ACCSCIENCE PUBLISHING

Innovative Medicines & Omics

REVIEW ARTICLE

Fermentation-derived compounds and their impact on skin health and dermatology: A review

Rawan Atef Essmat[1], Nour Altalla[1], and Radwa Abdallnasser Amen[2]*

[1]Faculty of Pharmacy, Modern University for Information and Technology, Cairo, Egypt

[2]Department of Biotechnology, Faculty of Science, Cairo University, Cairo, Egypt

Abstract

Fermented plant extracts have recently become popular ingredients in various cosmetic and dermal applications, mainly because of their superior biological activities. In fermentation by microorganisms, the concentration of the useful compound is increased or new phytochemicals are introduced, enhancing their biological activity in anti-inflammatory, antibacterial, wound-healing, anti-melanogenic, and antioxidant applications. The fermented state of *Panax ginseng* shows higher anti-wrinkle and whitening effects than its non-fermented counterpart. Black ginseng promotes collagen synthesis and inhibits melanogenesis after fermentation. Fermented extracts of *Magnolia denudata*, organic *Indica rice bran*, and unpolished *Black rice* also show very good antioxidant and skin-whitening activities. Hyaluronic acid, kojic acid, citric acid, glycolic acid, and ascorbic acid are acids produced by the fermentation of natural products, forming smaller molecules size that are more effective than high molecular size and able to penetrate deeply into the skin, maintaining its microbiota balance and providing antioxidant protection. Fermented vitamins include B3, A, and E produced through microbial fermentation with added stability and bioactivity to contribute toward better skin health, promotion of absorption, anti-inflammation, and antioxidant properties. Skin health is modulated by its resident microbiota and their metabolites, among which fermented microorganisms have gained interest as active skincare ingredients. It is known that metabolites from skin-associated bacteria improve skin pigmentation and wrinkle appearance, such as *Nitrosomonas eutropha*, which oxidizes ammonia produced from sweat into nitric oxide derivatives. Similarly, antimicrobial peptide from *Enterococcus faecalis* strain proved to be potent against *Cutibacterium acnes*; hence, anti-acne treatments have been commercialized. In addition, *Vitreoscilla filiformis* found in hot springs significantly ameliorated symptoms of atopic dermatitis and photoaging while *Streptococcus thermophilus* enhanced levels of the natural ceramides, thereby enhancing skin barrier and hydration.

Keywords: Fermented plant extracts; Anti-melanogenic; Antioxidant protection; Skin barrier; Anti-wrinkle effects; Anti-inflammatory; Wound healing; Skin microbiota balance

***Corresponding author:**
Radwa Abdallnasser Amen
(radwaabdallnasser@gmail.com)

Citation: Essmat RA, Altalla N, Amen RA. Fermentation-derived compounds and their impact on skin health and dermatology: A review. *Innov Med Omics*. 2025;2(1):19-35. doi: 10.36922/imo.5020

Received: October 01, 2024
Revised: November 05, 2024
Accepted: November 21, 2024
Published online: December 27, 2024

Copyright: © 2024 Author(s). This is an Open-Access article distributed under the terms of the Creative Commons Attribution License, permitting distribution, and reproduction in any medium, provided the original work is properly cited.

Publisher's Note: AccScience Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1. Introduction

Dermatology and cosmetic science increasingly embrace the use of fermented plant extracts (FPEs) with their profound effects on skin health and beauty. Fermentation is a time-honored process that avails itself of microorganisms in the deconstruction of organic materials into their constituent parts, therefore increasing bioavailability and allowing the creation of new phytochemicals with superior properties. This biotechnological development has had very positive results on the formulation of skincare products that are much more effective than their non-fermented counterparts. Fermentation will enhance the anti-inflammatory, antibacterial, wound-healing, anti-melanogenic, and antioxidant properties of plant materials substantially, which makes them valuable addenda in today's skincare regimens.[1] One impressive example regarding the benefits of fermentation involves the transformation of *Panax ginseng.* This traditional herb shows a more powerful anti-wrinkle and whitening effect when fermented, higher in efficacy to reduce the visible signs of aging and hyperpigmentation than the one that is non-fermented.[2] This improvement is due to an increase in the concentration of bioactive compounds and the generation of new phytochemicals produced through fermentation. Similarly, fermented black ginseng enhanced the synthesis of collagen and reduced melanogenesis, further supporting the maintenance of skin that is young and evenly toned.[3]

Besides plant extracts, other natural materials subjected to a fermentation process also serve beneficial purposes, including extracts from fermented extracts of *Magnolia denudata* (Common name: Yulan Magnolia) Scientific name: *Magnolia denudata*, unpolished black rice (Common name: forbidden rice or purple rice) Scientific name: *Oryza sativa japonica*, which have major antioxidant and skin-whitening properties.[4,5] These fermented materials also have strong protective activity against oxidative stress, one of the major causative agents in skin aging and damage. The increased efficiency of the extracts in question would be in turn a direct result of the fermentation process as a method enabling an increase in active ingredient content and introducing metabolic products not present within raw materials. Another group of valuable metabolites produced by fermentations are fermented acids, such as hyaluronic, kojic, citric, glycolic, and ascorbic acids. With a smaller molecule size than their non-fermented cousins, these acids are well recognized for superior penetration through the skin. This superior level of skin penetration enables them to exhibit deeper therapeutic effects, maintain microbiota balance, and provide antioxidant protection.[6] Moreover, the fermentation process generally enhances the stability of these acids, which may be one more reason for their effectiveness in cosmetic formulations. Besides acids, microbial fermentation of vitamins, such as B3, A, and E has also been shown to improve stability and bioactivity. Fermented vitamins help improve skin health by enhancing better skin absorption, reducing inflammation, and providing defense against oxidation. Fermentation enhances the bioactivity of such vitamin manifold, which thereby allows them to be much more effective in mitigating various skin concerns related to inflammation, dryness, and oxidative damage.[7] However, the role of fermented microorganisms in skin care does not stop at the mere fermentation of plant extracts and acids. Skin metabolites generated by skin-associated bacteria, such as *Nitrosomonas eutropha* and *Enterococcus faecalis*, have provided immense benefits to skin health. *N. eutropha* is known to convert ammonia that is formed from sweat to nitric oxide compounds that are known to be beneficial for toning down pigmentations and wrinkling, while *E. faecalis* excretes out antimicrobial peptides which are active against *Cutibacterium acnes* and hence result in new anti-acne treatments.[3,8] In addition, probiotics, such as *Lactobacillus paracasei* and *Lactobacillus rhamnosus* have other advantages, such as enhancing immune responses, inhibiting inflammation, and improving the skin barrier.[5] This review elucidates the heightened awareness in regard to fermentation playing a better role in skin health and further developments that are likely to emerge on the care of the skin. The aim of this review is to find different functional fermentation products from deferent source as plant, vitamins, amino acids, and microbiome metabolites as shown in (Figure 1).

2. Natural-derived functional substances using microbial fermentation

2.1. Plant fermentation effect on skin health

FPEs are practical liquids that are made by the fermentation of fresh plants by microorganisms, mostly bacteria and fungi. Fermentation must be carried out to provide a suitable matrix of biologically active molecules with a range of biological characteristics. Presenting verified data on the biological activity of FPEs for cutaneous and cosmetic applications is the aim as well as some potential applications for the skin. Furthermore, fermentation can increase the antioxidant activity of plant extracts associated with increased concentrations of phytochemicals, mainly by causing microbial hydrolysis or biotransformation to produce antioxidant peptides, antioxidant polyphenols, and antioxidant polysaccharides.[9]

Lactobacillus brevis has been used to assess *P. ginseng* (red ginseng [RG]) and fermented RG (FRG) as

