JOURNAL OF NATURAL REMEDIES
DOI: 10.18311/jnr/2025/47791

REVIEW ARTICLE

Probiotics: Novel Natural Rejuvenators for Skin's Health

Nandini Sinhmar, Bindu Battan*, Surender Verma, Sulekha Chahal and Jitender Sharma

Department of Biotechnology and Pharmaceutical Science, Kurukshetra University, Kurukshetra - 136119, Haryana, India; bbattan@kuk.ac.in

Abstract

Skin is the greatest external human organ that hosts a varied microbial ecosystem collectively known as the skin's microbiome. There are ample shreds of evidence that show any imbalances resulting in skin disorders such as acne, inflammation, psoriasis, atopic dermatitis, eczema, and even skin cancer. Therefore, researchers now emphasise from their findings the benefits of probiotics and their extracts as biotherapeutic tools for acute to chronic dermatological disorders, deadly cancer, by effectively rebalancing the microbial niche by eradicating pathogens, thus maintaining health naturally. Probiotics are non-pathogenic microorganisms, mainly of animal or natural origin, that are beneficial to the host when administered in adequate amounts. The application of probiotic-based dermal products is an emerging approach in dermatology. They are good microbes belonging to the *Lactobacillus* and *Bifidobacterium* genera, thought to mediate skin disorders by decolonising skin pathogens (*S. aureus, A. vulgaris, P. aeruginosa*, etc). The use of conventional treatments, including antibiotics, drug-based, immunosuppressive therapy, etc., may cause dysbiosis of the natural microbiome; therefore, the introduction of microorganism-based products against microorganisms is an advanced and attractive approach to re-establish the microbial equilibrium and maintain skin health. This approach has achieved popularity among researchers worldwide due to the absence of adverse effects and is thus considered safe. This review also provides pharmaceutical applications of probiotic strains and covers recent formulations isolated and cultivated from natural sources used in the development of dermal health products.

Major Findings: The main findings are that probiotics can help maintain healthy skin. By encouraging the growth of good bacteria and suppressing the growth of bad ones, probiotics, whether taken orally or topically, can affect the balance of commensals on the skin. This modulation can improve skin moisture, lessen the severity of several skin disorders, including eczema, acne, and allergic reactions.

Keywords: Dermal Disorders, Probiotics, Probiotic Patents, Skin Microbiome

1. Introduction

Dermal products are skin care products useful for balancing, preventing, or treating various dermatological conditions, including acne, rosacea, allergies, yeast and bacterial infections, atopic dermatitis, psoriasis, and external ageing, etc. Since they are employed in prevention and treatment of disease that impacts both skin's composition and function, they comprise both medication and cosmetics including personal care products like creams, lotions, soaps, liquid spray agents, lotions, etc. that are applied on the skin's surface by simply pouring, rubbing, or sprinkling/spraying for cleansing, beautifying, promoting attractiveness, or altering appearance. These products influence resident microbes on the applied skin area either positively or negatively[1].

The use of microorganism-based products against microorganisms as a new approach to restore and maintain human health has achieved popularity among researchers and consumers worldwide. Probiotics are live beneficial microorganisms naturally found in the human gut and found in both dairy and non-dairy products, and are taken as dietary supplements[2].

*Author for correspondence

Article Received on: 15.12.2024 Revised on: 01.08.2025 Accepted on: 11.08.2025

In comparison to conventional treatment using antibiotics or drug-based options for skin disorders, both oral and topical probiotic-based skincare products do not have adverse effects and are thus considered GRAS safe. Knowledge about the active role of the skin's microbiome has led to the direct approach of treatment that involves using probiotics both in oral and topical forms. Clinical studies have shown that both orally administered and topically applied probiotic-based formulations have been used for treating several skin issues and have effectively shown positive results on related disorders, including skin inflammations, acne, rosacea, atopic dermatitis, psoriasis, ageing, UV-induced photo-ageing, and even skin cancer[3,4].

Several diseases are due to imbalances in the gut-skin axis; therefore, this offers diverse avenues in the development of both oral and topical probiotic-based formulations useful for treating skin disorders. Orally administered probiotic-based formulations act through the gut axis, and topically applied formulations enhance the skin's natural barriers effectively at the target site and thus reduce host skin-related imbalances[5]. Development and application of topical probiotics represent the direct approach to restore the altered skin microbiome and modulate immune response at the applied site.

Compared with conventional treatment options, including drugs and chemically synthesised medicines for skin disorders, the use of both oral and topical probiotics or synbiotic-based formulations in skincare products is considered safe and devoid of any adverse effects. In general, the positive results available from clinical trials clearly show improvement in skin conditions after probiotic interventions. Although until now, limited clinical trials have demonstrated favourable results, a few cutaneous-associated diseases cured by probiotic formulations, along with evidence, are explained in this review.

2. Probiotics and Their Mode of Action

The term 'probiotics' is derived from the Greek word "for life" and is considered "living non-pathogenic organisms and their derived bioactive components showing favourable effects on the recipients." Over the decades, several different microorganisms have been used extensively due to their capability to cure and prevent different diseases, leading to the invention of probiotics, which are live microbes that, when administered in appropriate amounts, are beneficial to the receiving host. In 1907, "Nobel laureate Elie Metchnikoff stated that the consumption of Bulgarian yoghurt containing lactic acid bacteria was good for health[6]." In 1962, Lily and Stillwell first described probiotics as "The anaerobic bacteria that can produce lactic acid and stimulate the growth of other organisms," and then redefined them as "A product produced by one microorganism stimulating the growth of another microorganism[7,8]." In 1974, Parker concluded that the probiotics include not only microorganisms but also other bioactive substances contributing to intestinal microbial balance or homeostasis[9]." The first probiotic species, *Acidophilus,* was isolated by Hull *et al.,* in 1984, and *Bifidobacterium bifidum* by Holcombh *et al.,* in 1991. The term probiotics is an antonym of antibiotics, as probiotics are for life and antibiotics are against life[10].

In 2002, FAO and WHO experts defined probiotics as "live microorganisms that when administered in adequate amounts confer a health benefit on the host." In 2014, experts from the International Scientific Association for Probiotics and Prebiotics (ISAPP) termed it as "probiotics are referring to many types of microorganisms which demonstrate health benefits for the host, while remaining alive[11]."

Probiotics are isolated from both conventional and non-conventional sources including dairy products, lactating milk, fermented raw milk, sheep, buffalo, and cow milk cheese, yogurt, non-dairy products, fruits and vegetables, dietary supplements, pineapple waste, industrial sausages, ice- cream, corn slurry, rice curd (fermented), yeast extracts, meat extracts, chicken feed, glucose, sucrose, from natural antimicrobial agents, faeces of breast-fed infants, beverages, poultry sources, chicken intestine and faecal samples, honey and gut of honeybee, human colonial epithelial cells, human and animal vagina, fermented foods, etc[12]. They mainly belong to the *Lactobacillus* genus, but based on their respective physical characteristics, metabolic needs, and obtained end products, they are further grouped into species and strains[13].

The most used bacteria belong to the genera *Lactobacillus, Bifidobacterium, Enterococcus, Propionibacterium,* and some yeasts belonging to the *Saccharomyces* species. Their specific species and strains

have been studied extensively, with evidence that they possess most of the probiotics' properties[14-16]. The notable species include *Lactobacillus* (*Lactobacillus acidophilus, L. rhamnosus, L. fermentum, L. cellobiosus, L. brevis, L. reuteri, L. casei, L. bulgaricus, L. delbrueckii), Bifidobacterium* (*B. thermophilus, B. infantis, B. longum, B. bifidum, B. animalis, B. breve*), *Streptococcus* (*S. lactis, S. thermophilus, S. cremonis, S. alivarius), Saccharomyces* (*S. boulardii, S. cerevisiae, S. carlbergensis),* etc[17,18].

Both *in vitro* and *in vivo*, the role and effects of species belonging to *Lactobacillus* and *Bifidobacterium* have been extensively studied for showing promising results in curing, preventing, and diminishing the after-side effects of antibiotic therapy in different research fields and disorders including obesity, diabetes, colon cancer, cardiovascular diseases, urinary tract infections, atopic eczema, acne, obesity, food allergies, skin allergies, and even skin cancer[19].

Recent interest by the masses in naturally maintaining their health issues has boosted the production of probiotic-based natural products and has tremendously increased their commercialisation. There is a constant debate regarding the effectiveness of probiotics in today's lifestyle. Currently, probiotics-based projects are a multibillion-dollar industry with an estimated 7% growth globally. Probiotics can be in the form of liquid, gel, paste, granules, powder, and are also available in the form of capsules and sachets[20,21].

Probiotics positively influence the host, including mucosal barriers, epithelial cells, dendritic cells, macrophages, B and T cells, etc. In a broad concept, the mechanisms of action of probiotics include natural inhibition of adhesion of pathogens or competitively excluding pathogenic microbes, producing antimicrobial substances, modulating immune response at the primary level, and showing anti-inflammatory actions by modulating Th1/Th2 inflammatory response, enhancing epithelial barrier stability by restoring disturbed local conditions[22,23].

A diverse group of probiotic strains can produce potent antimicrobial agents against a broad spectrum of microorganisms, including bacteriocins, bacteriocin-like substances, and organic acids that successfully compete and thus prevent pathogen adhesion[24,25]. *L. acidophilus* produces acidolin, acidophilin, lactocidin, and lactocin B. *L. plantarum* produces lactolin, *L. brevis* produces lactobacillin, lactobrevin, *L. reuteri* produces reuterin, *L. johnsonii* produces lactocin F, and *S. thermophilus* produces streptophilin[26].

In the case of skincare, neutralisation or treatment of any issue is done by appropriate probiotics by increasing mucin secretion that, in turn, traps pathogenic microbes, inhibits colonisation by decreasing pH, secretes bacteriocin, and increases ceramide production without affecting the respective host[27]. Evidence also suggests that probiotics perform anti-pathogenic and anti-inflammatory immunogenic activities in favour of skin commensals, and a species of the *Lactobacillus* genus exhibits nonspecific immune system boosting and regulation[28,29].

Most probiotics may be temporary constituents of the natural microflora, but their amount is not enough for therapeutic purposes. Topical probiotics protect by competitive exclusion at cell surface receptor binding sites by blocking receptors from foreign attackers by competitive nutrient consumption and by regulating the host's innate immune response. A diverse range of species, subspecies, and strains belonging to probiotics show various mechanisms of action by modulating the host immune system, thus modifying simple to chronic inflammatory conditions, ranging from acne, rosacea, atopic dermatitis, photoaging, and even skin cancer. Probiotics are body-friendly bacteria that naturally modulate the immune system by restoring the unbalanced microbiome or the body's natural flora. The most important influencing factor responsible for human health and disease pathogenesis is the commensal bacterial population[30,31].

