A Randomized, Double-Blind, Placebo-Controlled Trial to Determine the Effectiveness of a Dietary Supplement (Viskin EX^{5®}) in Improving Skin Condition of Healthy Asian Women

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Abstract: The skin undergoes noticeable changes as it ages, such as the loss of moisture, uneven darkening of skin tone, pigmentation, and the formation of wrinkles. While traditional topical skin care products are commonly used, specific dietary supplements offer the potential to improve skin conditions from within and provide a more comprehensive approach to skincare. A randomized double-blind clinical intervention was conducted to evaluate the effectiveness of Viskin EX^{5®}, a nutritional supplement containing fruit extract and vitamins, in improving skin conditions. 32 healthy Asian women were randomly assigned to take either two tablets of Viskin EX^{5®} (150 mg) or a placebo daily for eight weeks. Skin water content, skin color, and wrinkle area were measured at the beginning of the study and after four and eight weeks. Additionally, participants completed questionnaires at four and eight weeks to provide subjective feedback. Objective measurements of skin parameters revealed that Viskin EX^{5®} significantly improved facial skin hydration compared to the placebo. The supplement also led to a significant reduction in skin melanin value, pigmentation density, and skin unevenness. Changes in skin colorimetric parameters, such as L* value, b* value, and ITA ° degree, indicated a lighter skin tone. Furthermore, the areas of crow's feet and nasolabial folds were significantly reduced, with most skin indicators showing significant improvement at four weeks and further enhancement at eight weeks (p<0.05). Participants in the Viskin EX^{5®} group generally reported that the supplement did not cause any bodily discomfort and resulted in improved skin condition. Viskin EX^{5®}, consisting of fruit extract and vitamins, was found to be a safe and effective method for increasing skin moisture content, whitening skin, and reducing wrinkles. The results suggest that this nutritional supplement can provide comprehensive benefits for skin health.

1. Introduction

Skin aging is a natural and inevitable process that occurs due to a combination of intrinsic and extrinsic factors. Intrinsic factors are primarily determined by genetics and include physiological changes such as decreased collagen production and slower cell turnover rates. Extrinsic factors, on the other hand, are environmental and lifestyle-related, such as exposure to UV radiation, pollution, smoking, and poor nutrition^[1,2]. The manifestations of facial skin aging include decreased skin moisture, increased roughness, uneven skin tone, hyperpigmentation, and the formation of wrinkles^[3].

In order to address the desire for youthful-looking skin, various measures have been taken to improve skin condition. Traditional approaches include the use of topical creams, serums, and cosmetic procedures such as chemical peels and laser treatments^[4–7]. These methods often provide immediate results and target specific skin concerns. However, they may have limitations and potential side effects, such as skin irritation or sensitivity. Additionally, the effects of these external measures may be temporary and require continuous usage for maintenance^[8,9].

In recent years, there has been a growing interest in the use of oral dietary supplements to improve skin health and appearance. These supplements typically contain a combination of essential nutrients and plant extracts, including ingredients like vitamin C, hyaluronic acid, and polyphenols^[1,2]. Compared to other methods such as topical applications or using specialized instruments, oral administration of these supplements is simpler and more convenient. Moreover, what sets dietary supplements apart is their ability to offer a holistic approach to skin care. When ingested, the active compounds in these supplements circulate through the bloodstream and continuously replenish the skin, reaching all areas including the epidermis, dermis, subcutaneous fat, and sebum^[10–12]. This allows the supplements to provide antioxidant and anti-inflammatory benefits and supplement key structural components throughout the skin, helping individuals combat damage caused by external factors and aging^[12].

With this in mind, we conducted a comprehensive evaluation of the skincare effects and subjective satisfaction of a patented oral dietary supplement (Viskin $EX^{5@}$), aiming to provide more knowledge for the development and utilization of dietary supplements to improve skin condition. As an award-winning patented skincare dietary supplement, Viskin $EX^{5@}$ is the world's first formula to utilize fruit-derived SOD and other antioxidants as the main ingredients to improve skin condition.