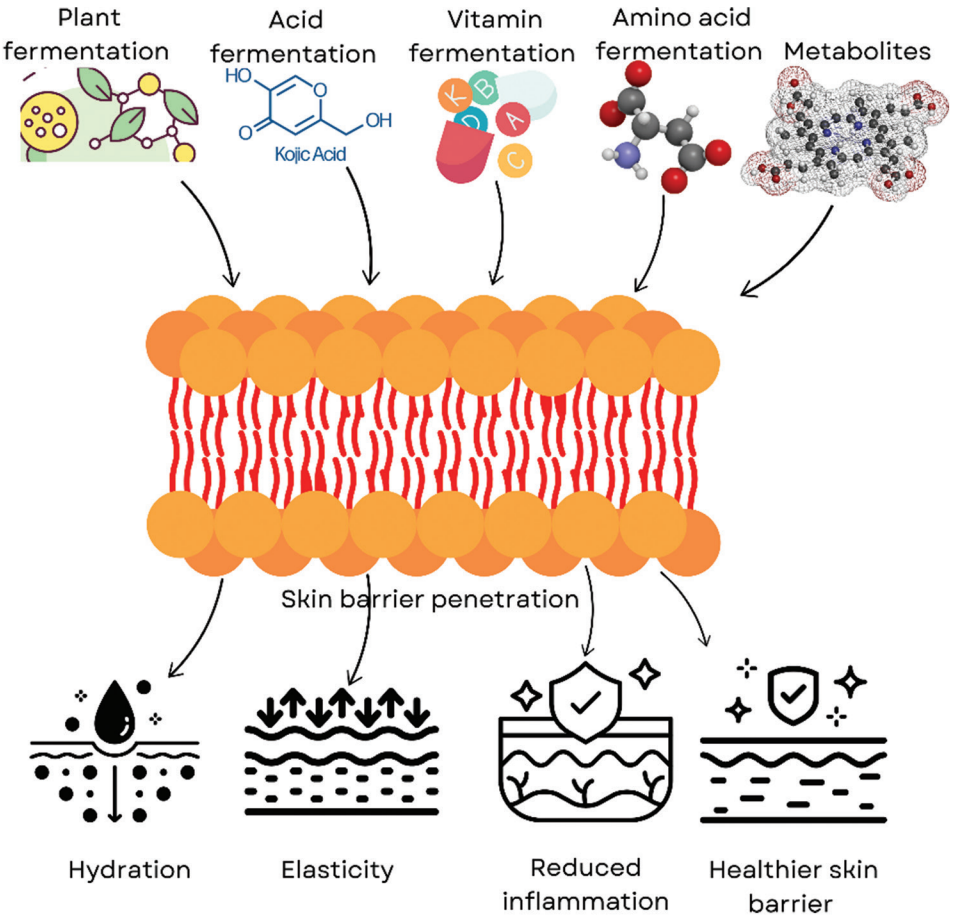


Figure 1. The mechanism of activity of the fermented compounds on skin

cosmetic components, specifically focusing on their anti-aging potential and skin safety. Compared to RG, FRG demonstrates higher concentrations of uronic acid, flavonoids, and polyphenols, as well as elevated antioxidant activity. Notably, no significant changes have been observed in the total ginsenoside content, although FRG exhibits higher levels of ginsenoside metabolites than RG. The tyrosinase inhibitory activity (half-maximal inhibitory concentration [IC^{50}) of FRG (27.63 μg/mL) is more potent than that of RG (34.14 μg/mL). Similarly, the elastase inhibitory activity (IC_{50}) of FRG (117.07 μg/mL) surpasses that of RG (157.90 μg/mL). Both 10% RG and 10% FRG are classified as essentially non-irritating materials in initial skin irritation tests. However, in skin sensitivity assessments, the RG group demonstrated a sensitization rate of 100% and an average irritation score of 1.4, as opposed to the FRG group, which demonstrated a sensitization rate of 20% and an average irritation score of 0.2. After fermentation, FRG possesses elevated levels of ginsenoside metabolites, including Rg3, Rg5, Rk1, compound K, Rh1, F2, Rg2, and flavonoids. Consequently, when compared to RG, FRG has better anti-wrinkle and whitening properties and lower toxicological potency.[10]

Fermented *Panax notoginseng* polysaccharide (FPNP) prevents the decline in antioxidant activity and the expression of the antioxidant enzymes catalase, glutathione peroxidase, and superoxide dismutase, which are typically induced by hydrogen peroxide (H_2O_2) and reduces reactive oxygen species (ROS) and malondialdehyde levels. Moreover, it was reported that FPNP, fermented by *Saccharomyces cerevisiae*, prevented the damage produced by H_2O_2 in collagen and elastin in human fibroblast cells.[11]

Using human fibroblasts (HS68), an *in vitro* experiment assessed FBG as a potential skin-whitening and anti-wrinkle ingredient. At concentrations below 10 μg/mL, FBG did not exhibit cytotoxicity, while at doses up to 100 μg/mL, the bio ferment was harmless to the eyes. In human fibroblasts, it significantly increased the type I procollagen expression level at doses ranging from 0.3 to 10 μg/mL when fermented by *S. cerevisiae*.[12] FBG's anti-wrinkle

action was accompanied by an increase in type I collagen synthesis and a decrease in matrix metalloproteinase-1 activity. Moreover, FBG has skin-whitening qualities as it inhibits tyrosinase, reduces melanogenesis, and decreases dihydroxyphenylalanine oxidation.[13]

The flower petal extract of *Magnolia denudate*, fermented by *Pediococcus acidilactici*, exhibits antioxidant and anti-cancer properties. The concentration of the fermented extract is 3 times higher than its non-fermented counterpart. Moreover, the radical-scavenging activity of fermented *M. denudate* against 1,1-diphenyl-2-picryl-hydrazyl (DPPH) increased from 85.1% to 91.4%, depending on the duration of fermentation.[14]

Fermented organic *Oryza sativa L.* (indica rice bran) has emerged as a key ingredient in skincare products, offering hydration, brightening, and anti-wrinkle benefits. Its effects are comparable to Pitera – a naturally occurring byproduct of sake lees fermentation – but it is free from alcohol-related irritation, making it highly effective for sensitive skin. It is fermented in a clean, safe environment by lactic acid bacteria. In terms of anti-oxidative properties, a 100.0 mg/mL bran fermentation solution demonstrates 71.4% higher DPPH radical-scavenging activity than Vitamin C at the same concentration and chelate Fe^{2+} ions 79.0% more effectively than ethylenediaminetetraacetic acid. Moreover, the superoxide anion-scavenging capacity of 10.0 mg/mL bran fermentation solution was 42.9% higher than butylated hydroxytoluene at the same dosage. The bran fermentation solution also inhibits the formation of dopachrome, a melanin intermediate, in a concentration-dependent manner, with higher concentrations providing greater inhibition. The IC_{50} of the bran fermentation solution and arbutin were 9.23 mg/mL and 0.52 mg/mL, respectively.[15] Fermented unpolished black rice (FUBRS), processed using a mixture of microbes isolated from *loog-pang*, demonstrates superior capacity to reduce melanin concentration in melanoma cells. In addition, it prevents melanogenesis in other melanoma cells by phosphorylating AKT, ERK, and p38. The marked decline in intracellular tyrosinase activity is in line with melanin reduction activity. The human fibroblast and melanoma cell lines are not cytotoxically affected by FUBRS. In addition, it decreases the expression levels of tyrosinase, tyrosinase-related protein 1 (TYRP-1), TYRP-2, and microphthalmia-associated transcription factors in both transcript and protein levels.[16]

A fermented extract of soybean, fermented with *Bacillus bacterium* and processed into a dry powder form, provides the skin with essential nutrients. By incorporating skin-aging inhibitors and whitening agents as active ingredients, the composition moisturizes the skin, improves elasticity, enhances skin tone, and provides antioxidant benefits.[17] Moreover, an extract of *Zanthoxylum schinifolium*, fermented with *L. rhamnosus* A6-5, showed greater antibacterial activity than raw extract when tested against *Propionibacterium acnes* and *Staphylococcus epidermidis*. Similarly, fermented blueberry fruit extract demonstrated antibacterial activity against *Brevibacterium linens*, *P. acnes*, *Bacillus cereus*, and *S. epidermidis* when fermented with particular probiotic bacteria (*Bacillus amyloliquefaciens* and *L. brevis*) and yeast (*Starmerella bombicola*) isolated from fermented starfish.[18]

2.2. Production of acids through fermentation for skin care

In the cosmetics industry, fermented acids are gaining attention by combining innovative and traditional methods to improve skincare regimens. Fermented acids are produced through fermentation, breaking down natural substances into smaller, more potent molecules. This increases the concentration of active chemicals and improves bioavailability, allowing them to penetrate the skin more deeply. Fermented acids have many advantages, including the capability to maintain the skin's microbiota. These compounds assist in minimizing acne, reduce inflammation, and relieve skin problems such as rosacea and eczema by maintaining a healthy balance of bacteria on the skin. Furthermore, the high antioxidant content of fermented acids shields the skin from ultraviolet (UV) rays and free radical damage. Moreover, the fermentation frequently yields novel, health-promoting compounds, including vitamins, peptides, and amino acids that improve the skin's overall appearance and health. These components greatly complement any skincare routine since they increase moisture retention, boost collagen production, and improve skin texture.[19]

Hyaluronic acid (HA) is a glycosaminoglycan widely distributed in humans and other mammalian tissues. It has numerous applications in both the medical and cosmetic industries, however, it excels as a humectant due to its capacity to form viscoelastic hydrogels in aqueous solutions, making it an ideal ingredient as a natural skincare moisturizer. The low yield of this polysaccharide when extracted from animal sources (such as rooster combs) was a key factor that prompted the commercial release of the biotechnologically produced version. Gram-positive endotoxins and proteins present in the membrane of the *Streptococcus* strain used to produce high molecular weight HA are potentially hazardous substances and must be removed through a sequence of filtration processes. These laborious purification steps are avoided by using recombinant *Bacillus subtilis*, which secretes HA into a fermentation medium. The medium is then sprayed and

dried at a high temperature to produce HA powder.[20] HA serves several functions based on its molecular weight.[21] High-molecular HA (about 1 MDa) increases the viscosity and stability of the product film that forms on the skin, hence decreasing transepidermal water loss and improving the hydration of the upper layers of the epidermis. At a lower molecular weight (about 250 kDa), HA interacts with skin cells and extracellular components, providing deeper hydration and wrinkle reduction. This enables HA to function as a signal molecule that triggers the synthesis of natural HA. Reports have suggested that more potent anti-aging effects may arise from molecules with smaller molecular weights.[22]

Another molecule that is becoming increasingly important is kojic acid, which primarily acts as a skin-lightening agent. It is synthesized by strains from the genera *Aspergillus* and *Penicillium*. Kojic acid improves the ability of skin care products to shield users from UV rays and reduces skin hyperpigmentation by inhibiting the production of tyrosinase. According to the Global Industry Analysts, there is a high demand for whitening creams in the Middle East, Asia, and Africa. Moreover, given its economic potential, kojic acid consistently draws attention for its environmentally friendly synthesis, with research continually being conducted to enhance its production.[23]

