weeks. The images of collagen and wrinkle are shown in figure 1. The skin collagen density was significantly increased 6.1% after consuming the collagen beverage for four weeks compared to baseline (week 0), and also significantly increased 2.8 % compared to the placebo group (Figure 1A). The skin elasticity significantly increased 8.2% after consuming the collagen beverage for four weeks compared to baseline (week 0) and significantly increased 8.2 % compared to the placebo group (Figure 1B). After consuming the collagen beverage for four weeks, the skin wrinkles decreased 19.1% compared to baseline (week 0) and decreased 14 % compared to the placebo group (Figure 1C). In addition, skin moisture content was significantly increased 5.2% compared to baseline (week 0) and significantly increased 4.4% compared to the placebo group (Figure 1D). These results indicated that the collagen beverage increased skin collagen, elasticity, moisture, and decreased wrinkles (Figure 2).

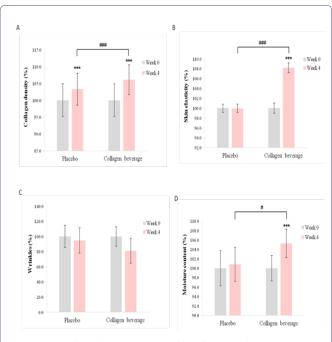


Figure 1: The collagen beverage improved skin collagen, elasticity, wrinkles, moisture. The (A) collagen, (B) elasticity, (C) wrinkles, (D) moisture, (n=30; mean value \pm S.E.M.) (*, compared with before using (week 0). #, compared with placebo) (*, p<0.05, ***, p<0.01, ****, p<0.001) (#, p<0.05, ###, p<0.001).

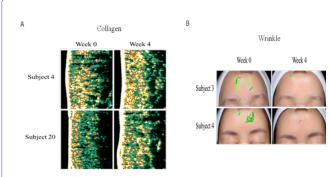


Figure 2: Improvement of skin collagen and wrinkles for the collagen beverage. The image of (A) skin collagen, (B) wrinkles.

Combined with goji berry, aloe vera, chamomile, and acerola cherry decreased skin melanin, visible and UV spots, and increased whitening.

Second, we want to explore whether the collagen beverage improved skin whitening, melanin, visible spot, and UV spot. After consuming the collagen beverage for four weeks, the L* value significantly increased 4.1% compared to baseline (week 0) and significantly increased 3.8% compared to the placebo group (Figure 3A). The skin melanin index significantly decreased 2.8% after consuming the collagen beverage for four weeks compared to baseline (week 0) and significantly decreased 4.2% in the placebo group (Figure 3B). The visible skin spots significantly decreased 6.3% after consuming the collagen beverage for four weeks compared to baseline (week 0) and decreased 2.5% in the placebo group (Figure 3C). The UV spots significantly decreased 4.4% after consuming the collagen beverage for four weeks compared to baseline (week 0) and decreased 3.4% compared to the placebo group (Figure 3D). The images of visible spots and UV spots are shown in figure 4. These results indicated that the collagen beverage decreased skin melanin, visible and UV spots, and increased whitening. The above results are summarized in table 1.

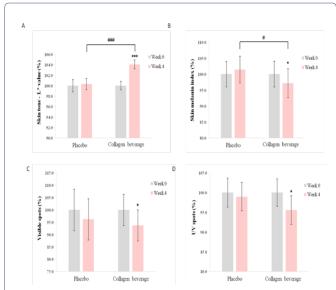


Figure 3: The collagen beverage improved skin whitening, melanin, spots, and UV spots. The (A) L value, (B) melanin, (C) spots, (D) UV spots, (n=30; mean value \pm S.E.M.) (*, compared with before using (week 0). #, compared with placebo) (*, p<0.05, **, p<0.01, ***, p<0.001) (#, p<0.05, ###, p<0.001)

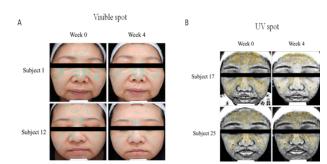


Figure 4: Improvement of skin collagen and wrinkles for the collagen beverage. The image of (A) visible spots, (B) UV spots.