2. Methods

2.1. Supplement formulation

The supplement under study is formulated as tablets made from a blend of 150mg Viskin EX^{5®} (3.8% cantaloupe extract, 38.5% grape seed extract, 38.5% vitamin C, and 19.2% vitamin E) and 50mg dextrin. Among them, melon extract is rich in superoxide dismutase (SOD, \geq 219 IU/g), while grape seed extract contains 95% proanthocyanidins, both of which have been proven to be beneficial for the skin. The placebo capsules contained 200 mg of dextrin, maintaining the same aspect as the product under study. Viskin EX^{5®} was provided by Eternal Grace PTE. LTD.(Singapore) (Patent Application Number LU501730).

2.2. Subjects

The randomized controlled study enrolled healthy Asian women with saggy, dry, fine lines on their facial skin in Shanghai, China, in May 2023. Inclusion criteria were as follows: (1) 18–

40 years of age; (2) facial wrinkles of grade 1-3 confirmed by the dermatologist(The highest level is 6 and the lowest level is 0); (3) having a sun protection habit, and be able to adhere to the sun protection during the testing process; (4) agree not to use any other cosmetics, drugs and health products that may affect the test; (5) no other clinical tests in the last month; (6) no cosmetic treatment in the last three months (7) don't participate in clinical trials at any other research center during the trial period and (8) ability to participate and to comply with all the requirements of the study protocol.

	Placebo	Supplemented	
No. enrolled	19	17	
No. completed	16	16	
Average age (yr)	33.88±5.14	34.63±5.02	
Average grade of wrinkles	2.06±0.68	1.94±0.68	

Table 1: Demographics of the participants in each group.

As shown in Table 1, a total of 36 healthy women participated in this study, of which 32 completed the intervention and were included in the final analysis. These 32 women were randomly divided into two groups, with an average age of around 34 years and an average facial wrinkle grade of around 2. The study objectives and protocol were carefully explained to the subjects and their written informed consent was obtained.

2.3. Study design

This was a randomized, double-blind, placebo-controlled, matched-pair study. After recruitment, the subjects were randomized into the placebo (n = 16) or Viskin EX^{5®} group (n = 16). The Viskin EX^{5®} and placebo tablets were prepared so that they were the same size, smell and color. The subjects were instructed to take two tablets 20-30 min before breakfast every day for 8 weeks. At 0 week, 4 weeks, and 8 weeks, subjects were asked to come to the lab for a variety of objective skin condition tests and to record subjective assessments.

2.4. Objective evaluations

Before each test, the subjects were asked to clean their face with a standard facial cleanser, dry their face with a paper towel, and sit still for 20 minutes at a temperature of $21\pm1^{\circ}$ C and a humidity of 50% $\pm10^{\circ}$ RH^[13].

Stratum corneum hyydration level of cheek surface was measured with the Corneometer CM 825 (Courage-Khazaka, Cologne, Germany)^[14]. Skin melanin index(MI) of cheek surface was measured with the Mexameter MX18 (Courage-Khazaka, Cologne, Germany)^[15]. Skin colorimetric parameters (skin color L*, skin color b* and skin color ITA °), mean value of density of pigmentation, uneven skin tone parameter and percentage of wrinkles area were measured with the VISIA-CR (Canfield Scientific Inc, Fairfield, America)^[16].

2.5. Subjective evaluations

A self-assessment questionnaire of product efficacy evaluation was filled out by each subject at 4 week and 8 week. Scores for each question were 1-5 points: 5, agreement; 4, relative agreement; 3, neutrality; 2, relative disagreement; and 1, disagreement. The proportion of subjects with 4 or 5 points for each question was calculated^[17].

2.6. Statistical analysis

The statistical analysis was carried out using the GraphPad Prism 6.0 (GraphPad Software, Inc., San Diego, CA, U.S.A.). Data were presented as mean \pm SD. The one-way ANOVA analysis was performed by SPSS software (version 21.0, SPSS Inc., Chicago, IL, U.S.A.), and the significance of the difference in data results was judged by Tukey's test (p<0.05).