Citric acid is a member of the class of molecules known as alpha hydroxyl acids (AHAs) and functions as an exfoliating agent in skin care products. AHAs can eliminate dead skin cells from the skin's outermost layer, a process known as exfoliation, leaving the skin radiant and youthful. Over the past few years, there has been a steady increase in demand for cosmetic products containing AHAs, particularly in the Western European and Asian markets. In 1916, research conducted by James Currie enabled the profitable industrial synthesis of citric acid from *Aspergillus niger* using molasses and sucrose as primary carbon sources. He discovered that several strains of *A. niger* can produce significant amounts of citric acid. The two most important findings were: (i) citric acid production could succeed at a pH of approximately 2.5 – 3.5, which inhibited the formation of gluconic and oxalic acid, and (ii) citric acid production increased as sugar content rose.[24] In addition, since the 1960s, scientists have made significant efforts to introduce *Yarrowia lipolytica* yeast as an alternative to conventional fungal technology. *Y. lipolytica* can produce citric acid using a variety of carbon sources. Furthermore, *Y. lipolytica* possesses several desirable properties, such as withstanding lower pH levels, making it more economical and tolerant to high quantities of carbon sources and contaminants found in substrates.[25]

In addition to citric acid, glycolic acid is another AHA known in the skincare industry. Fermentation of glycolic acid breaks it down into smaller molecules, allowing for easier absorption into the skin. This helps with exfoliation, resulting in a smoother and more radiant complexion. Glycolic acid improves skin hydration and barrier function by boosting collagen production, which helps to reduce the appearance of fine lines and wrinkles, giving the skin a more youthful and firmer appearance. It can also introduce beneficial antioxidants that protect the skin from environmental stressors and free radical damage. Currently, glycolic acid is primarily produced using petrochemical resources, which involves the usage of hazardous formaldehyde. Alternatively, a biotechnological production pathway offering a sustainable approach is more desirable. Producing glycolic acid from lignocellulosic biomass feedstocks would be more economically and environmentally viable. Numerous bacteria naturally produce glycolic acid by hydrolyzing glycolonitrile and oxidizing ethylene glycol. However, developing a pathway that allows for the flexible usage of alternative, more abundant carbon sources under standard bioprocessing conditions would be more advantageous, as current production pathways depend on ethylene glycol or glycolonitrile, and specific environmental conditions. One less-explored but promising production pathway is the glyoxylate cycle, where C2 molecules, such as ethanol are naturally converted into glyoxylate, which can be further converted into glycolic acid through metabolic engineering. Other than that, several methods have been proposed for modifying *Escherichia coli*'s glyoxylate cycle to enhance glycolic acid production.[26]

Ascorbic acid, also known as Vitamin C, is a water-soluble essential vitamin and functions as a crucial cofactor for several enzymatic reactions in the body.[27,28] The antioxidative ability of ascorbic acid to scavenge free radicals and minimize oxidative stress has led to its growing use in cosmetic products.[29] Ascorbic acid is produced through a fermentation process that frequently uses several microorganisms. In the first stage of the fermentation, the bacterium *Gluconobacter oxydans* converts D-Sorbitol into L-Sorbose. In the next stage, a mixed culture of *Ketogulonicigenium vulgare* and *Bacillus* species converts L-sorbose into 2-keto-L-gulonic acid, a pre-cursor of ascorbic acid. Together, these microbes perform a two-step fermentation process that effectively produces ascorbic acid.[30]

2.3. Production of vitamins through fermentation for skin care

Fermented vitamins are revolutionizing the cosmetics market with their potent skin benefits and enhanced

bioavailability. The fermentation process, driven by beneficial microbes, transforms the vitamins into more stable and bioactive forms that are particularly effective in skincare products. During fermentation, complex vitamin structures are broken down, enhancing the skin's ability to absorb and utilize the nutrients. The use of fermented vitamins in cosmetics includes two key benefits: (i) improved absorption and (ii) increased effectiveness. Moreover, fermented vitamins exhibit stronger antibacterial and anti-inflammatory properties compared to their non-fermented counterparts, making them valuable in treating various skin issues, such as aging and acne. Research on fermented vitamins in cosmetics can result in novel formulations with improved advantages for skin health, opening doors to more sustainable and effective beauty products.[19]

Niacinamide, also known as Vitamin PP, Vitamin B3, or nicotinamide, is a component of coenzymes involved in hydrogen transfer and has several positive effects on the skin. The topical application of niacinamide helps to cure atopic dermatitis by stabilizing the skin barrier, reducing transepidermal water loss, and promoting the synthesis of ceramides and proteins such as filaggrin, keratin, and involucrin. It has been observed that topical treatment with niacinamide lowered transepidermal water loss in dry skin and improved the synthesis of cholesterol, free fatty acids, and ceramide – the main pathogenic components responsible for barrier failure in atopic dermatitis. The anti-inflammatory properties of niacinamide and its ability to reduce the production of several inflammatory cytokines (interleukin [IL]-1β, IL-6, IL-8, and tumor necrosis factor), make it a promising treatment for acne, rosacea, and other inflammatory skin diseases.[31] As for the production of niacinamide, reports have demonstrated that Vitamin B3 can be produced using recombinant *E. coli* expressing *Rhodococcus rhodochrous* nitrile hydratase.[32]

Another vitamin of interest in skin care applications is Vitamin A, also known as retinoid or β-carotene. Vitamin A can be derived from several sources, such as animal products (meat, dairy products, and fish), colored fruits and vegetables (β-carotenoid or provitamin A), as well as retinol and retinyl ester. In addition to retinol and its natural counterparts, the retinoid family includes numerous synthetic compounds. Retinoids interact with several cellular and nucleic acid receptors, such as the nuclear retinoic acid receptor family, the cellular retinol-binding protein, and the cellular retinoic acid-binding protein types I and II. The mechanism of action of retinoids involves regulating cellular differentiation, which enhances photoaging by promoting epidermal proliferation, leading to epidermal thickening, and stimulating the deposition of glycosaminoglycans. In addition, Vitamin A, as an antioxidant, helps to reduce DNA damage from free radicals, thereby preventing neoplastic transformation and carcinogenesis.[31] In terms of production, Vitamin A or β-carotene is produced by the yeast, *Y. lipolytica*. The production of β-carotene is increased by overexpressing heterologous carotene synthase in *Y. lipolytica*. After screening for the most effective promoter, the modified strain achieved a fermentation yield of 1.5 g/L. By employing fed-batch fermentation and perfectly adjusting the fermentation conditions, the production titer of β-carotene was further increased to 6.5 g/L and 90 mg/g dry cell weight.[33]

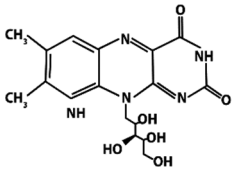
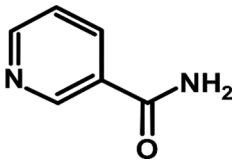
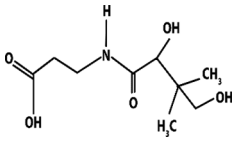
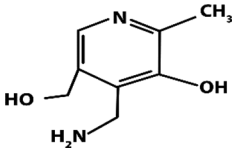
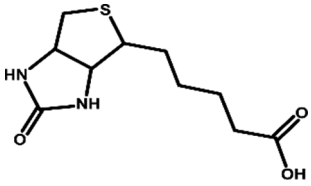
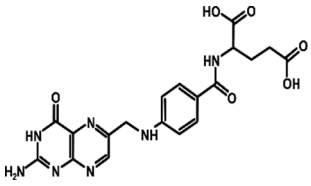
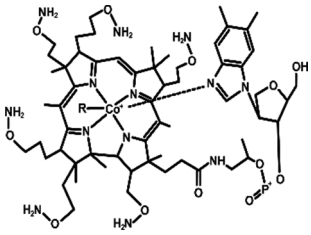
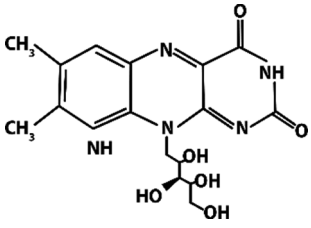
Vitamin E, including tocopherols and tocotrienols, is a group of lipid-soluble antioxidants. Vitamin E serves as the primary defense against lipid peroxidation by inhibiting the synthesis of ROS molecules, thereby preserving the integrity of cell membranes. The antioxidant activity of Vitamin E can be significantly enhanced by ascorbic acid, Vitamin B3, selenium, glutathione, and other biological factors. The potent antioxidant properties of Vitamin E make it an ideal compound for avoiding skin aging, treating several skin disorders such as atopic dermatitis, and melasma, and preventing scar formation. Topical application of Vitamin E is generally safe, with minimal reported side effects and a low frequency of minor irritations. Reports have shown that formulations containing 0.2% α-tocopherol effectively increased Vitamin E levels in the stratum corneum (SC) and decreased lipid peroxidation *in vivo*, thereby protecting the skin from the damaging effects of photoaging and oxidative stress.[34,35] Moreover, it has been recently discovered that the bacterium *Euglena gracilis* is highly effective in creating high-value compounds, such as Vitamin E. It is characterized by rapid growth and a high production of α-tocopherol, which accounts for over 97% of the total tocopherol content in the organism.