For the ramification on affected skin, probiotics don't need to reside for a long time on the applied surface as the application of probiotics on affected areas quickly triggers skin cells to produce strain-specific bioactive agents against pathogenic microbes, and meanwhile readjusts the skin's commensal balance[32]. Probiotic-based skin care products help to build cells and heal connective tissues on affected areas by forming a protective shield over the skin's surface, thus hindering the pathways of pathogenic bacteria that cause inflammation, ageing, and other dermal disorders or diseases[33,34].

Resident microbiota plays a significant role in maintaining an active immune system. Disturbance in the microbial biome invites opportunistic pathogenic bacterial species to colonise and thus become responsible

for the disease. Skin disorders are the outcome of downregulation of physiological, immunological activities, and neurological mechanisms; therefore, they can be prevented or remodulated either by appropriate nutritional support or by using suitable probiotic strains. An appropriate probiotic strain should be chosen based on its ability to adhere to skin tissue, exhibit competitive exclusion and antimicrobial activity, be tolerant to oxygen, high or low pH, and sensitive to antibiotics. Evidence reported that Lactic acid bacteria, having potential probiotic characteristics, including *Lactococcus, Lactobacillus, Pediococcus, and Propionibacterium,* produce bacteriocin or bioprotective agents against diverse microbes. Oh *et al.* 2006 reported the efficiency of bacteriocins from *Lactococcus* HY449 in controlling skin inflammation and acne by bacteriolytic action on the cell wall and cell membrane of skin inflammatory bacteria, including *S. epidermis, S. aureus,* and *Propionibacterium acnes*[35].

3. Skin Microbiome

Skin is the largest organ of the human body and a remarkably inhospitable environment for a rich and diverse community of microorganisms. On average, every human harbours 1000 species of bacteria belonging to more than 25 phyla adapted to the skin's surface[36]. The healthy skin of humans harbours myriads of complex and diverse communities of microorganisms belonging to bacteria, fungi, viruses, and archaea, broadly known as the skin microbiome or skin microbiota. 60% of phyla residing on the skin include genus *Corynebacterium, Propionibacterium, and Staphylococcus,* and the rest belong to *Actinobacteria, Firmicutes, Proteobacteria,* and *Bacteroides*[37,38].

Skin has a self-renewal property that sheds and colonises microbes throughout life. It acts as a physical barrier with additional roles including body temperature control, sensation, and storage of lipids and water[39]. The skin microbiome is affected by both microenvironment and macroenvironment, which is crucial for skin health. Skin microbiota must maintain a healthy, continual, and dynamic interaction with the skin immune system both at the cellular and molecular levels throughout life. Many studies have already revealed that the skin microbiome plays an important role in all physiological and immunological tasks in all challenging conditions throughout life[40]. The microbiota of skin is obtained after birth and is highly dynamic in composition at early stages of life, and later stabilises in response to host and environmental factors. The normal skin displays visible variations in relative microbial structure across different body sites, framed by their biological, physical, and chemical features[41,42]. Commensals have developed their blueprint to adapt and flourish accordingly on the skin. The total surface area of skin is differentiated into different micro niches, including dry, sebaceous, and moist regions. Sebaceous follicles are lipid-rich areas that are mainly colonised by *Propionibacterium.* Axillary areas colonise bacteria belonging to the genera *Staphylococcus, Corynebacterium, Micrococcus,* and *Propionibacterium.* Drier regions colonise *Staphylococcus, Micrococcus, Corynebacterium, Propionibacterium, and Streptococcus*. Fungal species such as *Malassezia,* including *M. restricta,* and *M. sympodialis,* colonise sebum-rich areas. Fungal species such as *Aspergillus, Epicoccum, and Rhodotorula* are present around the skin areas of the foot. *Staphylococcus epidermidis* is one of the dominant skin inhabitants that produces an antimicrobial product as a bioactive agent or by modulating the immune system, which restricts the development of biofilms by pathogenic species, and it can limit the pathogen invasion[43,44].

The skin microbiome can be organised into three broad groups: transitory or short-term, which are found randomly on the skin surface; temporary residents, which can maintain a survival rate for a shorter period; and permanent residents, which reside permanently on the skin surface[45]. Human skin is unique, and its associated microbiome is also unique and different due to genetics, diet, lifestyle, and the environment in which it lives[46,47].

The normal and healthy resident microbiome provides protection and is considered beneficial to the host, but when disturbed, it may become equally dangerous [48,49]. There are many factors responsible for disturbed skin resident microbiota, including host factors and environmental factors. Host factors include age, sex, and anatomic sites, and environmental factors include climate, temperature, and UV rays [50]. There are various factors responsible for skin ageing, including imbalanced skin microflora, altered pH, changes in the stratum corneum, lipid composition, increased

oxidative stress, reduced collagen level, and altered immune response[51].

4. Skin Disorders and Their Related Probiotic-Based Therapy

Since childhood, the skin's microbiome has been established and is considered a skin commensal, consisting of a varied community of microbes. All together occupies a definite niche and adapts accordingly to all prevailing conditions throughout life. The complexity and composition of these communities depend on certain physiological factors such as hydration, the number of sebaceous glands on the surface, temperature, external conditions of the environment, and genetics. All skin commensals generally provide passive protection against both abiotic and biotic factors by occupying similar niches to pathogen-prone sites, thus hampering their colonisation over affected areas without harming skin integrity. Commensals also actively compete with pathogens by secreting antimicrobial bioactive agents, altering local physiological conditions on the surface, and mediating and modulating local immune responses that directly protect against pathogens, maintaining homeostasis.

Skin conditions cause great discomfort and severely affect the quality of life because of their visibility. Any shift or alteration of the resident microbial population results in illness and even disorders. *Staphylococcus aureus* is one of the commensal microbes residing on the skin surface; only when it colonises less than 10^6 cfu/cm^2, but an equal or greater number is considered a skin infection. Approximately 80% of the population is at risk of opportunistic *Staphylococcus aureus,* which is responsible for skin barrier disturbance, skin burns, atopic dermatitis or eczema, acne, impetigo, furuncles, photo ageing, subcutaneous abscesses, and even skin cancer.

Out of all the associated skin issues prevailing nowadays, from acute to chronic, acne vulgaris, Atopic Dermatitis (AD), eczema, and skin cancer are conditions that require a protracted duration of treatment and perpetuation. Recent approaches related to chemotherapy-based treatment represent a definitive cure for many skin issues and thus adversely affect the quality of life. Therefore, restabilising, or rebalancing, the skin's natural microbial population may result in a positive influence on these conditions. Compared with aggressive therapies or systemic medications, biotherapeutic-based therapy shows a relevant decrease in adverse effects both during the treatment and afterwards. Knowledge about different microbial diversity over different body surface areas, time-to-time variations, and the factors affecting such diversity, including lifestyle, personal hygiene, and geographical spots, is very necessary. The skin microbiome studies are beneficial for dermatology as well as for the development of pharmaceutically based topical formulations, as they do not have adverse effects associated with drug- or antibiotic-based therapies. This positive impact on microbial composition and improvement in their interactions with skin cells boost the viability of this biotherapeutic-based technology[52].

Skin problems have a linear relationship with the gut axis, so in addition to orally designed formulations, probiotic-based dermal products also showed a significant reduction in dermal-related issues. Many studies have successfully investigated the positive effect of different probiotic formulations when administered orally and applied topically, resulting in the improvement in symptoms of dermal-associated issues. This article sheds light on the different skin disorders and their associated pathogens, the importance of probiotics, and their therapeutic potential by competing with persistent pathogens responsible for acute infections and chronic diseases.

5. Atopic Dermatitis (AD) or Eczema

Atopic Dermatitis (AD) or eczema is a frequent chronic skin condition characterised by inflammation, dryness, scaling of the skin, itching, and redness, followed by erythematous scaly lesions affecting 15% to 20% of children and 1% to 3% of adults worldwide, mainly prevailing in Western countries[53]. AD is a chronic inflammatory issue of the skin, and its therapy should be individually implemented following age, severity, extent, and distribution of the lesion. The occurrence of atopic dermatitis is particularly higher in children in comparison to adolescents and adults. The tri-directional relationship of atopic dermatitis-skin barrier-skin microbiome determines the cause and severity of the disease. *Staphylococcus aureus* is known to play a significant and dominant role, as toxins released

from *S. aureus* act as superantigens that aggravate atopic dermatitis, and its load reflects the disease severity[54]. *S. aureus* produces toxins that penetrate the stratum corneum and deform the epidermal epithelium, thereby compromising the physical barrier of the skin. Such compromises increase the penetration of pathogenic microbes into the epidermis and dermis. Excess *S. aureus* also unbalances the innate antimicrobial immune responses by activating Th-2 cells[55].

Evidence from research on the positive effects of probiotics shows that AD is still in its debut stages. The present-day treatment of AD includes skin barrier repair and protection with moisturisers, antihistamines, anti-inflammatory medications, and topical antimicrobial therapies[56].

Eczema is a chronic skin inflammatory issue; therefore, its therapy should be implemented individually by age, severity, extent, and distribution of lesions. To control the severity of the AE, in addition to the drug, other treatments, including basic treatment such as cutaneous hydration, adjuvant treatments including primrose oil, omega-3, and vitamin D supplements, and standard medical treatments including topical glucocorticoids, calcineurin inhibitors like antihistamines, and anti-infectious agents, are given. Systemic therapy includes the use of cyclosporine, glucocorticoids, azathioprine, mycophenolate, mofetil, and methotrexate. In addition to all the treatments, phototherapy and Allergen immunotherapy are also applicable nowadays. At the genetic level, atopic dermatitis is characterised by an impaired skin barrier due to a mutation in the FLG gene, which controls cutaneous hydration and thus decreases the natural moisturisers of the skin [57,58].

In basic treatment, cutaneous hydration is maintained with the help of emollients that reduce flare-ups of AD. Taking warm water baths hydrates the stratum corneum, eliminates crusts, scales, allergens, and irritants, and then suitable moisturisers, creams, lotions, and ointments should be applied. The appropriate moisturiser is decided depending on the patients' preferences, season, and symptoms[59,60]. The National Institute for Health and Clinical Excellence (NICE) issues standard guidelines that recommend the use of 250 g of emollients weekly[61].