3. Results

3.1. Objective evaluations

3.1.1. Skin moisture

From Figure 1, it can be seen that there was no significant difference in baseline skin moisture levels between the supplemented group and the placebo group in the stratum corneum hydration evaluation. The supplemented group showed a significant increase in cheek stratum corneum hydration at 4 weeks, which continued to increase significantly at 8 weeks. In contrast, there was no significant difference in skin moisture levels among the placebo group subjects in the three measurements. At 8 weeks, the stratum corneum hydration of the cheek skin in the supplemented group was 1.88 times that of the placebo group (Supplemented group: 56.19 ± 1.47 ; placebo group: 29.94 ± 1.84).

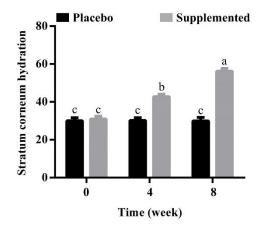


Figure 1: Changes in Stratum corneum hydration with Viskin EX^{5®} treatment.

3.1.2. Skin color

Regarding the changes in skin color, this study measured melanin index (Figure 2A), density of pigmentation (Figure 2B), uneven skin tone parameter (Figure 2C), and skin chromaticity parameters (Figure 2D-E). At week 0, the placebo group and supplement group showed similar values for these parameters.

The measurement results showed that there were no significant changes in the parameters of the placebo group during the testing process. However, in the supplemented group, participants who took Viskin $EX^{5@}$ for 4 weeks experienced a significant decrease in melanin index(Week 0: 144.19±6.52; Week 4: 136.27±6.31; Week 8:132.02±6.26, Figure 2A), mean value of density of pigmentation (Week 0: 98.13±2.03; Week 4: 95.95±2.16; Week 8: 94.20±2.22, Figure 2B), and Uneven skin color parameter (Week 0: 1.82±0.10; Week 4: 1.62±0.07; Week 8:1.55±0.08, Figure 2C), which continued to decrease at week 8.

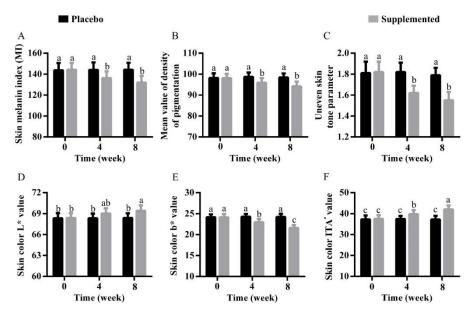


Figure 2: Moisture index, mean value of density of pigmentation, uneven skin tone parameter, and skin colorimetric parameters results during intervention. (A) Changes in moisture index values; (B) in mean value of density of pigmentation; (C) in uneven skin tone parameter; (D) in skin color L* value; (E) in skin color b* value; and (F) in skin color TIA °value with Viskin EX^{5®} treatment.

L* refers to the lightness or darkness of the skin color. It measures from 0 (black) to 100 (white), with higher values indicating lighter skin tones^[18,13]. From the Figure 2D, it can be observed that the group taking Viskin EX^{5®} showed a noticeable upward trend in skin color L* value. Although there was no significant difference at the week 4, the data at week 8 confirmed a significant improvement effect. At the same time, the placebo did not provide any improvement to the subjects.

b* refers to the yellowness or blueness of the skin color. It measures from -127 (blue) to +127 (yellow), with positive values indicating more yellowish tones and negative values indicating more bluish tones^[18,19]. Figure 2E shows that the subjects had a yellowish skin color. Compared to the ineffective control group, after 4 weeks of intervention with Viskin EX^{5®}, the subjects' skin b* value significantly decreased. By the 8th week, the decrease was measured at 10.54% $\pm 2.95\%$ (Week 0: 24.10 ± 0.79 ; Week 8: 21.56 ± 0.71).