In addition to the vitamins mentioned, many other vitamins are produced through microbial fermentation and exert beneficial effects on the skin. A summary of these vitamins and their respective functions on skin health is tabulated in Table 1.[36]

2.4. Production of amino acids through fermentation for skin care

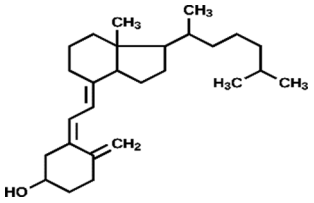
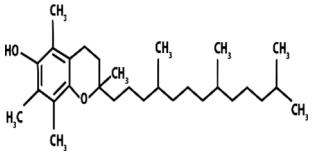
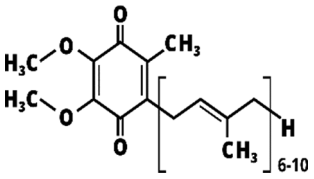
Fermented amino acids are revolutionizing the fields of nutrition and skincare. Fermentation increases the bioavailability and efficacy of amino acids, allowing better absorption by the body than their synthetic counterparts, thereby improving overall skin health and general wellness. Fermented amino acids help strengthen the skin's protective barrier, enhance moisture retention, and

Table 1. Examples of other vitamins produced by microorganisms and their respective functions on skin

Vitamin	Chemical structure	Microbes involved	Function on skin	Description of benefits
Vitamin B2 (Riboflavin)		*Staphylococcus epidermidis, Corynebacterium* spp.	Acts as an antioxidant, supports cellular energy production, enhances skin integrity, and repair	Riboflavin protects skin cells from oxidative damage and helps in repairing skin exposed to environmental stressors, such as UV rays.[37]
Vitamin B3 (Niacin/ Niacinamide)		*Staphylococcus epidermidis, Cutibacterium acnes*	Functions as an anti-inflammatory agent, improves skin hydration, helps reduce redness	Niacinamide helps in building keratin, keeps skin firm and healthy, improves skin barrier function, and reduces signs of aging.[38]
Vitamin B5 (Pantothenic acid)		*Propionibacterium* spp., *Staphylococcus* spp.	Functions as an anti-inflammatory agent, enhances wound healing, maintains skin hydration	Pantothenic acid supports the synthesis of coenzyme A which is important for cell regeneration and soothing irritated or damaged skin.[39]
Vitamin B6 (Pyridoxine)		*Cutibacterium acnes, Streptococcus* spp.	Reduces skin irritation, enhances immune defense	Pyridoxine supports skin health by helping enzymes that regulate metabolism and protein production, providing protection against pathogens.[40]
Vitamin B7 (Biotin)		*Propionibacterium* acnes, *Corynebacterium* spp.	Improves skin barrier function, supports anti-inflammatory processes	Biotin maintains skin hydration, elasticity, and smoothness, aiding in the formation of fatty acids essential for skin health.[41]
Vitamin B9 (Folate)		*Lactobacillus* spp., *Bifidobacterium* spp.	Promotes cell renewal, supports DNA synthesis, helps maintain youthful skin	Folate is essential for cell division, and in the skin, it can promote faster regeneration, beneficial for healing wounds and blemishes.[42]
Vitamin B12 (Cobalamin)		*Propionibacterium* acnes, *Staphylococcus* aureus	Regulates microbiota, essential for DNA synthesis and cell metabolism	Cobalamin supports cellular energy production and may help control inflammation and acne by regulating skin microbial balance.[43]
Vitamin K2 (Menaquinone)		*Staphylococcus epidermidis, Bacillus* spp.	Supports blood clotting, provides antioxidant benefits	Menaquinone helps with wound healing due to its role in blood clotting and provides antioxidant protection, which may reduce wrinkles and sunspots.[44]

(Cont'd...)

Table 1. ***(Continued)***

Vitamin	Chemical structure	Microbes involved	Function on skin	Description of benefits
Vitamin D3 (Cholecalciferol)		UV-activated synthesis on skin with *Staphylococcus* spp.	Enhances skin immunity, reduces inflammation, strengthens skin barrier	Cholecalciferol, produced in response to sunlight, is vital for skin immunity, protecting against pathogens and inflammation.[45]
Vitamin E		Skin microbiota contribution not fully established	Acts as an antioxidant, protects skin from UV damage, promotes healing	Though primarily acquired through diet, Vitamin E on the skin provides photoprotection and repairs cell membranes damaged by free radicals.[46]
Coenzyme Q10		*Cutibacterium acnes* and other anaerobes	Acts as an antioxidant, helps in collagen production, protects skin cells from oxidative stress	Although not a vitamin, coenzyme Q10 functions similarly by protecting the skin from oxidative stress and maintaining cellular energy levels. [47]

Abbreviation: UV: Ultraviolet.

promote a youthful appearance, making them valuable in skincare applications. They are renowned for their ability to boost collagen synthesis, a crucial process in maintaining skin elasticity and reducing the appearance of wrinkles and fine lines. Furthermore, fermentation is both sustainable and environmentally friendly, aligning with the growing demand for eco-friendly and clean beauty products. Harnessing the power of fermentation enables the production of potent and natural ingredients that benefit the skin and contribute to a more sustainable planet. The production of fermented amino acids frequently uses two bacteria: *Corynebacterium glutamicum* and *E. coli*.[48] These bacteria can create a wide range of amino acids, and their productivity as amino acid producers has increased by applying different metabolic engineering modifications. For instance, genetically engineered *C. glutamicum* is utilized to manufacture high yields of glutamic acid or lysine (up to 50% w/w), whereas *E. coli* has been modified to produce aromatic amino acids such as L-tryptophan, L-phenylalanine (L-Phe), and L-tyrosine (L-Tyr).[49]

C. glutamicum is an aerobic, non-pathogenic Gram-positive soil bacterium primarily used in amino acid production. Amino acids produced by *C. glutamicum*, such as L-glutamate, L-lysine, L-serine, L-proline, L-arginine, and L-isoleucine, have a favorable effect on the skin. The bacterium primarily prefers glucose as a carbon source in amino acid production but can also utilize other sugars such as sucrose, fructose, ribose, mannose, and maltose.[50] Glutamic acid is an amino acid involved in the central nervous system, known for its ability to enhance the antioxidant activity of the skin, regulate redox balance, prevent apoptosis, and play a vital role in the development of fibroblasts and keratinocytes. It is also recognized for its beneficial effects in treating various conditions such as large wounds, surgical wounds, and wounds from radiation and chemotherapy. Despite these benefits, glutamic acid's low water solubility (7.5 g/L at 20°C) limits its applications in cosmetics and ointments at high doses.[51]

Arginine, a semi-essential amino acid known for its role in skin immunity, wound healing, collagen synthesis, and cell division, is metabolized by the enzymes nitric oxide synthase II or arginase I. It has been reported to play a role in the management of serious wounds, including burns, diabetic wounds, bedsores, and UV-induced erythema.[52]

L-lysine has been noted for its beneficial effects in managing pityriasis rosea (PR), a skin condition primarily affecting young individuals aged 10 – 35. PR typically presents as an erythemato-papulosquamous eruption on the trunk and extremities in otherwise healthy individuals. The condition generally resolves on its own within six to eight weeks but may persist for three to six months, sometimes causing reversible skin discoloration. L-lysine can reduce the frequency of yearly symptoms and accelerate lesion healing, offering potential benefits in managing PR.[53]

Serine, an amino acid containing a hydroxyl group,

is found in keratin and naturally occurring moisturizing agents. Its ability to interact actively with water molecules suggests that it could improve the skin's ability to retain moisture when effectively delivered into the skin's SC.[54]

L-proline is a crucial amino acid for collagen synthesis, providing stability to skin, bones, tendons, and connective tissues. As humans age, collagen levels decline, leading to changes in skin texture. L-proline supports collagen synthesis, aiding skin repair and maintaining its structural integrity. It plays a key role in the four stages of wound healing – hemostasis, inflammation, proliferation, and maturation – facilitating the growth of new, healthy tissue in damaged areas. I addition, L-proline contributes to anti-aging by promoting collagen production to help delay or repair age-related skin changes. It also supports the healing of burns, cuts, and wounds by boosting collagen synthesis.[55-57]

L-isoleucine is an amino acid used in the treatment of atopic eczema. It stimulates epithelial cells to produce antimicrobial peptides, strengthening the skin's innate immune response. L-isoleucine, used topically, has been demonstrated to enhance skin barrier function, lower inflammation, and reduce eczema symptoms, including itching and redness. Research has shown that L-isoleucine-containing creams, used in combination with ceramides and rhamnosoft, significantly improved clinical outcomes for individuals suffering from mild-to-moderate eczema.[58,59]

E. coli, is a naturally occurring Gram-negative aerobic bacteria mostly found in plants and the gut flora of mammals. It produces numerous amino acids, including the aromatics, L-Phe, L-Tyr, L-methionine (Met), L-cysteine (Cys), and L-threonine (Thr). Although there is no direct evidence linking the availability of these amino acids and the production of skin proteins, these volatile amino acids play a crucial role as melanin pre-cursors. Melanin is the primary cutaneous photoprotective pigment preventing DNA damage and certain forms of skin cancer by absorbing harmful UV rays from the sun.[60,61] Melanocytes, the specialized cells responsible for the creation of melanin, contain the enzymes tyrosinase (a copper enzyme) and Phe (a tetrahydrobiopterin-dependent enzyme).[62] After activation, Phe hydroxylase in human melanocytes converts Phe into Tyr. Phe hydroxylase can be activated by ROS and the oxidant condition produced following UV exposure.[63] Tyrosinase then further oxidizes Tyr to produce melanin.[64] Melanosomes, the subcellular organelle of melanocytes, transport the melanin to keratinocytes.[65] Freckles and moles are areas of the skin with a higher concentration of these melanocytes and melanin. The amount of Phe and Tyr required for melanin production depends on sun exposure and skin type. The type and amount of melanin determine an individual's tanning response and overall skin health.[66]