Given the failure of basic conventional treatments, a systemic treatment is required, consisting of cyclosporin and glucocorticoids. Alternative therapies

Table 1. List of systemic medical treatments against Atopic dermatitis

S. No.	Name	Mode of action	Adverse effects
1	Topical calcineurin inhibitors are Tacrolimus at 0.03% and pimecrolimus at1%	By binding to the FK-binding protein, it thus inhibits the production of cytokines from activated T cells and inflammatory cells.	Transient burning or itching[64,65].
2	Antihistamines like hydroxyzine, chlorpheniramine	Relieves histamine-induced itching sensations by blocking H1 receptors.	It can impair adults' driving ability or children's learning ability[66].
3	Anti-infectious agents such as cephalosporins and penicillinase-resistant penicillin (Dicloxacillin, oxacillin, or cloxacillin)	Effective against superantigen *Staphylococcus aureus* and other bacteria, fungi, etc., responsible for AE symptoms.	Antibiotic resistance occurs occasionally[67,68].
4	Cyclosporine as an immunomodulator The recommended dose is for both children and adults.	The main target is T cells because they bind to intracellular cyclophilin and inhibit the transcription of cytokines.	Hypertension and functional impairment of the Kidney or liver[69].
5	Methotrexate, azathioprine, and mycophenolate mofetil as antimetabolites are recommended at a dose of 2 g daily for adults.	It acts as a folate antagonist that inhibits cytokine synthesis and cell chemotaxis. Azathioprine is a purine analogue with anti-inflammatory and antiproliferative effects. Mycophenolate mofetil inhibits purine biosynthesis.	Patients undergoing treatment with mycophenolate should be monitored for herpes retinitis and dose-related bone marrow suppression[70,71].
6	Interferons-γ	IgE level gets lower, thus downregulating Th2 cells.	Headache Fever and flu-like symptoms[72,73].

include phototherapy, interferon-gamma, allergen immunotherapy, antimetabolites, and biologics, depending on the cases reported during the trial[62]. Topical glucocorticoids are major and more effective pharmaceutical agents in controlling eczema and its related symptoms, including itchiness and inflammation, as described in Table 1. There are many factors influencing the effectiveness of topical steroids that include amount, potency, and vehicles of agents, duration of application, type and area of lesions, existence of infection and allergic reactions, and compliance of patients towards therapy[63].

In addition, some antibodies, named after Rituximab, Omalizumab, Infliximab, Dupilumab, Mepolizumab, and Tocilizumab, are monoclonal antibodies that act against B cells and neutralise IgE, anti-TNFα, anti-IL-4, IL-5, and IL-6 cytokine receptors, thus interrupting signalling pathways. These biological antibacterial agents have shown adverse effects to date[74-79].

These treatments are insufficient and have adverse effects, mainly on sensitive patients; therefore, probiotic-based bacterial therapy could be helpful for the treatment of eczema[80]. Certain microorganisms belonging to probiotics are clinically shown to have a preventive role in AD and its associated symptoms. They do so by influencing several biological processes, like acting as microbial antagonists by exerting antimicrobial components[81] that compete with pathogenic bacteria for adhesion to the epithelium and nutrients[82]. They immunomodulate the host and inhibit the production of bacterial toxins[83,84].

The application of a formulation containing *Streptococcus thermophilus* as a probiotic on AD patients' skin. A fifteen-day application containing a sonicated formulation of lactic acid bacteria *Streptococcus thermophilus* on the forearm of AD-infected patients significantly increases ceramides in the stratum corneum by producing protease sphingomyelinase that hydrolyses sphingomyelin, leading to improvement in scaling, erythema, and pruritus-like symptoms in AD-infected patients[85].

The topically applied cream containing 5% lysate of *Vitreoscilla filiformis*, a Gram-negative bacterium found in hot water springs, mediates the symptoms associated with AD[86]. The application of a thermally treated probiotic-based lotion containing 3.1×10^{11} CFU/g *Lactobacillus johnsonii* NCC 533 on an infected area to 52 patients, both female and male, aged between 18-75 years, for three weeks, twice a day, inhibited colonisation of *S. aureus,* thus improving Scoring Atopic Dermatitis Index (SCORD)[87]. A placebo-controlled trial indicated that the treatment with the use of *Roseomonas mucosa* was associated with a decrease in pruritus, SCORD by significantly decreasing the main coloniser *S. aureus* load at the affected areas without adverse effects or complications[88,89]. A trial of a topically applied formulation containing a combination of *Lactobacilli paracasei* and *Bifidobacterium longum reuter* in 33 females for 8 weeks showed a significant decrease in the dryness on the leg and roughness on the face. Another trial included 66 female volunteers with sensitive or reactive skin. Topical application of *Bifidobacterium longum reuter* lysate for 2 months twice a day showed measurable improvement in skin resistance ability by reducing trans- epidermal water loss, improvement in skin sensitivity, and reduction in dryness in response to physical and chemical changes[90]. The application of *Lactobacillus rhamnosus*-based product improves the scoring of the atopic dermatitis index (SCORD) even in IgE-sensitised AD patients[91]. *L. rhamnosus* AD1 shows improvement in the severity of eczema, thus reducing the risk of AD, especially in infants [92,93]. *Bifidobacterium lactis* and *L. acidophilus* showed a reduction in the development of AD in infants by reducing IgE production [94,95]. *L. reuteri* showed improvement in eczema by blocking integrins, thus reducing cell death by *S. aureus*[96].

6. Acne

Acne vulgaris is the most common skin disease caused by *Propionibacterium acnes,* with a lifetime prevalence affecting approximately 80-85 % of the population. The main culprit is an anaerobic Gram-positive bacterium commonly found in sebum-rich areas. It metabolises sebaceous triglycerides into fatty acids, forms a part of the skin's natural microbial flora, and interacts with other skin commensals, including *Staphylococcus epidermis, Pseudomonas species,* and *Streptococcus pyogenes*. Its over-proliferation action contributes to the development of acne[97]. Acne vulgaris is a complex inflammatory mechanism involving both innate and acquired immunity caused by a series of factors, including altered follicular keratinisation,

unbalanced sebum production due to disturbed hormones, and follicular colonisation at pilosebaceous areas by *Propionibacterium acnes*[98]. The microbiota of the affected area is disturbed and is different from the normal microbiome of the skin. Antibiotic-based therapy for acne is facing several challenges as it disrupts the natural physiology of the skin, making it dry, irritated, and even sensitive. Several studies have already demonstrated that the skin-gut axis is interdependent, as both possess somewhat similar microbial populations, implying that most skin-related issues are due to an imbalanced gut microbiome. The skin-gut axis relationship in acne indicates that appropriate probiotic strains can help rebalance the disturbed immune system beyond the gut and expand it towards the skin[99].

The study revealed that the daily consumption of *Lactobacillus bulgaricus* and *S. thermophilus* for 12 weeks resulted in a 30% reduction in inflammatory lesions. The concentration of sebum and free fatty acid clusters in the skin decreased by 50% after consuming the above-mentioned oral probiotic. Another study revealed that patients after receiving an oral probiotic formulation containing *Lactobacillus rhamnosus* SP1 strain for 3 months showed significant improvement in their acne as compared to placebo[100].

Till now, there is little data analysed from clinically proven evidence about the efficacy of topical probiotics for acne-associated issues. The studies suggest that *Cutibacterium acnes* is one of the commensals of natural skin; therefore, topical application of the phylotype of *C. acnes* as probiotics may be used as a preventative regimen against acne-associated opportunistic pathogens. Such a targeted strategy following nearly similar species of bacteria sharing a similar ecological niche is more effective than using other microbial species, as they showed significantly faster and long-lasting improvement of the overall skin microbiome[101].

Many studies have already revealed that species belonging to the Lactic acid bacteria *Streptococcus thermophilus* enhance ceramide production both *in vivo* and *in vitro* when applied topically. Ceramides contain ceramide sphingolipids that show antibacterial activity against *C. acnes,* thereby improving acne and soothing the irritated skin [102].

The application of *Streptococcus thermophilus* found in yoghurts on the skin would increase ceramide production[103]. Increased levels of ceramide provide anti-inflammatory activity and antimicrobial activity against the main coloniser, *Propionibacterium acne,* in affected areas and thus are relevant for acne therapy by reducing papules and pustules[104]. The lyophilised powder containing *Enterococcus faecalis* SL-5-derived bioactive enterocins exhibits potential activity against *Propionibacterium acnes* and is useful for treating acne by decreasing inflammatory lesions by 60% as compared to control after 8 weeks [105]. An *in vitro* assay was performed, which demonstrated that cell-free supernatants of selected probiotic strains, including "*Lactobacillus acidophilus* La-5, *Lactobacillus delbrueckii, L. acidophilus* La-10, *Lactobacillus paracasei* La-26, *Bifidobacterium lactis* B-94, and *Bifidobacterium animalis* Bb-12," showed the highest adhesion to keratinocytes and thus exhibited the antimicrobial activity against skin pathogens *E. coli, P. acnes, Staphylococcus aureus,* and *Pseudomonas aeruginosa* by preventing their biofilm formation or colonisation by competitive inhibition for binding sites at affected areas[106-108]. It was clinically investigated that Lactic Acid bacteria, including *Lactobacillus acidophilus, Lactobacillus plantarum, Lactobacillus casei, Lactobacillus lactis,* and *Lactobacillus gasseri* as probiotic strains, along with konjac glucomannan hydrolysate as prebiotics, were active against *Propionibacterium acnes* NCTC 737, which is responsible for acne vulgaris in in-vitro conditions[109,110].

One of the topical formulations consists of *C. acnes* bacteriophages that lyse bacteria. Studies have revealed that some *C. acnes* bacteriophages lyse pathogens responsible for acne and other pathogenic phylotypes without harming commensals of healthy skin[111,112].

7. Wound Healing

A wound is any sort of injury or disruption of the cutaneous microbiome of skin, caused by cuts, burns, etc., and is associated with local changes in the microbiome of the affected area of skin. Studies revealed that the probiotics may follow a mode of action by modulating the inflammatory response by inhibiting pathogen colonisation and thus promoting the healing process. Topically designed probiotic formulations have been reviewed for the elimination of inflammation and infection by inhibiting the formation of pathogen

biofilm over the infected area, thus augmenting the healing process[113]. There are a series of mechanisms that are involved in healing the wound area, concerning immunomodulatory mechanisms, macrophages, and lymphocytes activation, species-specific antipathy by modulating skin microflora, and decreasing inflammation that helps to maintain skin's integrity[114].