The Individual Typology Angle (ITA $^{\circ}$) is a comprehensive index calculated based on the skin color L* and b* values. It is used in dermatology and cosmetic research to objectively classify skin color. Using ITA $^{\circ}$, skin color can be classified into one of the following categories: Very light >55 $^{\circ}$, Light 55-41 $^{\circ}$, Intermediate 41-28 $^{\circ}$, Tan 28-10 $^{\circ}$, Brown 10-30 $^{\circ}$, and Dark < 30 $^{418,20]}$. From Figure 2F, it can be observed that the baseline values of skin ITA $^{\circ}$ for both groups of subjects are close to 37, indicating a moderate level. Compared to the ineffective placebo, Viskin EX^{5®} gradually increased the subjects' skin color ITA $^{\circ}$ values, reaching the light category by the 8th week (Week 0: 37.48 ±1.78; Week 8: 42.01 ±1.89).

3.1.3. Skin wrinkles

The outer corners of the eyes and the nasolabial folds are areas on the face that are particularly prone to developing wrinkles and fine lines during the aging process^[21]. By focusing on crow's feet and nasolabial folds in wrinkle tests, researchers can accurately assess the ability of products to reduce the appearance of wrinkles and improve skin texture.

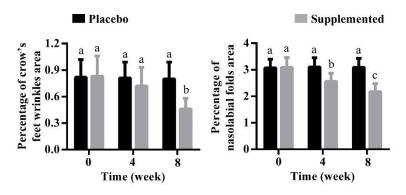


Figure 3: Percentage of crow's feet wrinkles area and percentage of nasolabial folds area results during intervention. (A) Changes in percentage of crow's feet wrinkles area; and (B) in percentage of nasolabial folds area with Viskin EX^{5®} treatment.

From Figure 3A, it can be observed that the proportion of crow's feet area for both groups of subjects was close to 0.8% at week 0. The reduction in the proportion of crow's feet area was not significant for the supplement group after 4 weeks of taking Viskin $EX^{5@}$. However, after 8 weeks of taking Viskin $EX^{5@}$, the proportion of crow's feet area decreased by 44.58% ±14.46% (Week 0: 0.83% ±0.23%; Week 8: 0.46% ±0.12%). Meanwhile, the crow's feet condition of the placebo group did not show effective improvement.

Similarly, in Figure 3B, the improvement of wrinkles by Viskin $EX^{5@}$ was also confirmed. As shown in Figure 3B, the baseline levels of nasolabial folds were similar in both groups of subjects. Compared to the ineffective control group, the subjects who took Viskin $EX^{5@}$ showed significant improvement in nasolabial folds as early as the 4th week, and the proportion of nasolabial folds further decreased significantly by the 8th week (Week 0: 3.09% ±0.37%; Week 4: 2.56% ±0.31%; Week 8: 2.17% ±0.31%).

3.2. Subjective evaluations

According to Table 2, the placebo group had a lower level of agreement regarding the effectiveness of the product. However, subjective rating results from the subjects taking Viskin EX^{5®}indicated that after 4 and 8 weeks of product consumption, 100% of the subjects believed that the research product could enhance skin hydration, brightness, lightness, and reduce skin acne marks. Over 93.5% of the subjects felt that the roughness and wrinkles of their skin had improved. Additionally, 100% of the subjects found the product to be gentle, with no observed burning, stinging, allergy, or other adverse reactions or discomfort throughout the study period.

	Placebo (n=16)		Supplemented (n=16)	
Question	28d	56d	28d	56d
Skin feels more hydrated	12.5%	6.25%	100%	100%
Skin dullness looks reduced/ Skin looks brighter	6.25%	0%	100%	100%
Lightening of skin	12.5%	18.75%	100%	100%
Reduce skin roughness	0%	6.25%	100%	93.75%
Reduce skin wrinkles	6.25%	6.25%	93.75%	93.75%
Reduce skin acne marks	0%	0%	100%	100%
The product is gentle	100%	100%	100%	100%

4. Discussion

The skin is constantly exposed to various environmental factors that can lead to skin aging, and while traditional skincare methods have been effective to some extent, there has been a growing interest in an inside-out approach to skincare through the use of dietary supplements^[12].