Met is a sulfur-containing amino acid required to synthesize glutathione and Cys. Sulfur is needed to sustain the skin's elasticity and strength. Met serves as a pre-cursor to glutathione, an effective antioxidant that shields the skin from UV ray damage and oxidative stress, which can cause pre-mature aging. Moreover, it serves as an essential amino acid in collagen and elastin synthesis, preserving the firmness and elasticity of skin, while promoting skin restoration and wound healing. In addition, Met can improve the skin's natural barrier against environmental stressors while helping to keep the skin clear through detoxification. Furthermore, in the context of Cys in keratins, it can be obtained endogenously from oral consumption of Met. Cys is crucial in producing the disulfide bridges found in integumentary skin structures. These sulfur-containing amino acids and other sulfated molecules provide sulfur, which is needed for several purposes.[67] The body requires an adequate intake of Met and Cys to produce glycosaminoglycans and skin structural polysaccharides. Besides that, Met can serve as an antioxidant complex to treat inflammatory cutaneous lesions and acne by acting as a zinc carrier rather than a sulfur provider.[68]

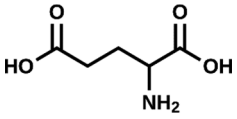
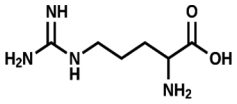
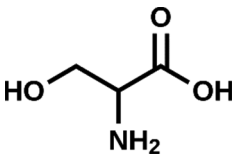
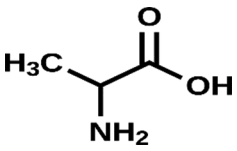
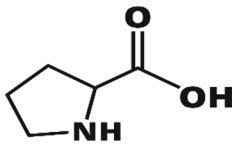
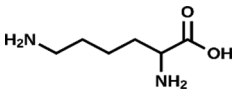
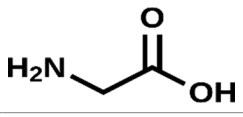
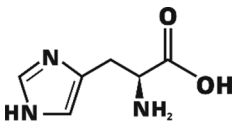
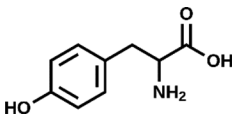
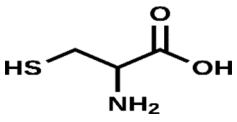
Thr, produced from the formation of collagen and elastin, aids in preserving the moisture balance of the skin, giving it a smoother, more youthful appearance. However, there is limited information regarding the dietary requirement for maintaining skin or any other tissues. Thr and serine are amino acids essential in maintaining the moisture of the SC. Both amino acids can be phosphorylated by many kinases, and this phosphorylation is crucial for proper structural function and regulation of skin metabolism.[69]

Other than the mentioned amino acids, various types of amino acids possess functional effects on skin health, as shown in Table 2.[70]

3. Benefits of microorganism-derived metabolites on the skin

The skin is home to 1,000 species of commensal bacteria, viruses, fungi, and other microorganisms. It has been shown that metabolites, such as glycerol and fatty acids produced by naturally occurring skin microorganisms, benefit skin health. As a result, probiotic cosmetics and skin-domesticating microorganisms and their metabolites are common constituents in skincare products. Currently, traditional Japanese fermented ingredients are employed as fermented cosmetics

Table 2. Amino acids and their respective beneficial compounds for skin health

Amino acid	Chemical structure	Microbes involved	Function on skin	Description of benefits
L-glutamic		*Staphylococcus epidermidis, Corynebacterium* spp.	Functions as a moisturizer promotes hydration	L-glutamic acid helps retain moisture and maintain the skin's natural hydration barrier.[38]
L-arginine		*Cutibacterium* acnes, *Staphylococcus* spp.	Acts as an antioxidant, promotes wound healing	L-arginine plays a role in collagen synthesis, supporting wound repair and skin elasticity.[39]
L-serine		*Staphylococcus* spp., Micrococcus luteus	Hydrates skin, maintains elasticity	L-serine is essential for skin hydration and softness, contributing to the skin's natural moisturizing factor.[71]
L-alanine		*Staphylococcus epidermidis, Corynebacterium* spp.	Strengthens skin barrier, enhances moisture retention	L-alanine provides hydration and supports the skin barrier, helping protect against environmental stress.[44]
L-proline		*Cutibacterium* acnes, *Corynebacterium* spp.	Synthesizes collagen, improves skin texture	L-proline aids in collagen formation, enhancing skin firmness and reducing the appearance of fine lines.[72]
L-lysine		*Cutibacterium* acnes, *Staphylococcus* aureus	Acts as an anti-inflammatory agent, supports skin repair	L-lysine contributes to collagen formation, aids in wound healing and inflammation reduction.[73]
L-glycine		*Corynebacterium* spp., Micrococcus luteus	Provides hydration, enhances skin texture	L-glycine supports collagen production, maintains hydration, and improves overall skin texture.[74]
L-histidine		*Staphylococcus epidermidis, Corynebacterium* spp.	Acts as an antioxidant, enhances moisture retention	L-histidine is an antioxidant that hydrates the skin, promoting softness and resilience.[75]
L-tyrosine		*Propionibacterium* acnes, *Staphylococcus* spp.	Regulates skin pigmentation	L-tyrosine is a pre-cursor for melanin synthesis, regulates pigmentation, and protects against UV radiation.[76]
L-cysteine		*Cutibacterium* acnes, *Staphylococcus* aureus	Acts as an antioxidant, supports skin healing	L-cysteine helps with collagen production and provides antioxidant protection, aiding skin regeneration.[77]

Abbreviation: UV: Ultraviolet.

after using these ingredients as food for more than 1,300 years. It is anticipated that fermented cosmetics will continue to expand as a category of products in the natural skincare product market and offer many health benefits.[78]

N. eutropha is an ammonia-oxidizing bacterium that oxidizes sweat-derived ammonia to create nitric oxide and nitrogen on the skin.[79] Clinical trials on topical treatment of *N. eutropha* showed improvement in pigmentation and wrinkles between the eyebrows and on the forehead.[80] This

discovery prompted the creation of a mist lotion with *N. eutropha*, currently available for purchase and has been demonstrated to improve the appearance and texture of skin. *E. faecalis* is a type of lactic acid bacterium found in the intestines and is known to benefit human health. Studies have demonstrated that the antibacterial peptides produced by *E. faecalis* possess antibacterial activity against *C. acnes*, confirming its potential as an effective new anti-inflammatory drug for acne. This has led to the commercialization of *E. faecalis* in skincare cosmetics and other therapies, intended to reduce inflammation associated with acne.[81]

Vitreoscilla filiformis is a fungus present in hot spring water and hydrothermal vents. The fungal extract was observed to balance the skin's immunological homeostasis. According to a previous study, patients with mild to moderate atopic dermatitis showed a reduction in the level of pruritus upon application of ointments containing *V. filiformis* twice daily to the site of inflammation.[82] Moreover, an extract of *V. filiformis* cultured in Vasi Volcanic Mineral Water is known to fortify the skin against exposome attack, mend damaged skin, regenerate the skin barrier, and avoid photoaging through increased immunological response. The results showed that *V. filiformis* is highly effective in repairing damaged skin, reducing photoaging, and enhancing immunological function by restoring the skin barrier.[83] Moreover, clinical trials have proven the benefits of fungus in balancing the skin flora and relieving itching in skin prone to allergies and the condition. Consequently, body washes and lotions containing *V. filiformis* cultures have been commercialized in the market.[84]

Another lactic acid bacterium, *Streptococcus thermophilus*, sometimes known as the cheese and yogurt seed, was observed to elucidate positive effects on skin health. An increase in ceramide levels was observed in healthy individuals who were given creams containing *S. thermophilus*. Ceramides are essential in maintaining the barrier and moisture of a healthy SC.[85] In addition, atopic dermatitis patients who received topical treatment of *S. thermophilus* also demonstrated elevated ceramide levels in their skin, followed by improvements in erythema, scaling, and pruritus.[86]

L. paracasei, a lactic acid bacterium inhabiting the digestive tract and oral cavity, was reported to improve atopic dermatitis and benefit the skin.[87] Furthermore, an investigation on the impact of *Pueraria lobata* extract fermented with *L. paracasei* on the skin's immune response revealed differential expression of seven skin-related proteins and a moisturizing effect on the skin upon treatment. Hence, *L. paracasei* can be used as a nutricosmetic resource for its hydrating and anti-inflammatory properties. In addition, it has been discovered that *L. paracasei* produces the same antioxidant and bioactive peptides, which reduce wrinkles and may be utilized as a more advantageous probiotic for

Table 3. Effects of microbiome metabolites on skin health

Microorganism	Metabolite	Effect on skin
Nitrosomonas eutropha	Nitric oxide compounds	Improves skin pigmentation and reduces wrinkle appearance by oxidizing sweat-derived ammonia.[92]
Enterococcus faecalis	Antimicrobial peptides	Effective against *Cutibacterium* acnes, leading to reduced acne and commercialization of anti-acne treatments.[93]
Vitreoscilla filiformis	Unknown metabolites	Reduces symptoms of atopic dermatitis and photoaging due to its anti-inflammatory properties.[84]
Streptococcus thermophilus	Ceramide synthesis enhancement	Increases ceramide levels, supporting skin barrier function and hydration.[94]
Lactobacillus paracasei	Unknown metabolites	Improves immune response, reduces inflammation, and enhances skin barrier function.[95]
Lactobacillus rhamnosus	Unknown metabolites	Reduces inflammation and promotes skin barrier repair.[96]
Bifidobacterium breve	Polysaccharide A	Modulates immune responses and enhances skin hydration by stimulating T-regulatory cells.[97]
Lactobacillus plantarum	Lipoteichoic acid	Reduces skin sensitivity, provides anti-inflammatory effects, and improves skin barrier function.[98]
Cutibacterium acnes	Short-chain fatty acids	Modulates skin pH and inhibits pathogenic bacteria, promoting a healthy skin microbiome.[99]
Staphylococcus epidermidis	Phenol-soluble modulins	Enhances skin defense mechanisms by promoting antimicrobial peptide production.[100]
Lactobacillus reuteri	Reuterin	Displays antimicrobial activity against skin pathogens and promotes skin barrier function.[101]
Bacillus subtilis	Surfactin	Provides anti-inflammatory and wound-healing properties.[102]

the skin.[88] L. *rhamnosus* is a probiotic known to enhance the intestinal barrier's performance and is anticipated to be used in cosmetics.[89] Research has indicated that topical application of *L. rhamnosus* lysate to a human epidermal model for 16 days increased the expression of skin barrier proteins and promoted SC formation, which may have beneficial effects in preserving skin barrier function.[90] Although more investigation is necessary, these results imply that topical probiotics could have potential applications in skincare products. In addition, *L. rhamnosus* showed a high inhibition of tyrosinase and melanin synthesis and increased collagen production when co-cultured with *L. paracasei*.[91] Besides the mentioned microorganisms and metabolites, there are many other examples of microorganism-derived metabolites affecting the skin, as shown in Table 3.