In case of burn victims, *Staphylococcus aureus*, gram-positive bacteria, are the main colonisers in the first 48 h, and then, opportunistic, sometimes life-threatening, gram-negative *Pseudomonas aeruginosa* bacteria predominate. It causes infection and inflammation in burn patients using a (TLR-4) toll-like receptor-4 associated with (LRC) lipopolysaccharide receptor complex by modulating adaptive immune responses[115].

Recent studies have shown that probiotic-based formulations containing a combination of *Lactobacillus brevis*, *Lactobacillus plantarum,* and *Lactobacillus fermentum* reduce inflammation, thereby accelerating the wound healing process. It was clinically evaluated that the positive role of probiotic formulations when applied topically on burn injuries and wound healing by reducing bacterial load, apoptotic and necrotic cells, neutrophils, and modifying the immune system by increasing interleukin-8 production at the infected site [116]. Studies have been conducted using animals as models with burn injuries, skin ulcers, and irritated wounds to determine the efficacy of topically applied probiotics in healing procedures by promoting tissue granulation, increasing collagen concentration, and quickening angiogenesis. Kefir, a cultured probiotic beverage, when applied topically, showed antibacterial activity against *Salmonella, Helicobacter, Shigella, Staphylococcus,* and *E. coli*. A probiotic *Lactobacillus plantarum* reduces *Pseudomonas aeruginosa* when applied to burn wounds in a mouse model. Studies also demonstrated clinically in humans that *Lactobacillus plantarum* is as effective as silver sulfadiazine solution in reducing the risks of infection in second and third-degree burn injuries[117,118]. The probiotic *Lactobacillus plantarum* has been shown to regulate and boost immune response non-specifically. 10^5 cfu/ml of *L. plantarum,* when injected into infected areas for 3 to 9 days, inhibited *P. aeruginosa* PA100 colonisation in an *in vivo* burned-murine model[119,120].

Skin commensals also act as excellent candidates when applied to prevent pathogenic biofilm formation, e.g, *Propioniferax innocua*, a skin commensal, has been found to degrade already established pathogenic biofilms. *Staphylococcus caprae* exerts antimicrobial activity against methicillin-resistant *S. aureus* by inhibiting colonisation in an *in vivo* model of mice. *Staphylococcus epidermis* suppresses skin inflammation by producing antimicrobial agents that selectively target *S. aureus* and *S. pyogenes. C. acnes* has also been shown to inhibit the *S. aureus* growth in an open wound mouse model by producing propionic acid[121,122].

8. Photoaging and Skin Ageing

Skin is directly exposed to environmental stress, including UV irradiation, which causes oxidative stress, generating Reactive Oxygen and Nitrogen Species (ROS/RNS) at the exposed surface[123]. UVR exposure accounts for 80-85 % of skin ageing, scaling, wrinkling, uneven pigmentations, dryness, and freckles[124]. Investigations have shown that long-term exposure to UV-A, as compared to UV-B, leads to photoaging and free radical production, and damage to both the epidermis and dermis[125]. The skin microbiome is known to change over time when exposed to external stress, influenced by physiological and chronological changes that cause photoaging[126]. Many clinical trials on animals and humans as models showed that the probiotic-based biotherapy may slow down both intrinsic and extrinsic ageing-induced factors or processes. It was demonstrated that probiotics can restore the acidic pH of skin naturally, alleviate oxidative stress, reduce or diminish photoaging, and improve skin barrier[127]. UV rays alleviate the ROS/RNS production at the genetic level and activate cytokines at the molecular level, which is responsible for photoaging. Probiotics belonging to *Lactobacillus* and *Bifidobacterium* strains may be regarded as effective biotherapeutic agents that are demonstrated clinically to have antioxidant potential under both *ex vivo* and *in vivo* conditions, thus useful for impeding skin's oxidative stress either via the topical way or via the oral route. Also, both *Lactobacillus* and *Bifidobacterium* strains, as whole cells or their respective cell-free extracts containing antioxidant enzymes, were able to exert autoxidation of ascorbate, metal-chelation, scavenging superoxides and other reactive species, thus inhibiting lipid peroxidation[128,129]. Microbial-derived extracts of Lactic acid species or fermented

milk were investigated for reducing or delaying human low-density lipoprotein oxidation[130,131]. Experiments were performed to study the antioxidant potential of *S. thermophilus* S244 extracts, which possess good free radical scavenger ability by VSL Pharmaceuticals, USA. Kimchi is a well-studied and investigated plant; its derived extracts were fermented with *Lactobacillus buchneri* (PELB) concerning their anti-photoaging effect on UV-exposed keratinocytes and dermal fibroblasts *in vitro* models[132]. Studies revealed that the *Lactobacillus buchneri*-based skincare or cosmetic products are useful against UV-induced photoaging due to their protective effects[133]. Also, *Lactobacillus helveticus* supernatant, when applied on the surface of skin, shows antioxidant activity on rats as experimental models. Therefore, the use of live biotherapeutic agents as photo-protectants is considered an innovative outlook to remodulate uneven pigmentation by utilising their antioxidant potential, thus preventing photoaging and even skin cancer[134].

9. Disturbed Skin Barriers

Human skin provides a barrier against diverse pathogenic microorganisms. Collagen is one of the major skeletal constituents of the skin, responsible for its physical integrity and elasticity. Many abiotic and biotic stresses damage skin integrity, and skin repairs the damage itself, but fails to do so in chronic conditions. The skin epidermis and dermis consist of ceramides, hyaluronic acids, and collagens that function as a single unit and maintain the elasticity of skin, epidermal permeability, and stratum corneum integrity, building a homeostatic barrier. Any damage to the skin microbiome is associated with dermal diseases such as atopic dermatitis or eczema, seborrheic dermatitis, and psoriasis[135,136].

The use of microbes from *Lactobacillus* species as probiotics produces lactic acid from lactose, glucose, and other sugars through fermentative metabolism, thereby lowering the pH of the skin and maintaining stratum corneum integrity. The acid-producing mechanism prevents the growth of other organisms because low pH favours the growth of Lactobacilli and benefits the host[137].

In psoriasis, the altered composition of the skin microbiome may trigger Th17 pathway activation, which very well demonstrates a difference in microbial population of psoriatic skin compared to healthy skin. The main colonisers in psoriatic lesions are *Staphylococcus aureus* and *Streptococcus pyogenes,* and species from the Actinobacteria also dominate[138].

Probiotics are still under trial for determining their role in psoriasis; however, there is some indication that they have positive immunoregulatory effects via lowering inflammation. For treating psoriasis, oral administration of *Bifidobacterium infantis* for 8 weeks significantly decreases the levels of C-reactive protein responsible for inflammation[139]. Another study concluded that oral administration of *Lactobacillus pentosus* GMNL-77 reduces tumour necrosis factor-α and IL-23, IL-17 cytokines, thus decreasing erythematous scaly lesions in an experimental mouse model infected with psoriasis[140].

Seborrheic dermatitis is an inflammatory response to free fatty acids produced by the *Malassezia furfur*, a normal fungus resident of the skin. A more accurate indicator of illness severity is disturbed and reduced bacterial diversity[141]. Application of a probiotic-based topical formulation containing *Vitreoscilla filiformis* to 60 volunteers showed a visible decrease in symptoms, including erythema, scaling, and pruritus, due to an elevation in production of IL-10 by dendritic cells, increasing the action of T-cells. In addition to the topically designed product mentioned above, patients receiving *Lactobacillus paracasei,* one of the probiotics, orally showed significant improvement in erythema and seborrhoea[142].

Hyaluronic acid is a key ingredient in many skin care treatments. By having strong water-holding capacities, hyaluronic acid, the main component of the extracellular matrix of skin tissues, and fibroblasts help to preserve the health of the skin and delay the ageing process[143]. Lactic acid bacteria produce hyaluronic acid as the main product in addition to other by-products by the fermentation process, thus benefiting and maintaining skin health. It was clinically observed in mouse skin that *Bifidobacterium-fermented* soymilk extracts significantly enhanced hyaluronic acid production both *in vitro* and *in vivo* and were able to improve the viscoelasticity and elasticity of skin, preventing age-dependent loss of cutaneous hyaluronic acid production[144]. The application of a probiotic containing *S. thermophilus* YIT 2084 significantly increased hyaluronic acid[145].

Ceramides, cholesterol, and FFA of the stratum corneum are among the lipid components necessary to properly maintain homeostasis in the permeability barrier. Keratinocytes are secreted to maintain epidermal membrane integrity, thus playing a crucial role in maintaining the structural integrity and permeability of the skin. Any imbalance of ceramides, cholesterol, and FFA results in water loss and dysregulation in the barrier, ultimately resulting in an easily available surface for pathogens, causing skin disorders.

It was investigated that the milk fermented with *S. thermophilus* and *L. bulgaricus* could generate skin collagen naturally and thus prevent elastosis[146]. The premise of Cavaliere and De Simone's (2001) discovery was the use of SMase, a bacterial enzyme produced from lactic acid, to raise the level of ceramides in topical dermatological and cosmetic formulations. According to this patent, the bacterial SMase, either alone or with a suitable enhancer, could be used for the preparation of pharmaceutical-based cosmetics to improve skin permeation or as an absorption enhancer. Thus, this method claims to cure or treat all abnormal ceramide level-associated disorders of skin, including atopic dermatitis or eczema, psoriasis, ichthyosis, skin ageing, Gaucher's disease, Tay-Sachs' disease, and Fabry's disease[147]. The use of sonicated *S. thermophilus-based* formulations could improve dysmetabolism of systemic mastocytosis in AD patients by increasing the level of ceramides in *in vivo* skin. A fifteen-day application of formulations consisting of *S. thermophilus* on the patient's forearm skin showed a significant increase in the level of ceramides and caused improvement in erythema, scaling, and pruritus. In addition, sonicated *S. thermophilus* when applied topically may help to strengthen the lipid barrier and effectively fend off skin xerosis caused by age[148].

Disturbance in the skin microbiome may be involved in dermal or subcutaneous neoplasms and aid in carcinogenesis, which causes skin cancer. A blooming microbiota may suppress this health hazard through the regulation of its immune system as a natural therapeutic agent. Cutaneous T-cell lymphoma disease severity is linked to *Staphylococcus aureus* infection, as *Staphylococcal* superantigens play a potential role in carcinogenesis. Oral intake of lipoteichoic acid from *Lactobacilli* reduces the risk of UV-induced skin cancer[149]. Another recent finding process that strain *S. epidermis* selectively inhibits tumour proliferation by producing a certain nucleobase molecule that reduces the incidence of UV-induced tumours in mice as a model. Therefore, it is conceivable that the use of probiotics as biotherapeutics is beneficial in reducing the risk of cutaneous neoplasms[150]. Table 2 shows a list of *Lactobacillus* and *Bifidobacterium* strains as probiotics that have been patented, along with their effects on skin.