The results of this study showed that Viskin EX^{5®} significantly improved skin moisture, reduced skin pigmentation, improved skin color, and reduced wrinkle formation at 4 weeks. These improvements were further enhanced at 8 weeks, with a significant decrease in the area of crow's feet observed. The subjective evaluations of the Viskin EX^{5®} group were also positive at both 4 and 8 weeks compared to the placebo group, indicating that the majority of subjects were satisfied with its effects.

Viskin EX^{5®} is equipped with a protective antioxidant network for the skin. They include enzymatic antioxidants such as SOD and non-enzymatic low molecular weight antioxidants such as vitamin E, vitamin C, and anthocyanins^[2]. SOD is an endogenous enzyme that can neutralize superoxide radicals and has been proven to prevent premature aging of the skin, reduce inflammation, and promote overall skin health^[22,23]. Anthocyanins, vitamin C, and vitamin E have a wider range of antioxidant activity and can neutralize various free radicals. The combination of these ingredients has been proven to work synergistically, promoting an increase in skin moisture content and inhibiting melanin deposition^[13,24–27].

In summary, Viskin EX^{5®} as a specially formulated dietary supplement, can safely and effectively make the skin of Asian women become radiant and healthier. This groundbreaking study reveals the significant benefits and necessity of integrating antioxidant-rich dietary supplements into daily skincare routines.

Acknowledgments

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References

[1] Schagen, S. K., Zampeli, V. A., Makrantonaki, E. and Zouboulis, C. C. (2012). Discovering the link between nutrition and skin aging. Dermato-Endocrinology, 4(3), 298–307.

[2] Poljšak, B. and Dahmane, R. (2012). Free radicals and extrinsic skin aging. Dermatology Research and Practice, 2012, 1–4.

[3] Krieg, T., Bickers, D. R. and Miyachi, Y. (2010). Therapy of skin diseases: A worldwide perspective on therapeutic approaches and their molecular basis. Therapy of Skin Diseases: A Worldwide Perspective on Therapeutic Approaches and Their Molecular Basis, 13(3), 705–716.

[4] Draelos, Z. D. (2018). The science behind skin care: Moisturizers. Journal of Cosmetic Dermatology, 17(2), 138–144.

[5] O'Connor, A. A., Lowe, P. M., Shumack, S. and Lim, A. C. (2018). Chemical peels: A review of current practice. Australasian Journal of Dermatology, 59(3), 171–181.

[6] Agbai, O., Hamzavi, I. and Jagdeo, J. (2017). Laser treatments for postinflammatory hyperpigmentation a systematic review. JAMA Dermatology, 153(2), 199–206.

[7] Guthrie, A., Kadakia, S., Hu, S., Sawhney, R., Schumacher, J. and Ducic, Y. (2017). Modern approaches to skin care. Facial Plastic Surgery, 33(6), 653–660.

[8] Gibson, F. B. and Perkins, S. W. (2019). Complications of chemical peels, dermabrasion, and Laser resurfacing. Complications in Head and Neck Surgery, 49, 655–669.

[9] Šahu, T., Patel, T., Sahu, S. and Gidwani, B. (2016). Skin cream as topical drug delivery system: A review. Journal of Pharmaceutical and Biological Sciences, 4(5), 149–154.

[10] Taburet, A. M., Singlas, E., Glass, R. C., Thomas, F. and Leutenegger, E. (1995). Pharmacokinetic comparison of oral and local action transcutaneous flurbiprofen in healthy volunteers. Journal of Clinical Pharmacy and Therapeutics, 20(2), 101–107.

[11] Braithwaite, M. C., Tyagi, C., Tomar, L. K., Kumar, P., Choonara, Y. E. and Pillay, V. (2014). Nutraceutical-based

therapeutics and formulation strategies augmenting their efficiency to complement modern medicine: An overview. Journal of Functional Foods, 6(1), 82–99.