4. Conclusion

FPEs are superior among the reviewed skincare ingredients, due to their increased biological activity and varied benefits. In these extracts, fermentation enhances anti-inflammatory, antibacterial, and antioxidant properties, and accelerates wound-healing processes, making these fermented extracts more potent than their non-fermented counterparts. For example, fermented *P. ginseng* is remarkably effective in anti-aging and skin whitening, while fermented *M. denudata* and rice bran have significant antioxidant and skin-brightening properties. Fermentation enhances the bioavailability of bioactive phytochemicals toward better skin hydration, collagen synthesis, and barrier function. The integration of microorganisms and their metabolites in skincare products highlights the tendency of industry productions to shift toward more advanced natural solutions. Probiotic strains, including *N. eutropha, E. faecalis*, and *V. filiformis*, impart beneficial properties such as skin texture improvement, anti-inflammation, and barrier support. Fermented acids, vitamins, and amino acids enhance the functionality of ingredients, thereby increasing hydration, skin lightening, and exfoliation. These advancements within fermentation technology would enable the development of innovative skincare products, offering better and more sustainable solutions for achieving healthier, brighter skin.

Acknowledgments

None.

Funding

None.

Conflict of interest

The authors declare they have no competing interests.

Author contributions

Conceptualization: Rawan Atef Essmat, Radwa Abdallnasser
Writing-original draft: Rawan Atef Essmat, Nour Altalla
Writing-review & editing: Radwa Abdallnasser

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

Not applicable.

References

1. Zofia NŁ, Aleksandra Z, Tomasz B, *et al*. Effect of fermentation time on antioxidant and anti-ageing properties of green coffee kombucha ferments. *Molecules*. 2020;25(22):5394.

   doi: 10.3390/molecules25225394

2. Ramadhania ZM, Yang DU, Moektiwardojo M, *et al*. Enhanced anti-skin aging effects of fermented black ginseng (*Panax ginseng* CA Meyer) by *Aspergillus niger* KHNT-1. *Appl Sci*. 2022;13(1):550.

   doi: 10.3390/app13010550

3. Corbu VM, Gheorghe-Barbu I, Dumbrava AS, Vrâncianu CO. Current insights in fungal importance-a comprehensive review. *Microorganisms*. 2023;11:1384.

   doi: 10.3390/microorganisms11061384

4. Ragusa I, Nardone GN, Zanatta S, Bertin W, Amadio E. *Spirulina* for skin care: A bright blue future. *Cosmetics*. 2021;8:7.

   doi: 10.3390/cosmetics8010007

5. Liu Z, Liu X, Ma Z, Guan T. Phytosterols in rice bran and their health benefits. *Front Nutr*. 2023;10:1287405.

   doi: 10.3389/fnut.2023.1287405

6. Sourabh A, Rai AK, Chauhan A, *et al*. Health related issues and indigenous fermented products. In: *Indigenous fermented foods of South Asia*. Vol. 7. United States: CRC Press; 2015. p. 309.

7. Hrubša M, Siatka T, Nejmanová I, *et al*. Biological properties of vitamins of the B-complex, part 1: Vitamins B_1, B_2, B_3, and B_5. *Nutrients*. 2022;14(3):484.

   doi: 10.3390/nu14030484

8. Stavrakidis KKS. *Probiotics: Benefits on Skin Health and Therapeutical Potential*. Doctoral dissertation, University of Rijeka; 2024.

9. Zhao YS, Eweys AS, Zhang JY, *et al*. Fermentation affects the antioxidant activity of plant-based food material through

the release and production of bioactive components. *Antioxidants* (*Basel*). 2021;10(12):2004.

doi: 10.3390/antiox10122004

10. Lee HS, Kim MR Park Y, *et al*. Fermenting red ginseng enhances its safety and efficacy as a novel skin care anti-aging ingredient: *In vitro* and animal study. *J Med Food*. 2012;15(11):1015-1023.

doi: 10.1089/jmf.2012.2187

11. You S, Shi X, Yu D, *et al*. Fermentation of *Panax notoginseng* root extract polysaccharides attenuates oxidative stress and promotes type I procollagen synthesis in human dermal fibroblast cells. *BMC Complement Med Ther*. 2021;21(1):34.

doi: 10.1186/s12906-020-03197-8

12. Pham QL, Jang HJ, Kim KB. Anti-wrinkle effect of fermented black ginseng on human fibroblasts. *Int J Mol Med*. 2017;39(3):681-686.

doi: 10.3892/ijmm.2017.2858

13. Park JJ, An J, Lee JD, *et al*. Effects of anti-wrinkle and skin-whitening fermented black ginseng on human subjects and underlying mechanism of action. *J Toxicol Environ Health A*. 2020;83(11-12):470-484.

doi: 10.1080/15287394.2020.1777492

14. Herman A, Herman AP. Biological activity of fermented plant extracts for potential dermal applications. *Pharmaceutics*. 2023;15(12):2775.

doi: 10.3390/pharmaceutics15122775

15. Chen LH, Chen IC, Chen PY, Huang PH. Efficacy of rice bran fermentation in cosmetics and skin care products. *Biosci J*. 2018;34:1102-1113.

doi: 10.14393/BJ-v34n1a2018-39976

16. Sangkaew O, Yompakdee C. Fermented unpolished black rice (*Oryza sativa* L.) inhibits melanogenesis via ERK, p38, and AKT phosphorylation in B16F10 melanoma cells. *J Microbiol Biotechnol*. 2020;30(8):1184-1194.

doi: 10.4014/jmb.2003.03019

17. Korea Intellectual Property Office. *Registered Patent Gazette. Patent No. 0884424*. Korea Intellectual Property Office; 2006. p. 1-71.

18. Lee SW, Lim JM, Mohan H, *et al*. Enhanced bioactivity of *Zanthoxylum schinifolium* fermented extract: Anti-inflammatory, anti-bacterial, and anti-melanogenic activity. *J Biosci Bioeng*. 2020;129(5):638-645.

doi: 10.1016/j.jbiosc.2019.12.003

19. Pérez-Rivero C, López-Gómez JP. Unlocking the potential of fermentation in cosmetics: A review. *Fermentation*. 2023;9(5):463.

doi: 10.3390/fermentation9050463

20. Ciriminna R, Scurria A, Pagliaro M. Microbial production of hyaluronic acid: The case of an emergent technology in the bioeconomy. *Biofuels Bioprod Biorefin*. 2021;15(6):1604-1610.

doi: 10.1002/bbb.2285

21. Mohan N, Balakrishnan R, Sivaprakasam S. Optimization and effect of dairy industrial waste as media components in the production of hyaluronic acid by *Streptococcus thermophilus*. *Prep Biochem Biotechnol*. 2016;46(6):628-638.

doi: 10.1080/10826068.2015.1128446

22. Pavicic T, Gauglitz GG, Lersch P, *et al*. Efficacy of cream-based novel formulations of hyaluronic acid of different molecular weights in anti-wrinkle treatment. *J Drugs Dermatol*. 2011;10(9):990-1000.