10. Probiotics: Safety and Challenges

Although most of the probiotics are safe, following Anadón and co-workers' appraisal of probiotic safety represents a delicate task[153]. According to the World Health Organisation (WHO) and Food and Agriculture Organisation (FAO), microorganism strains belonging to the genera *Lactobacilli* and *Bifidobacteria* are well distinguished as beneficial by their safety aspect with GRAS status (Generally Regarded as Safe) compared to other microbes due to a lack of field trials[154]. There is no such thing as zero risk from a conventional point of view, but according to Snydman, probiotic strains should also be distinguished by low virulence and low antibiotic resistance. The selective criteria of new potential probiotic microorganisms targeting new bacterial strains and even new genera with higher beneficial potential and with more properties is not an easy task[155,156]. According to Fedorak and Madsen, public apprehension about the idea of risk/benefit ratio is not up to the mark. Although the risk seems to be low with probiotic products now on the market, the capacity of antibiotic resistance transfer is a real concern when working with probiotics. Regarding other various forms of therapeutic agents, probiotics and their biosafety must be assessed on a strain-by-strain basis before their commercialisation[157].

Another wave of challenges, for probiotic-based products, either as food or therapeutics, before commercialisation, encompasses inoculation, appraisal of viable counts, particularly when multiple strains are added, and when starter bacterial cultures are added[158]. It also includes maintaining probiotics, diversity, and origin of beneficial microbes, probiotic survival rate, their active state, dealing with host

Table 2. List of patents of probiotics beneficial for skin health

S. No.	Patent No.	Strain	Effect [151-153]
1	US11007137B2 (2021)	*Lactobacillus plantarum*	An increase in collagen secretion and ceramide synthesis leads to improvement in the skin condition.
2	BR112021/004538A2 (2021) and WO 2020/056359 (2020)	*Streptococcus* named after *S. captitis* N030_E12, *S. epidermidis* N018_F3, *S. epidermidis* AMT5_C5, and *S. epidermidis* N009_G7	Applied topically to restore and maintain the disbalanced microbiome of the skin, scalp, or associated mucous membranes, as well as for the treatment of acne.
3	US10695386B2 (2020)	*Bacillus licheniformis, Bifidobacterium breve, B. infantis, Lactobacillus fermentum, L. plantarum, L. rhamnosus, L. sakei, L. paracasei, Staphylococcus epidermis* and *Staphylococcus xylosus*	The treatment of dysbiosis of the infected skin.
4	ES2751994T3 (2020) and ES2677905T3 (2018)	*Lactobacillus paracasei*	Lysates are useful for the prevention of irritation of the skin due to external aggression and fatty disorders of the scalp.
5	EP3727594A1 (2020)	*Lactobacillus* species	Maintains the balance of the cutaneous microbiome and reinforces the cutaneous barriers.
6	CN111601583A (2020)	*Bacillus* genus lysate	In the treatment of seborrheic disease, sebum-dependent or proliferation inflammatory disorders are caused by microorganisms on the skin.
7	US10238597B2 (2019)	*Lactobacillus jensenii,* and *Lactobacillus vaginalis*	Useful for resolving scalp dandruff.
8	BR112019017962A2 WO 2018/1832889 (2018)	*S. epidermidis* MO34 and MO38	Useful for the treatment of neoplastic diseases and disorders, and even cancer.
9	WO201763066A1(2017)	*Bifidobacterial longum, B. bifidum, B. breve,* and *B. psuedolongum*	As cleansing and anti-ageing agents.
10	US9649346B2 (2017)	*Streptococcus thermophilus, S. salivarus* and its subspecies *thermophilus* type 1131, *Bifidobacterium longum*, *Lactobacillus paracasei*	They maintained the hydration of skin, reduced wrinkles, and proved useful for the treatment of acne and skin inflammations.
11	WO2015/181534A1(2015)	*Lactobacillus rhamnosus*	Useful for the repair of skin tissue and wound repair.
12	EP2704704B1(2012)	Species of *Bifidobacterium, Brevibacterium, Propionibacterium, Lactococcus, Lactobacillus, Streptococcus, Enterococcus, Pediococcus, Leuconostoc, Oenococcus*	Used for the improvement and maintenance of the integrity of the tight junctions of human epidermal keratinocytes.
13	FR2938429B1(2010)	*Lactobacilli and Bifidobacterium* species	Help in restoring a normal scalp, reducing irritation, itching, and dandruff.
14	JP2009503042A (2009)	*L. johnsonni* CNCM1-1225, *L. paracasei* CNCM1-21116, *Bifidobacterium adrecentis* CNCM1-2168, *B. longum* CNCM1-2170, *B. lactis* CNCM1-3446, *B. logum* BB536	Investigated for the prevention and treatment of dry and sensitive skin.
15	US6723326B1 (2008) and EPO975227A1(2009)	*Pseudomonas lindbergii, Bacillus coagulans* spores	Inhibits the growth of bacteria, yeast, and fungi in the infected area.
16	US20080107699A1 (2008)	*Lactobacillus acidophilus* strains NCFM, La-14, and *Lactobacillus paracasei* strain Lpc-37	Investigated for the prevention of contamination by pathogenic microorganisms.
17	WO2006/013441A2 (2006)	*Lactobacillus plantarum*	Evidence for preventing and treating many skin microbial diseases.
18	No. 253262 (2003)	*Lactobacillus gasseri*	Showed antioxidant properties.
19	No. 112466 (2001)	*Lactobacillus delbrueckii* subspecies *bulgarius*	It is effective on the skin by preserving moisture content and enhancing immunity.

inhabitant microflora, intrinsic intricate factors, and their potential health benefits[159].

To sum up, the probiotics industry is constantly expanding due to the wide range of probiotic strains and their derived unique products that are offered in the market in various forms and dosages, thus increasing the number of people who use probiotics. The probiotic microbe to be studied in future research and scientific studies needs to be described in greater detail, including the genus, species, and strain levels, in addition to the daily dosage and the length of the treatment. To focus on international norms and standards, three major elements, composed of the public, healthcare providers, and manufacturers, must overcome the challenges and thus guide strain-specific evidence-based therapy[160,161].

11. Probiotics Regulation: Global Scenario

With the emphasis on health, probiotics have exploded into a vast market potential as they are used as food, supplements, pharmaceuticals, therapeutic items, and even now in the cosmetic business. Nowadays, these live bacteria and their metabolites or specific extracts are the driving force behind health promotion; however, there are differences between regions or countries in terms of regulation and safety evaluation[162,163]. Probiotics are mostly classified as foods and/or dietary supplements in North America and Europe, natural health products in Canada, and foods for special medical purposes in Japan. The Generally Recognised as Safe (GRAS) status represents an exceptional standard for microbiological safety around the world, especially in the United States[164]. Health Department of Canada accepts 1×10^9 CFU for probiotic-based product per serving for *Bifidobacterium* and *Lactobacillus* spp[165]. The QPS status (Qualified Presumption of Safety) was proposed by the European Food Safety Authority (EFSA). The QPS status was proposed based on characterisation, taxonomy, pathogenicity, and conclusive statistical data that might be appropriate to a specific beneficial microbes' group that is confirmed as probiotic for direct human utilisation. The minimum quantity of viable cells in food per serving per day stipulated by the Italian Ministry of Health for the use of probiotic bacteria in food items is 1×10^9 CFU, and for cosmetic use, not more than 1×10^6 CFU[166]. Functional foods and nutraceuticals are regulated and supervised in China by the Chinese State Food and Drug Administration (SFDA). Probiotics have a substantial market share among functional food items in China, where traditional eating customs and economic development have a strong influence[167,168].

Probiotics are governed in Japan by the Food for Specific Health Use agency (FOSHU), which permits the labelling of foods or ingredients with health claims if the claims are supported by scientific evidence and are safe and effective[169]. The health characteristics may cover blood pressure, blood sugar, bone minerals, etc; in addition, the origin and conventional application of foods and/or food ingredients are considered when evaluating any innovation[170].

According to the current scenario, the Indian market now contributes less than 1% in terms of revenue to the global probiotic market. The probiotic sector in India is at a burgeoning stage. Major pharmaceutical companies are actively working to develop novel medications and packaged goods, such as nutritional supplements based on probiotics for people like lactation, pregnancy, immunodeficiency, etc., as well as items tailored to children and older people. Currently, it stands at Rs 50 crore and is growing at 20%. Some probiotic-based pharmaceutical formulations in this regard include Sporolac, ViBact, Darolac, Biglac, and Bifilac[171].

The FAO/WHO recommendation states that probiotic products should be labelled with a variety of specifications and information, including the genus, species, strain designations, minimum viability of each probiotic strain at the end of the shelf life, storage conditions, and traceability, such as the cooperating party. Probiotics do not, however, need to adhere to any worldwide regulatory standards, which emphasises the critical need for more frequent evaluations of the product's safety and quality. Microbial contamination and a decline in technologically functional probiotic qualities, which are influenced by handling and processing, are two major barriers that challenge the development of probiotic-based products[172,173].

12. Conclusion

The diverse microbiota of skin itself plays a significant role in the field of dermatology and functions as a potential therapeutic tool for cutaneous illnesses. Probiotics improve healing and microbiome balance

by lowering inflammation, rebalancing immune responses, and preventing the colonisation of vulnerable microorganisms. Even though the studies and evidence presented in this review regarding the efficacy of probiotics on skin disorders have positive and encouraging results, the development of probiotic-based topical products used in dermal treatment is in its preliminary stages. Therefore, more advanced research will be required to gain knowledge about the respective actions of mechanisms in skin-related issues to prove their efficacy and safety aspects. Improved rules and regulations are also required for the use and safety of biotherapeutic products based on probiotics. They may also offer new biotherapeutic tools to help patients with acute to chronic dermatological disorders. To support the replacement strategy for the microbiome, additional probiotic trials, either alone or in combination with prebiotics or with antibiotic treatment, may produce interesting and positive results in the future.

13. Author Contribution:

Nandini Sinhmar: Writing- original draft. **Bindu Battan:** Conceptualisation, Supervision. **Surender Verma:** The Idea of Concept. **Sulekha Chahal and Jitender Sharma:** Manuscript editing. All the authors have reviewed and agreed to the published version of the manuscript.