Skin Parameter	Placebo Beverage (% change)	Collagen Beverage (% change)
Collagen density	3.3%***	6.1%***, ###
Skin elasticity	0.00%	8.2%***, ###
Wrinkles	-5.10%	-19.10%
Moisture content	0.80%	5.2%***,#
L* value	0.30%	4.1%***, ###
Melanin index	1.40%	-2.8%*,#
Visible spots	-3.80%	-6.3%*
UV spots	-1.00%	-4.4%*

Table 1: Summary of the skin parameter changes after collagen and placebo supplementation.

Note: Significant difference versus baseline: *, p<0.05; **, p<0.01; ***, p<0.001; Significant difference versus placebo: #, p<0.05; ##, p<0.01; ###, p<0.001

Discussion

This study found that a collagen beverage containing goji berry, aloe vera, chamomile, and acerola cherry promoted collagen production, improved elasticity, anti-wrinkle, and increased moisture, whitened, and removed spots, suggesting the potential of collagen beverage for improving skin conditions. These findings support other studies documenting the skin health benefits of collagen and hydrolyzed collagen supplementation (18-20).

Goji berry was rich in many biologically active compounds with high antioxidant potential, such as vitamin A carotenoids, compounds associated with skin health [6]. Carotenoids also exhibit antioxidant properties, protecting the skin barrier and fighting free radicals, while vitamin A can promote cell renewal and keep the skin bright and white [16]. Goji berry was rich in vitamin B2, which maintained immune and digestive functions, increased skin moisture, and decreased spots and wrinkles [6]. Goji berry also contains a lot of vitamin C, promoting collagen production and keeping the skin elastic [2,17]. Goji berry had been proven to inhibit photoaging caused by UVB exposure [18]. Goji berry can inhibit the formation of UVB-induced wrinkles and collagen damage by inhibiting Extracellular Signal-Regulated Kinase (ERK), Mitogen-Activated Protein Kinase (MAPK), and Matrix Metalloproteinase 9 (MMP-9) [19].

Most cosmetic and medicinal products were produced from aloe vera, and a variety of active ingredients had been identified in aloe vera extract, including vitamins, minerals, lignin, saponins, anthraquinones, phenolic compounds, sterols, and salicylic acid [20]. Aloe polysaccharides can regulate immune function, activate immune cells

in the basal layer of skin, enhance local immune function and repair function, remove skin melanin, reduce free radical damage, and increase skin elasticity [21]. The subjects took aloe vera gel powder for eight weeks and found that it can increase skin moisture content and reduce wrinkles and pores [22]. The sterols in aloe vera powder can reduce facial wrinkles and treat dry skin [22]. Aloe vera gel can significantly improve the wrinkles and elasticity of photoaging human skin, increase collagen production, and decrease the collagen-degrading MMP-1 gene expression [23].

Chamomile has flavonoids, among which apigenin and apigenin-7-glycoside were the most abundant [24]. Moreover, chamomile extract can effectively reduce free radicals, reduce skin moisture loss and spots, and maintain skin barrier function [25]. The flavonoids in chamomile can penetrate below the skin surface into deeper skin layers [11]. The formulas containing chamomile do not cause skin irritation and can improve skin hydration through Kelch-like erythroid cell-derived protein with cap-n-collar homology-associated protein 1 (KEAP1)/NF-E2-Related Factor 2 (NRF2) signaling [26]. Acerola cherry extract can inhibit tyrosinase activity in melanocytes to inhibit melanin production, and acerola cherry extract can prevent UVB-induced skin pigmentation in brown guinea pigs [14]. In addition, acerola cherry extract has a high antioxidant capacity, can delay skin aging, and make skin smooth because it is rich in vitamin C and can further promote collagen synthesis [13].

Aloe vera dietary supplements with goji berry extract can reduce and strengthen the immune system and repair the body's metabolism [27]. In addition, the combined use of chamomile and acerola cherries can reduce the damage of free radicals to the skin [28]. Consistent with our results, combined with goji berry, aloe vera, chamomile, and acerola cherry, can improve skin conditions.

Conclusion

In short, through clinical studies, we had confirmed that hydrolyzed collagen beverages containing goji berry, aloe vera, chamomile, and acerola cherry could significantly improve skin conditions, which may be due to the combination of different effective substances in various plant extracts.

Conflicts of Interest

EG is currently Director of Research and Science at Isagenix International, LLC. He had no role in the design, interpretation, or analysis of the results. Other authors declare no conflict of interest.

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