[12] Myriam, M., Sabatier, M., Steiling, H. and Williamson, G. (2006). Skin bioavailability of dietary vitamin E, carotenoids, polyphenols, vitamin C, zinc and selenium. British Journal of Nutrition, 96(2), 227–238.

[13] Dumoulin, M., Gaudout, D. and Lemaire, B. (2016). Clinical effects of an oral supplement rich in antioxidants on skin radiance in women. Clinical, Cosmetic and Investigational Dermatology, 9, 315–324.

[14] Zhu, Y. H., Song, S. P., Luo, W., Elias, P. M. and Man, M. Q. (2011). Characterization of skin friction coefficient, and relationship to stratum corneum hydration in a normal chinese population. Skin Pharmacology and Physiology, 24(2), 81–86.

[15] Mackiewicz-Wysocka, M., Araszkiewicz, A., Schlaffke, J., Kuczynski, S., Micek, I. and Zozulinska-Ziolkiewicz, D. (2014). Lower melanin content in the skin of type 1 diabetic patients and the risk of microangiopathy. Experimental and Clinical Endocrinology and Diabetes, 122(4), 231–235.

[16] Chajra, H., Redziniak, G., Auriol, D., Schweikert, K. and Lefevre, F. (2015). Trihydroxybenzoic acid glucoside as a global skin color modulator and photo-protectant. Clinical, Cosmetic and Investigational Dermatology, 8, 579–589.

[17] Li, S., He, X., Zhang, Z., Zhang, X., Niu, Y., Steel, A. and Wang, H. (2023). Efficacy and safety of a facial serum and a mask containing salicylic acid and lipohydroxy acid in acne management: A randomized controlled trial. Journal of Cosmetic Dermatology, 22(9), 2502–2511.

[18] Ly, B. C. K., Dyer, E. B., Feig, J. L., Chien, A. L. and Del Bino, S. (2020). Research techniques made simple: Cutaneous colorimetry: A reliable technique for objective skin color measurement. Journal of Investigative Dermatology, 140(1), 3–12.

[19] Bissett, D. L., Oblong, J. E. and Berge, C. A. (2005). Niacinamide: A B vitamin that improves aging facial skin appearance. Dermatologic Surgery, 31(7), 860–866.

[20] Au, L. E., Harris, S. S., Dwyer, J. T., Jacques, P. F. and Sacheck, J. M. (2014). Association of serum 25-hydroxyvitamin D with race/ethnicity and constitutive skin color in urban schoolchildren. Journal of Pediatric Endocrinology and Metabolism, 27(11–12), 1095–1100.

[21] Mendelson, B. C. and Brien, J. X. O. (2016). The aging face. International Textbook of Aesthetic Surgery, 8, 855–865.

[22] Menvielle-Bourg, F. (2005). Superoxide Dismutase (SOD), a Powerful Antioxidant, is now available Orally. Phytoth érapie, 3, 1–4.

[23] Le Qu ér é, S., Lacan, D., Lemaire, B., Carillon, J. and Schmitt, K. (2014). The role of superoxide dismutase (SOD) in skin disorders A review. Nutrafoods, 13, 13–27.

[24] Correia, P., Araújo, P., Ribeiro, C., Oliveira, H., Pereira, A. R., Mateus, N., de Freitas, V., Brás, N. F., Gameiro, P., Coelho, P., Bessa, L. J., Oliveira, J. and Fernandes, I. (2021). Anthocyanin-related pigments: Natural allies for skin health maintenance and protection. Antioxidants, 10, 1038.

[25] Pullar, J. M., Carr, A. C. and Vissers, M. C. M. (2017). The roles of vitamin C in skin health. Nutrients, 9, 866.

[26] Eberlein-Konig, B., Placzek, M. and Przybilla, B. (1998). Protective effect against sunburn of combined systemic ascorbic acid (vitamin C) and d- α -tocopherol (vitamin E). Journal of the American Academy of Dermatology, 38(1), 45–48.

[27] Aren, K. and Urke, E. B. (2007). Interaction of vitamins C and E as better cosmeceuticals. Dermatologic Therapy, 20(2), 314–321.