14. References

1. Huang MCJ, Tang J. Probiotics in personal care products. Microbiol Discov. 2015; 3:5. https://doi.org/10.7243/2052-6180-3-5
2. Patil E, Rawtal B, Sakharwade S. Magical approach of probiotics in cosmetics. World J Pharm Res. 2020; 9(11):404-16.
3. França K. Topical probiotics in dermatological therapy and skincare: a concise review. Dermatol Ther (Heidelb). 2021; 11(1):71-7. https://doi.org/10.1007/s13555-020-00476-7
4. Barankin B, DeKoven J. Psychosocial effect of common skin diseases. Can Fam Physician. 2002; 48:712-6.
5. Al-Ghazzewi FH, Tester RF. Impact of prebiotics and probiotics on skin health. Benef Microbes. 2014; 5(2):99-107. https://doi.org/10.3920/BM2013.0040
6. Suvana VC, Boby VU. Probiotics in human health: a current assessment. Curr Sci. 2005; 88(11):1744-8.
7. Lilly DM, Stillwell RH. Probiotics: growth-promoting factors produced by microorganisms. Science. 1965; 147(3659):747-8. https://doi.org/10.1126/science.147.3659.747
8. Pandey KR, Naik SR, Vakil BV. Probiotics, prebiotics and synbiotics - a review. J Food Sci Technol. 2015; 52(12):7577-87. https://doi.org/10.1007/s13197-015-1921-1
9. Parker RB. The other half of the antibiotic story. Anim Nutr Health. 1974; 29:4-8.
10. Hammerman C, Bin-Nun A, Kaplan M. Germ warfare: probiotics in defence of the premature. Clin Perinatol. 2004; 31(3):489-500. https://doi.org/10.1016/j.clp.2004.04.015
11. Zielinska D, Kolozyn-Krajewska D. Food-origin lactic acid bacteria may exhibit probiotic properties: review. Biomed Res Int. 2018; 2018:5063185. https://doi.org/10.1155/2018/5063185
12. Arshad F, Mehmood R, Hussain S, Khan MA, Khan MS. Lactobacilli as probiotics and their isolation from different sources. Br J Res. 2018; 5(3):43. https://doi.org/10.21767/2394-3718.100043
13. Scharschmidt TC, Fischbach MA. What lives on our skin: ecology, genomics, and therapeutic opportunities of the skin microbiome. Drug Discov Today Dis Mech. 2013; 10(3-4):e83-9. https://doi.org/10.1016/j.ddmec.2012.12.003
14. Khare A, Thorat G, Bhimte A, Yadav V. Mechanism of action of prebiotics and probiotics. J Entomol Zool Stud. 2018; 6(4):51-3.
15. Notay M, Mittal R, Arora A, Dhingra N, Manhas D. Probiotics, prebiotics and synbiotics for the treatment and prevention of adult dermatological diseases. Am J Clin Dermatol. 2017; 18(6):721-32. https://doi.org/10.1007/s40257-017-0300-2
16. Shenderov BA. Metabiotics: novel idea or natural development of probiotic conception. Microb Ecol Health Dis. 2013; 24:20399. https://doi.org/10.3402/mehd.v24i0.20399
17. Nazemian V, Shadnoush M, Manaheji H, Zaringhalam J. Probiotics and inflammatory pain: a literature review study. Middle East J Rehabil Health Stud. 2016; 3(2):e36087. https://doi.org/10.17795/mejrh-36087
18. Lew LC, Liong MT. Bioactives from probiotics for dermal health: functions and benefits. J Appl Microbiol. 2013; 114(5):1241-53. https://doi.org/10.1111/jam.12137
19. Singh H, Singh H. Probiotics: an emerging concept. Int J Sci Res Publ. 2014;4(6):1-4.
20. Foligné B, Daniel C, Pot B. Probiotics from research to market: the possibilities, risks, and challenges. Curr Opin Microbiol. 2013; 16(3):284-92. https://doi.org/10.1016/j.mib.2013.06.008
21. Teran C. Probiotic technology. Active Concepts; 2011.
22. Bermudez-Brito M, Plaza-Díaz J, Muñoz-Quezada S, Gómez-Llorente C, Gil A. Probiotic mechanisms of action. Ann Nutr Metab. 2012; 61(2):160-74. https://doi.org/10.1159/000342079

23. Kang BS, Seo JG, Lee GS, Kim JH, Kim SY, Han YS, *et al.* Antimicrobial activity of enterocins from *Enterococcus faecalis* SL-5 against Propionibacterium acnes, the causative agent in acne vulgaris, and its therapeutic effect. J Microbiol. 2009; 47(1):101-9. https://doi.org/10.1007/s12275-008-0179-y
24. Gillor O, Etzion A, Riley MA. The dual role of bacteriocins as anti- and probiotics. Appl Microbiol Biotechnol. 2008; 81(4):591-606. https://doi.org/10.1007/s00253-008-1726-5
25. Cinque B, La Torre C, Melchiorre E, Marchesani G, Zoccali G, Palumbo P, *et al.* Use of probiotics for dermal applications. In: Riccò M, editor. Probiotics. Berlin: Springer; 2011. p. 221-41. (Microbiology Monographs; vol. 21). https://doi.org/10.1007/978-3-642-20838-6_9
26. Saeed MW. Characterisation of the potential of probiotics or their extracts as therapy for skin [dissertation]. Manchester (UK): The University of Manchester; 2014.
27. Valdéz JC, Peral MC, Rachid M, Santana M, Perdigón G. Interference of *Lactobacillus plantarum* with *Pseudomonas aeruginosa in vitro* and infected burns: the potential use of probiotics in wound treatment. Clin Microbiol Infect. 2005; 11(6):472-9. https://doi.org/10.1111/j.1469-0691.2005.01142.x
28. West NP, Pyne DB, Peake JM, Cripps AW. Probiotics, immunity, and exercise: a review. Exerc Immunol Rev. 2009; 15:107-26.
29. Benyacoub J, Bosco N, Blanchard C, Demont A, Philippe D, Castiel-Higounenc I, *et al.* Immune modulation property of *Lactobacillus paracasei* NCC2461 (ST11) strain and impact on skin defences. Benef Microbes. 2014; 5(2):129-36. https://doi.org/10.3920/BM2013.0014
30. Bowe WP, Logan AC. Acne vulgaris, probiotics and the gut-brain-skin axis - back to the future? Gut Pathog. 2011; 3:1. https://doi.org/10.1186/1757-4749-3-1
31. Gardner R. Probiotics for the skin. Nutr Outlook. 2014; 17:8.
32. Herbal Dynamics Beauty. Topical probiotics for skin health [Internet]. 2018 [cited 2025 Aug 22]. Available from: https://www.herbaldynamicsbeauty.com/blogs/herbal-dynamics-beauty/topical-probioticsfor-skin-health
33. Herbal Dynamics Beauty. Topical probiotics for skin health [Internet]. 2019 [cited 2025 Aug 22]. Available from: https://www.herbaldynamicsbeauty.com/blogs/herbal-dynamics-beauty/topicalprobiotics-for-skin-health
34. Patra VK, Wagner K, Arulampalam V, Wolf-Watz H. Potential of skin microbiome, pro- and/or prebiotics to affect local cutaneous responses to UV exposure. Nutrients. 2020; 12(6):1795. https://doi.org/10.3390/nu12061795
35. Oh S, Kim SH, Ko Y, Sim JH, Kim KS, Lee SH, *et al.* Effect of bacteriocin produced by *Lactococcus* sp. HY 449 on skin-inflammatory bacteria. Food Chem Toxicol. 2006; 44(4):552-9. https://doi.org/10.1016/j.fct.2005.08.030
36. Egert M, Simmering R. The microbiota of the human skin. In: Grice EA, editor. The human microbiota. Cham: Springer; 2016. p. 61-81. https://doi.org/10.1007/978-3-319-31248-4_5
37. Dréno B, Araviiskaia E, Berardesca E, Gontijo G, Sanchez Viera M, Xiang LF, *et al.* Microbiome in healthy skin, update for dermatologists. J Eur Acad Dermatol Venereol. 2016; 30(12):2038-47. https://doi.org/10.1111/jdv.13965
38. Grice EA, Kong HH, Renaud G, Young AC, Bouffard GG, Blakesley RW, *et al.* Topographical and temporal diversity of the human skin microbiome. Science. 2009; 324(5931):1190-2. https://doi.org/10.1126/science.1171700
39. Reid G, Younes JA, Van der Mei HC, Gloor GB, Knight R, Busscher HJ. Microbiota restoration: natural and supplemented recovery of human microbial communities. Nat Rev Microbiol. 2011; 9(1):27-38. https://doi.org/10.1038/nrmicro2473
40. Grice EA, Segre JA. The skin microbiome. Nat Rev Microbiol. 2011; 9(4):244-53. https://doi.org/10.1038/nrmicro2537
41. Byrd AL, Belkaid Y, Segre JA. The human skin microbiome. Nat Rev Microbiol. 2018; 16(3):143-55. https://doi.org/10.1038/nrmicro.2017.157
42. Gao Z, Perez-Perez GI, Chen Y, Blaser MJ. Quantitation of major human cutaneous bacterial and fungal populations. J Clin Microbiol. 2010; 48(10):3575-81. https://doi.org/10.1128/JCM.00597-10
43. Litwin D, Chen W, Dzika E, Korycińska J. Human permanent ectoparasites: recent advances on biology and clinical significance of Demodex mites. Iran J Parasitol. 2017; 12(1):12-21.
44. Schommer NN, Gallo RL. Structure and function of the human skin microbiome. Trends Microbiol. 2013; 21(12):660-8. https://doi.org/10.1016/j.tim.2013.10.001
45. Holland KT, Bojar RA. Cosmetics: what is their influence on the skin microflora? Am J Clin Dermatol. 2002; 3(7):445-9. https://doi.org/10.2165/00128071-200203070-00001
46. U.S. Food and Drug Administration. Federal Food, Drug and Cosmetic Act (FD and C Act), Sec. 201 [21 U.S.C. 321], Chapter II - Definitions [Internet]. 2012 [cited 2025 Aug 22]. Available from: https://www.fda.gov/regulatory-information/laws-enforced-fda/federal-food-drug-and-cosmetic-act-fdc-act
47. Krutmann J. Pre- and probiotics for human skin. J Dermatol Sci. 2009; 54(1):1-5. https://doi.org/10.1016/j.jdermsci.2009.01.002
48. Simmering R, Breves R. Pre- and probiotics in cosmetics. Hautarzt. 2009; 60(10):809-14. https://doi.org/10.1007/s00105-009-1759-4
49. Maleki D, Homayouni A, Khalili L, Golkhalkhali B. Probiotics in cancer prevention: updating the evidence. In: Watson RR, Preedy VR, editors. Probiotics, prebiotics,