23. Chib S, Jamwal VL, Kumar V, Gandhi SG, Saran S. Fungal production of kojic acid and its industrial applications. *Appl Microbiol Biotechnol*. 2023;107(7-8):2111-2130.

doi: 10.1007/s00253-023-12451-1

24. Show PL, Oladele KO, Siew QY, Aziz Zakry FA, Lan JCW, Ling TC. Overview of citric acid production from *Aspergillus niger*. *Front Life Sci*. 2015;8(3):271-283.

doi: 10.1080/21553769.2015.1033653

25. Kamzolova SV. A review on citric acid production by *Yarrowia lipolytica* yeast: Past and present challenges and developments. *Processes*. 2023;11(12):3435.

doi: 10.3390/pr11123435

26. Lu X, Yao Y, Yang Y, *et al*. Ethylene glycol and glycolic acid production by wild-type *Escherichia coli*. *Biotechnol Appl Biochem*. 2021;68(4):744-755.

doi: 10.1002/bab.1987

27. Paciolla C, Fortunato S, Dipierro N, *et al*. Vitamin C in plants: From functions to biofortification. *Antioxidants* (*Basel*). 2019;8(11):519.

doi: 10.3390/antiox8110519

28. Kawahori K, Kondo Y, Yuan X, *et al*. Ascorbic acid during the suckling period is required for proper DNA demethylation in the liver. *Sci Rep*. 2020;10(1):21228.

doi: 10.1038/s41598-020-77962-7

29. Timoshnikov VA, Kobzeva TV, Polyakov NE, Kontoghiorghes GJ. Redox interactions of vitamin C and iron: Inhibition of the pro-oxidant activity by deferiprone. *Int J Mol Sci*. 2020;21(11):3967.

doi: 10.3390/ijms21113967

30. Zhang Q, Lyu S. Microbial interactions in a vitamin C industrial fermentation system: Novel insights and perspectives. *Appl Environ Microbiol*. 2022;88(18):e0121222.

doi: 10.1128/aem.01212-22

31. Dattola A, Silvestri M, Bennardo L, *et al*. Role of vitamins in skin health: A systematic review. *Curr Nutr Rep*. 2020;9(3):226-235.

doi: 10.1007/s13668-020-00322-4

32. Wang J, Wu Y, Ning F, Zhang C, Zhang D. The association between leisure-time physical activity and risk of undetected prediabetes. *J Diabetes Res*. 2017;2017:4845108.

doi: 10.1155/2017/4845108

33. Larroude M, Rossignol T, Nicaud JM, Ledesma-Amaro R. Synthetic biology tools for engineering *Yarrowia lipolytica*. *Biotechnol Adv*. 2018;36(8):2150-2164.

doi: 10.1016/j.biotechadv.2018.10.004

34. Thiele JJ, Hsieh SN, Ekanayake-Mudiyanselage S. Vitamin E: Critical review of its current use in cosmetic and clinical dermatology. *Dermatol Surg*. 2005;31(7):805-813; discussion 813.

doi: 10.1111/j.1524-4725.2005.31724

35. Zussman J, Ahdout J, Kim J. Vitamins and photoaging: Do scientific data support their use? *J Am Acad Dermatol*. 2010;63(3):507-525.

doi: 10.1016/j.jaad.2009.07.037

36. Wang Y, Liu L, Jin Z, Zhang D. Microbial cell factories for green production of vitamins. *Front Bioeng Biotechnol*. 2021;9:661562.

doi: 10.3389/fbioe.2021.661562

37. Harris-Tryon TA, Grice EA. Microbiota and maintenance of skin barrier function. *Science*. 2022;376(6596):940-945.

doi: 10.1126/science.abo0693

38. Belkaid Y, Segre JA. Dialogue between skin microbiota and immunity. *Science*. 2014;346(6212):954-959.

doi: 10.1126/science.1260144

39. Pessôa R, Clissa PB, Sanabani SS. The interaction between the host genome, epigenome, and the gut-skin axis microbiome in atopic dermatitis. *Int J Mol Sci*. 2023;24(18):14322.

doi: 10.3390/ijms241814322

40. Blume-Peytavi U, Bagot M, Tennstedt D, *et al*. Dermatology today and tomorrow: From symptom control to targeted therapy. *J Eur Acad Dermatol Venereol*. 2019;33:3-36.

doi: 10.1111/jdv.15335

41. Levin BJ. *Discovery and Characterization of Glycyl Radical Enzymes Found in the Human Gut Microbiota and Other Environments*. Doctoral dissertation, Harvard University; 2019.

42. Kamble NS, Bera S, Bhedase SA, Gaur V, Chowdhury D. Review on applied applications of microbiome on human lives. *Bacteria*. 2024;3(3):141-159.

doi: 10.3390/bacteria3030010

43. Tóth KF, Ádám D, Bíró T, Oláh A. Cannabinoid signaling in the skin: Therapeutic potential of the "C(ut)annabinoid" system. *Molecules*. 2019;24(5):918.

doi: 10.3390/molecules24050918

44. Mourelle ML, Gómez CP, Legido JL, Pereira L. Role of nutribiotics in skin care. *Appl Sci*. 2024;14(8):3505.

doi: 10.3390/app14083505

45. Bikle DD. Vitamin D metabolism, mechanism of action, and clinical applications. *Chem Biol*. 2014;21(3):319-329.

doi: 10.1016/j.chembiol.2013.12.016

46. Joshi M, Hiremath P, John J, Ranadive N, Nandakumar K, Mudgal J. Modulatory role of vitamins A, B3, C, D, and E on skin health, immunity, microbiome, and diseases. *Pharmacol Rep*. 2023;75(5):1096-1114.

doi: 10.1007/s43440-023-00520-1

47. Peng H, Chu C, Jin L, *et al*. Study on *Oleum cinnamomi* inhibiting *Cutibacterium acnes* and its covalent inhibition mechanism. *Molecules*. 2024;29(13):3165.

doi: 10.3390/molecules29133165

48. Ikeda M, Nakagawa S. The *Corynebacterium glutamicum* genome: Features and impacts on biotechnological processes. *Appl Microbiol Biotechnol*. 2003;62(2-3):99-109.

doi: 10.1007/s00253-003-1328-1

49. Aoki R, Wada M, Takesue N, Tanaka K, Yokota A. Enhanced glutamic acid production by a H+-ATPase-defective mutant of *Corynebacterium glutamicum*. *Biosci Biotechnol Biochem*. 2005;69(8):1466-1472.

doi: 10.1271/bbb.69.1466

50. Zahoor A, Lindner SN, Wendisch VF. Metabolic engineering of *Corynebacterium glutamicum* aimed at alternative carbon sources and new products. *Comput Struct Biotechnol J*. 2012;3(4):e201210004.

doi: 10.5936/csbj.201210004

51. Jara CP, de Andrade Berti B, Mendes NF, *et al*. Glutamic acid promotes hair growth in mice. *Sci Rep*. 2021;11(1):15453.

doi: 10.1038/s41598-021-94816-y

52. Arribas-López E, Zand N, Ojo O, Snowden MJ, Kochhar T. The effect of amino acids on wound healing: A systematic review and meta-analysis on arginine and glutamine. *Nutrients*. 2021;13(8):2498.

doi: 10.3390/nu13082498

53. Pedrazini MC, Groppo FC. L-lysine therapy to control the clinical evolution of Pityriasis rosea: Clinical case report and literature review. *Dermatol Ther*. 2021;34(1):e14679.

doi: 10.1111/dth.14679

54. Kim H, Ro J, Barua S, *et al*. Combined skin moisturization of liposomal serine incorporated in hydrogels prepared with Carbopol ETD 2020, Rhesperse RM 100, and hyaluronic

acid. *Korean J Physiol Pharmacol*. 2015;19(6):543-547.

doi: 10.4196/kjpp.2015.19.6.543

55. Marini A, Grether-Beck S, Jaenicke T, *et al*. Prolidase in skin aging and its relation to photoaging. *Exp Dermatol*. 2012;21(5):347-350.

56. Proksch E, Segger D, Degwert J, *et al*. Oral supplementation of specific collagen peptides has beneficial effects on human skin physiology: A double-blind, placebo-controlled study. *Skin Pharmacol Physiol*. 2014;27(1):47-55.

doi: 10.1159/000351376

57. Karna E, Miltyk W, Pałka JA, Wołczyński S, Kedzierska M. Proline-dependent and basophilic protein kinases in human skin fibroblasts. *Acta Biochim Pol*. 2006;53(3):591-597.

58. Licari A, Marseglia A, Agostinis F, Milani M, Marseglia GL. Barrier repair therapy in atopic eczema: Effects of isoleucine, rhamnosoft, ceramides, and niacinamide facial and body creams on clinical, itch, and *Staphylococcus aureus* skin colonization: A prospective assessor-blinded study. *Clin Pediatr Dermatol*. 2016;2:1.

doi: 10.21767/2472-0143.100010

59. Marseglia A, Licari A, Agostinis F, *et al*. Local rhamnosoft, ceramides and L-isoleucine in atopic eczema: A randomized, placebo controlled trial. *Pediatr Allergy Immunol*. 2014;25(3):271-275.

doi: 10.1111/pai.12227

60. Brenner M, Hearing VJ. The protective role of melanin against UV damage in human skin. *Photochem Photobiol*. 2008;84(3):539-549.

doi: 10.1111/j.1751-1097.2007.00226.x

61. Solano F. Photoprotection versus photodamage: Updating an old but still unsolved controversy about melanin. *Polym Int*. 2016;65:1276-1287.

doi: 10.1002/pi.5117

62. Solano F. Melanins: Skin pigments and much more-Types, structural models, biological functions, and formation routes. *New J Sci*. 2014;2014:498276.

doi: 10.1155/2014/498276

63. Fajuyigbe D, Lwin SM, Diffey BL, *et al*. Melanin distribution in human epidermis affords localized protection against DNA photodamage and concurs with skin cancer incidence difference in extreme phototypes. *FASEB J*. 2018; 32(7):3700-3706.

doi: 10.1096/fj.201701472R

64. Schallreuter KU, Wazira U, Kothari S, Gibbons NCJ, Moore J, Wood JM. Human phenylalanine hydroxylase is activated by H_2O_2: A novel mechanism for increasing the l-tyrosine supply for melanogenesis in melanocytes. *Biochem Biophys Res Commun*. 2004;322(1):88-92.

doi: 10.1016/j.bbrc.2004.07.082

65. Slominski A, Moellmann G, Kuklinska E, Bomirski A, Pawelek J. Positive regulation of melanin pigmentation by two key substrates of the melanogenic pathway, L-tyrosine and L-dopa. *J Cell Sci*. 1988;89:287-296.

doi: 10.1242/jcs.89.3.287

66. Serre C, Busuttil V, Botto JM. Intrinsic and extrinsic regulation of human skin melanogenesis and pigmentation. *Int J Cosmet Sci*. 2018;40:328-347.

doi: 10.1111/ics.12466

67. Sardana K, Garg VK. An observational study of methionine-bound zinc with antioxidants for mild to moderate acne vulgaris. *Dermatol Ther*. 2010;23(4):411-418.

doi: 10.1111/j.1529-8019.2010.01342.x

68. Danzberger J, Donovan M, Rankl C, *et al*. Glycan distribution and density in native skin's stratum corneum. *Skin Res Technol*. 2018;24(3):450-458.

doi: 10.1111/srt.12453

69. Reilly DM, Lozano J. Skin collagen through the lifestages: Importance for skin health and beauty. *Plast Aesthetic Res*. 2021;8:2.

doi: 10.20517/2347-9264.2020.153

70. Miniaci MC, Irace C, Capuozzo A, *et al.* Cysteine prevents the reduction in keratin synthesis induced by iron deficiency in human keratinocytes. *J Cell Biochem*. 2016;117(2):402-412.

doi: 10.1002/jcb.25286

71. Altunbulakli C. *Microbiome and Transcriptome Interactions in Epithelial Tissues in the Context of Allergic Diseases*. [dissertation], University of Zurich; 2018.