and synbiotics: bioactive foods in health promotion. Amsterdam: Academic Press; 2016. p. 780-91. https://doi.org/10.1016/B978-0-12-802189-7.00059-9
50. Cinque B, Palumbo P, La Torre C, Melchiorre E, Corridoni D, Miconi G, *et al.* Probiotics in ageing skin. In: Farage MA, Miller KW, Maibach HI, editors. Textbook of ageing skin. 2nd ed. Berlin: Springer; 2010. p. 2-78.
51. Victoria HM, Edna SS. An approach to the potential use of probiotics in the treatment of skin conditions: acne and atopic dermatitis. Int J Dermatol. 2018; 57(12):1425-32. https://doi.org/10.1111/ijd.13972
52. Pothmann A, Illing T, Wiegand C, Hartmann AA, Elsner P. The microbiome and atopic dermatitis: a review. Am J Clin Dermatol. 2019; 20(6):749-61. https://doi.org/10.1007/s40257-019-00467-1
53. Baldwin H, Aguh C, Andriessen A, Benjamin L, Fercee MA, Glowacki R, *et al.* Atopic dermatitis and the role of the skin microbiome in choosing prevention, treatment, and maintenance options. J Drugs Dermatol. 2020; 19(10):935-40. https://doi.org/10.36849/JDD.2020.5393
54. Nakatsuji T, Gallo RL. The role of the skin microbiome in atopic dermatitis. Ann Allergy Asthma Immunol. 2019; 122(3):263-9. https://doi.org/10.1016/j.anai.2018.12.003
55. Correa C, Nebus J. Management of patients with atopic dermatitis: the role of emollient therapy. Dermatol Res Pract. 2012; 2012:836931. https://doi.org/10.1155/2012/836931
56. Krakowski AC, Eichenfield LF, Dohil MA. Management of atopic dermatitis in the pediatric population. Pediatrics. 2008; 122(4):812-24. https://doi.org/10.1542/peds.2007-2232
57. Nemoto-Hasebe I, Akiyama M, Nomura T, Sandilands A, McLean WH, Shimizu H. Clinical severity correlates with impaired barrier in filaggrin-related eczema. J Invest Dermatol. 2009; 129(3):682-9. https://doi.org/10.1038/jid.2008.280
58. Sher LG, Chang J, Patel IB, Balkrishnan R, Fleischer AB Jr. Relieving the pruritus of atopic dermatitis: a meta-analysis. Acta Derm Venereol. 2012; 92(5):455-61. https://doi.org/10.2340/00015555-1360
59. Lee JH, Son SW, Cho SH. A comprehensive review of the treatment of atopic eczema. Allergy Asthma Immunol Res. 2016; 8(3):181-90. https://doi.org/10.4168/aair.2016.8.3.181
60. Boguniewicz M, Nicol N, Kelsay K, Leung DY. A multidisciplinary approach to the evaluation and treatment of atopic dermatitis. Semin Cutan Med Surg. 2008; 27(2):115-27. https://doi.org/10.1016/j.sder.2008.05.001
61. Queille-Roussel C, Paul C, Duteil L, Lefebvre MC, Rapatz G, Zagula M, *et al.* The new topical ascomycin derivative SDZ ASM 981 does not induce skin atrophy: a randomised, double-blind controlled study. Br J Dermatol. 2001; 144(3):507-13. https://doi.org/10.1046/j.1365-2133.2001.04076.x
62. Frankel HC, Qureshi AA. Comparative effectiveness of topical calcineurin inhibitors in adult patients with atopic dermatitis. Am J Clin Dermatol. 2012; 13(2):113-23. https://doi.org/10.2165/11597780-000000000-00000
63. Hultsch T, Kapp A, Spergel J. Immunomodulation and safety of topical calcineurin inhibitors for the treatment of atopic dermatitis. Dermatology. 2005; 211(2):174-87. https://doi.org/10.1159/000086739
64. Simons FE, Simons KJ. Histamine and H1-antihistamines: celebrating a century of progress. J Allergy Clin Immunol. 2011; 128(6):1139-50. https://doi.org/10.1016/j.jaci.2011.09.005
65. Bae JM, Choi YY, Park CO, Chung KY, Lee KH. Efficacy of allergen-specific immunotherapy for atopic dermatitis: a systematic review and meta-analysis. J Allergy Clin Immunol. 2013; 132(1):110-7. https://doi.org/10.1016/j.jaci.2013.02.044
66. Niebuhr M, Mai U, Kapp A, Werfel T. Antibiotic treatment of *Staphylococcus aureus* infections in atopic dermatitis: resistance and susceptibility. Exp Dermatol. 2008; 17(11):953-7. https://doi.org/10.1111/j.1600-0625.2008.00734.x
67. Leung DY. Infection in atopic dermatitis. Curr Opin Pediatr. 2003; 15(4):399-404. https://doi.org/10.1097/00008480-200308000-00008
68. Czech W, Bräutigam M, Weidinger G, Schöpf E. Cyclosporine microemulsion effective in severe atopic dermatitis. J Am Acad Dermatol. 2000; 42(4):653-9. https://doi.org/10.1016/S0190-9622(00)90180-4
69. Lyakhovitsky A, Barzilai A, Heyman R, Baum S, Amichai B, Solomon M, *et al.* Low-dose methotrexate for moderate-to-severe atopic dermatitis in adults. J Eur Acad Dermatol Venereol. 2010; 24(1):43-9. https://doi.org/10.1111/j.1468-3083.2009.03351.x
70. Berth-Jones J, Takwale A, Tan E, Barclay G, Agarwal S, Ahmed I, *et al.* Azathioprine in severe adult atopic dermatitis: a double-blind, placebo-controlled trial. Br J Dermatol. 2002; 147(2):324-30. https://doi.org/10.1046/j.1365-2133.2002.04989.x
71. Hanifin JM, Paller AS, Eichenfield L, Wagner AM, Shurman D, Papp KA, *et al.* Efficacy and safety of tacrolimus ointment up to 4 years in atopic dermatitis. J Am Acad Dermatol. 2005; 53(2 Suppl 2):S186-94. https://doi.org/10.1016/j.jaad.2005.04.062
72. Schneider LC, Baz Z, Zarcone C, Zurakowski D. Long-term therapy with recombinant interferon-gamma for atopic dermatitis. Ann Allergy Asthma Immunol. 1998; 80(3):263-8. https://doi.org/10.1016/S1081-1206(10)62968-7
73. Simon D, Hösli S, Kostylina G, Yawalkar N, Simon HU. Anti-CD20 (rituximab) improves atopic eczema. J Allergy Clin Immunol. 2008; 121(1):122-8. https://doi.org/10.1016/j.jaci.2007.11.016

74. Beck LA, Thaçi D, Hamilton JD, Graham NM, Bieber T, Rocklin R, *et al.* Dupilumab in adults with moderate-to-severe atopic dermatitis. N Engl J Med. 2014; 371(2):130-9. https://doi.org/10.1056/NEJMoa1314768
75. Jacobi A, Antoni C, Manger B, Schuler G, Hertl M. Infliximab in moderate to severe atopic dermatitis. J Am Acad Dermatol. 2005; 52(3 Pt 1):522-6. https://doi.org/10.1016/j.jaad.2004.11.022
76. Oldhoff JM, Darsow U, Werfel T, Katzer K, Wulf A, Laifaoui J, *et al.* Mepolizumab in atopic dermatitis. Allergy. 2005; 60(5):693-6. https://doi.org/10.1111/j.1398-9995.2005.00791.x
77. Bel EH, Wenzel SE, Thompson PJ, Prazma CM, Keene ON, Yancey SW, *et al.* Mepolizumab oral glucocorticoid-sparing in eosinophilic asthma. N Engl J Med. 2014; 371(13):1189-97. https://doi.org/10.1056/NEJMoa1403291
78. Navarini AA, French LE, Hofbauer GF. IL-6 receptor inhibition improves atopic dermatitis but risks superinfection. J Allergy Clin Immunol. 2011; 128(5):1128-30. https://doi.org/10.1016/j.jaci.2011.09.009
79. Raap U, Weißmantel S, Gehring M, Eisenberg AM, Kapp A, Fölster-Holst R. IL-31 correlates with disease activity in children with atopic dermatitis. Pediatr Allergy Immunol. 2012; 23(3):285-8. https://doi.org/10.1111/j.1399-3038.2011.01241.x
80. Lopes EG, Moreira DA, Gullón P, Gullón J, Saldaña G, Gómez JM, *et al.* Topical application of probiotics: adhesion, antimicrobial and antibiofilm assays. J Appl Microbiol. 2017; 122(2):450-61. https://doi.org/10.1111/jam.13349
81. Zommiti M, Feuilloley MGJ, Connil N. Update of probiotics in the human world. Microorganisms. 2020; 8(12):1907. https://doi.org/10.3390/microorganisms8121907
82. Vandenbergh PA. Lactic acid bacteria and their metabolic products. FEMS Microbiol Rev. 1993; 12(1-3):221-38. https://doi.org/10.1111/j.1574-6976.1993.tb00020.x
83. Guillot JF. Probiotic feed additives. J Vet Pharmacol Ther. 2003; 26(Suppl 1):52-5.
84. Isolauri E, Sütas Y, Kankaanpää P, Arvilommi H, Salminen S. Probiotics: effects on immunity. Am J Clin Nutr. 2001; 73(2 Suppl):444S-50S. https://doi.org/10.1093/ajcn/73.2.444s
85. Di Marzio L, Centi C, Cinque B, Masci S, Giuliani M, Arcieri A, *et al.* Effect of *Streptococcus thermophilus* on ceramide levels and symptoms in atopic dermatitis. Exp Dermatol. 2003; 12(5):615-20. https://doi.org/10.1034/j.1600-0625.2003.00051.x
86. Guéniche A, Knaudt B, Schuck E, Volz T, Bastien P, Martin R, *et al. Vitreoscilla filiformis* lysate in atopic dermatitis: double-blind study. Br J Dermatol. 2008; 159(6):1357-63. https://doi.org/10.1111/j.1365-2133.2008.08836.x
87. Blanchet-Réthoré S, Bourdès V, Mercenier A, Haddar CH, Verhoeven PO, Andres P. Effect of a lotion containing the heat-treated probiotic strain *Lactobacillus johnsonii* NCC 533 in atopic dermatitis. Clin Cosmet Investig Dermatol. 2017; 10:249-57. https://doi.org/10.2147/CCID.S135529
88. Myles IA, Earland NJ, Anderson ED, Moore IN, Kieh MD, Williams KW, *et al.* First-in-human topical microbiome transplantation for atopic dermatitis. JCI Insight. 2018; 3(9):e120608. https://doi.org/10.1172/jci.insight.120608
89. Myles IA, Castillo CR, Barbian KD, Kanakabandi K, Virtaneva K, Fitzmeyer E, *et al. Roseomonas mucosa* therapy may involve TNF-mediated epithelial repair. Sci Transl Med. 2020; 12(561):eaaz8631. https://doi.org/10.1126/scitranslmed.aaz8631
90. Bustamante M, Oomah BD, Oliveira WP, Burgos-Díaz C, Rubilar M, Shene C. Probiotics and prebiotics for skin and urogenital care. Folia Microbiol (Praha). 2020; 65(2):245-64. https://doi.org/10.1007/s12223-019-00759-3
91. Rosenfeldt V, Benfeldt E, Valerius NH, Paerregaard A, Michaelsen KF. Probiotics in children with atopic dermatitis: permeability and GI symptoms. J Pediatr. 2004; 145(5):612-6. https://doi.org/10.1016/j.jpeds.2004.06.068
92. Kalliomäki M, Salminen S, Poussa T, Isolauri E. Probiotics for eczema prevention: 7-year randomised trial. J Allergy Clin Immunol. 2007; 119(4):1019-21. https://doi.org/10.1016/j.jaci.2006.12.608
93. Kim JY, Kwon JH, Ahn SH, Lee SI, Han YS, Choi YO, *et al.* Probiotic mix for eczema prevention: randomised trial. Pediatr Allergy Immunol. 2010; 21(2 Pt 2):e386-93. https://doi.org/10.1111/j.1399-3038.2009.00958.x
94. Jung GW, Tse JE, Guiha I, Rao J. Acne treatment with/without probiotics and minocycline: open-label trial. J Cutan Med Surg. 2013; 17(2):114-22. https://doi.org/10.2310/7750.2012.12026
95. Prince T, McBain AJ, O'Neill CA. *Lactobacillus reuteri* protects keratinocytes from *Staphylococcus aureus*-induced death. Appl Environ Microbiol. 2012; 78(15):5119-26. https://doi.org/10.1128/AEM.00595-12
96. Tan AU, Schlosser BJ, Paller AS. Diagnosis and treatment of acne in adult women. Int J Womens Dermatol. 2018; 4(2):56-71. https://doi.org/10.1016/j.ijwd.2017.10.006
97. Park SY, Kim HS, Lee SH, Kim S. Skin microbiota in acne: effects of systemic antibiotics. J Clin Med. 2020; 9(1):168. https://doi.org/10.3390/jcm9010168
98. Kim J, Ko Y, Park YK, Kim NI, Ha WK, Cho Y. Lactoferrin-enriched milk improves acne and lipid profile. Nutrition. 2010; 26(9):902-9. https://doi.org/10.1016/j.nut.2010.05.011
99. Fabbrocini G, Bertona M, Picazo Ó, Pareja-Galeano H, Monfrecola G, Emanuele E. *Lactobacillus rhamnosus* SP1 modulates gene expression in adult acne. Benef Microbes. 2016; 7(5):625-30. https://doi.org/10.3920/BM2016.0089
100. Yu Y, Dunaway S, Champer J, Kim J, Alikhan A. Changing our microbiome: probiotics in dermatology. Br J Dermatol. 2020; 182(1):39-46. https://doi.org/10.1111/bjd.18088