72. Dua A, Nigam A, Saxena A, Dhingra GG, Kumar R. Microbial bioproduction of antiaging molecules. In: *Microbial Bioreactors for Industrial Molecules*. United States: John Wiley & Sons; 2023. p. 465-485.

73. Joshi AA, Vocanson M, Nicolas JF, Wolf P, Patra V. Microbial derived antimicrobial peptides as potential therapeutics in atopic dermatitis. *Front Immunol*. 2023;14:1125635.

doi: 10.3389/fimmu.2023.1125635

74. Chen YE, Fischbach MA, Belkaid Y. Skin microbiota-host interactions. *Nature*. 2018;553(7689):427-436.

doi: 10.1038/nature25177

75. Stone PM. The Skin, selected dermatologic conditions, and medical nutrition therapy. In: *Integrative and Functional Medical Nutrition Therapy: Principles and Practices*. Berlin, Germany: Springer Nature; 2020. p. 969-1002.

76. Dej-Adisai S, Parndaeng K, Wattanapiromsakul C. Determination of phytochemical compounds, and tyrosinase inhibitory and antimicrobial activities of bioactive

compounds from *Streblus ilicifolius* (S Vidal) Corner. *Trop J Pharm Res*. 2016;15(3):497-506.

doi: 10.4314/tjpr.v15i3.10

77. Shafiuddin M, Prather GW, Huang WC, *et al*. *Cutibacterium* adaptation to life on humans provides a novel biomarker of *C. acnes* infections. bioRxiv [Preprint]. 2024.

doi: 10.1101/2024.09.18.613542

78. Otsuka A, Moriguchi C, Shigematsu Y, *et al*. Fermented cosmetics and metabolites of skin microbiota-A new approach to skin health. *Fermentation*. 2022;8(12):703.

doi: 10.3390/fermentation8120703

79. Manisha N. The use of topical *Nitrosomonas eutropha* for cosmetic improvement of facial wrinkles. *J Cosmet Dermatol*. 2020;19(2):689-693.

doi: 10.1111/jocd.13060

80. Lee YJ, Choi HJ, Kang TW, Kim HO, Chung MJ, Park YM. CBT-SL5, a bacteriocin from *Enterococcus faecalis*, suppresses the expression of interleukin-8 induced by *Propionibacterium acnes* in cultured human keratinocytes. *J Microbiol Biotechnol*. 2008;18(12):1308-1316.

81. Guéniche A, Hennino A, Goujon C, *et al*. Improvement of atopic dermatitis skin symptoms by *Vitreoscilla filiformis* bacterial extract. *Eur J Dermatol*. 2006;16(4):380-384.

82. Gueniche A, Valois A, Kerob D, Rasmont V, Nielsen M. A combination of *Vitreoscilla filiformis* extract and Vichy volcanic mineralizing water strengthens the skin defenses and skin barrier. *J Eur Acad Dermatol Venereol*. 2022;36(Suppl S2):16-25.

doi: 10.1111/jdv.17786

83. Seite S, Zelenkova H, Martin R. Clinical efficacy of emollients in atopic dermatitis patients-relationship with the skin microbiota modification. *Clin Cosmet Investig Dermatol*. 2017;10:25-33.

doi: 10.2147/CCID.S121910

84. Di Marzio L, Cinque B, Cupelli F, De Simone C, Cifone MG, Giuliani M. Increase of skin-ceramide levels in aged subjects following a short-term topical application of bacterial sphingomyelinase from *Streptococcus thermophilus*. *Int J Immunopathol Pharmacol*. 2008;21(1):137-143.

doi: 10.1177/039463200802100115

85. Di Marzio L, Centi C, Cinque B, *et al*. Effect of the lactic acid bacterium *Streptococcus thermophilus* on stratum corneum ceramide levels and signs and symptoms of atopic dermatitis patients. *Exp Dermatol*. 2003;12(6):615-620.

doi: 10.1034/j.1600-0625.2003.00051.x

86. Kim WK, Jang YJ, Han DH, *et al*. *Lactobacillus paracasei* KBL382 administration attenuates atopic dermatitis by modulating immune response and gut microbiota. *Gut Microbes*. 2020;12:1-14.

doi: 10.1080/19490976.2020.1819156

87. Kwon JE, Lim J, Bang I, Kim I, Kim D, Kang SC. Fermentation product with new equol-producing *Lactobacillus paracasei* as a probiotic-like product candidate for prevention of skin and intestinal disorder. *J Sci Food Agric*. 2019;99(9):4200-4210.

doi: 10.1002/jsfa.9648

88. Miyaguchi E. *Lactobacillus rhamnosus* alleviates intestinal barrier dysfunction in part by increasing expression of zonula occludens-1 and myosin light-chain kinase *in vivo*. *J Dairy Sci*. 2009;92(5):2400-2408.

doi: 10.3168/jds.2008-1698

89. Jung YO, Jeong H, Cho Y, *et al*. Lysates of a probiotic, *Lactobacillus rhamnosus*, can improve skin barrier function in a reconstructed human epidermis model. *Int J Mol Sci*. 2019;20(17):4289.

doi: 10.3390/ijms20174289

90. Kim NY, Lee HY. Enhancement of skin whitening and anti-wrinkle activities of the co-culture of *Lactobacillus rhamnosus* and *Lactobacillus paracasei*. *J Soc Cosmet Sci Korea*. 2015;41(4):253-261.

doi: 10.15230/SCSK.2015.41.3.253

91. Huang X, Liu S, Xu W, Wang Q, Zhou Z, Zhang Q. Skin microbiota composition and functional diversity of ammonia-oxidizing bacteria: A potential role in skin health. *Sci Rep.* 2020;10(1):15591.

92. Kim JE, Lee YM, Lim Y. Evaluation of the anti-acne effects of *Enterococcus faecalis*-derived antimicrobial peptides. *J Microbiol Biotechnol*. 2019;29(11):1694-1702.

93. Gueniche A, Bastien P, Ovigne JM, *et al*. *Bifidobacterium longum* lysate, a new ingredient for reactive skin. *Exp Dermatol*. 2010;19(8):e1-e8.

doi: 10.1111/j.1600-0625.2009.00932.x

94. Kober MM, Bowe WP, Gallo RL. Skin microbiome and acne. *J Drugs Dermatol*. 2015;14(10):1093-1096.

95. Gueniche A, Philippe D, Bastien P, Reuteler G, Blum S, Castiel-Higounenc I, Breton L. Randomized double-blind placebo-controlled study of the effect of *Vitreoscilla filiformis* extract on skin microbiota in atopic dermatitis. *Eur J Dermatol*. 2006;16(1):52-57.

96. Jeong D, Kim DH, Kang IB, Kim H, Song KY, Kim H. Modulation of the skin microbiome by fermenting strains of *Lactobacillus plantarum* improves atopic dermatitis. *J Dermatol Sci*. 2013;71(3):121-125.

97. Nakatsuji T, Chen TH, Butcher AM, *et al*. *Staphylococcus epidermidis* produces antimicrobial peptides that kill pathogens and protect the skin. *Nat Commun*. 2017;8(1):1-9.

98. Cogen AL, Yamasaki K, Sanchez KM, *et al*. Selective

antimicrobial action is provided by phenol-soluble modulins derived from *Staphylococcus epidermidis*, a normal resident of the skin. *J Invest Dermatol*. 2010;130(1):192-200.

doi: 10.1038/jid.2009.243

99. Yu Q, Jia Z, Liang X. Probiotic *Lactobacillus reuteri* reduces endodontic infection and promotes skin health. *J Endod*. 2015;41(12):2037-2045.

100. Thiyagarajan P, Sivasankari S, Latha S. Characterization and biological potential of surfactin produced by *Bacillus subtilis* strain MZ-7. *Braz Arch Biol Technol*. 2016;59:e16150515.

101. Mu Q, Tavella VJ, Luo XM. Role of *Lactobacillus reuteri* in human health and diseases. *Front Microbiol*. 2018;9:757.

doi: 10.3389/fmicb.2018.00757

102. Alara JA, Alara OR, Abdurahman NH. Role of biosurfactants in biocidal activity and wound healing. In: *Advancements in Biosurfactants Research*. Cham: Springer International Publishing; 2023. p. 399-437.