101. Lee YB, Byun EJ, Kim HS. Potential role of the microbiome in acne: a comprehensive review. J Clin Med. 2019; 8(7):987. https://doi.org/10.3390/jcm8070987
102. Di Marzio L, Cinque B, De Simone C, Cifone MG. Effect of *Streptococcus thermophilus* on ceramide levels in keratinocytes and stratum corneum *in vivo*. J Invest Dermatol. 1999; 113(1):98-106. https://doi.org/10.1046/j.1523-1747.1999.00633.x
103. Bowe WP, Logan AC. Acne vulgaris, probiotics and the gut-brain-skin axis - back to the future? Gut Pathog. 2011; 3:1. https://doi.org/10.1186/1757-4749-3-1
104. Pavicic T, Wollenweber U, Farwick M, Korting HC. Anti-microbial and -inflammatory activity and efficacy of phytosphingosine: an *in vitro* and *in vivo* study addressing acne vulgaris. Int J Cosmet Sci. 2007; 29(3):181-90. https://doi.org/10.1111/j.1467-2494.2007.00378.x
105. Lopes EG, Moreira DA, Gullón P, Gullón B, Cardelle-Cobas A, Tavaria FK. Topical application of probiotics in skin: adhesion, antimicrobial and antibiofilm *in vitro* assays. J Appl Microbiol. 2017; 122(2):450-61. https://doi.org/10.1111/jam.13349
106. Brook, I. Bacterial interference. Crit Rev Microbiol. 1999; 25(3):155-72. https://doi.org/10.1080/10408419991299211
107. Al-Ghazzewi FH, Tester RF. Effect of konjac glucomannan hydrolysate and probiotics on the growth of the skin bacterium Propionibacterium acnes *in vitro*. Int J Cosmet Sci. 2010; 32(2):139-42. https://doi.org/10.1111/j.1468-2494.2009.00555.x
108. Marinelli L, Fitz-Gibbon S, Hayes C, Bowman C, Inkeles M, Loncaric A, *et al*. Propionibacterium acnes bacteriophages display limited genetic diversity and broad killing activity against bacterial skin isolates. mBio. 2012; 3(5):e00279-12. https://doi.org/10.1128/mBio.00279-12
109. Brown TL, Petrovski S, Dyson ZA, Seviour R, Tucci J. The formulation of bacteriophage in a semi-solid preparation for the control of Propionibacterium acnes growth. PLoS One. 2016; 11(3):e0151184. https://doi.org/10.1371/journal.pone.0151184
110. Jończyk-Matysiak E, Weber-Dąbrowska B, Żaczek M, Międzybrodzki R, Letkiewicz S, Łusiak-Szelachowska M, *et al*. Prospects of phage therapy in the treatment of acne caused by Propionibacterium acnes. Front Microbiol. 2017; 8:164. https://doi.org/10.3389/fmicb.2017.00164
111. Knackstedt R, Knackstedt T, Gatherwright J. The role of topical probiotics in skin conditions: a narrative review. Int Wound J. 2020; 17(5):1345-51. https://doi.org/10.1111/iwj.13451
112. Foligné B, Dewulf J, Breton J, Claisse O, Lonvaud-Funel A, Pot B. Probiotic properties of non-conventional lactic acid bacteria: immunomodulation by *Oenococcus oeni*. Int J Food Microbiol. 2010; 140(2-3):136-45. https://doi.org/10.1016/j.ijfoodmicro.2010.04.007
113. Nayak BS, Marshall JR, Isitor G. Wound healing potential of ethanolic extract of *Kalanchoe pinnata* Lam. leaf: a preliminary study. Indian J Exp Biol. 2010; 48(6):572-6.
114. Peral MC, Huaman Martinez MA, Valdez JC. Bacteriotherapy with *Lactobacillus plantarum* in burns. Int Wound J. 2009; 6(1):73-81. https://doi.org/10.1111/j.1742-481X.2008.00577.x
115. Peral MC, Rachid MM, Gobbato NM, Huaman Martinez MA, Valdez JC. Interleukin-8 production by polymorphonuclear leukocytes from patients with chronically infected leg ulcers treated with *Lactobacillus plantarum*. Clin Microbiol Infect. 2010; 16(3):281-6. https://doi.org/10.1111/j.1469-0691.2009.02793.x
116. Notay M, Saric-Bosanac S, Vaughn AR, Dhaliwal S, Trivedi M, Reiter PN, *et al.* The use of topical *Nitrosomonas eutropha* for cosmetic improvement of facial wrinkles. J Cosmet Dermatol. 2020; 19(3):689-93. https://doi.org/10.1111/jocd.13060
117. Guéniche A, Bastien P, Ovigne JM, Kermici M, Courchay G, Chevalier V, *et al. Bifidobacterium longum* lysate, a new ingredient for reactive skin. Exp Dermatol. 2010; 19(8):e1-8. https://doi.org/10.1111/j.1600-0625.2009.00932.x
118. Nwanodi O. Skin protective nutraceuticals: the current evidence in brief. Healthcare (Basel). 2018; 6(2):40. https://doi.org/10.3390/healthcare6020040
119. Mirvish JJ, Pomerantz RG, Falo LD Jr, Geskin LJ. Role of infectious agents in cutaneous T-cell lymphoma: viral and bacterial. Clin Dermatol. 2013; 31(4):423-31. https://doi.org/10.1016/j.clindermatol.2013.01.009
120. Xu Y, Fisher GJ. Ultraviolet (UV) induced signal transduction in skin photoaging. J Dermatol Sci Suppl. 2005; 1(Suppl):S1-8. https://doi.org/10.1016/j.descs.2005.06.002
121. Grant WB. Solar UVB, vitamin D, skin cancer action spectra, and smoking are linked to solid tumours. Eur J Cancer. 2008; 44(1):12-5. https://doi.org/10.1016/j.ejca.2007.09.009
122. Wendt J, Schanab O, Binder M, Pehamberger H, Okun J, Kindermann J, *et al.* Site-dependent actinic skin damage as a risk factor for melanoma in Central Europe. Pigment Cell Melanoma Res. 2012; 25(2):234-42. https://doi.org/10.1111/j.1755-148X.2011.00946.x
123. Bocheva G, Slominski RM, Slominski AT. Neuroendocrine aspects of skin ageing. Int J Mol Sci. 2019; 20(11):2798. https://doi.org/10.3390/ijms20112798
124. Shibagaki N, Suda W, Clavaud C, Bastien P, Takayasu L, Iioka E, *et al.* Ageing-related changes in the diversity of women's skin microbiomes associated with oral bacteria. Sci Rep. 2017; 7(1):10567. https://doi.org/10.1038/s41598-017-10834-9
125. Sharma D, Kober MM, Bowe WP. Anti-ageing effects of probiotics. J Drugs Dermatol. 2016; 15(1):9-12.
126. Lin MY, Yen CL. Antioxidative ability of lactic acid bacteria. J Agric Food Chem. 1999; 47(4):1460-6. https://doi.org/10.1021/jf981149l
127. Lin MY, Chang FJ. Antioxidative effect of intestinal bacteria *Bifidobacterium longum* ATCC 15708 and Lactobacillus acidophilus ATCC 4356. Dig Dis Sci. 2000; 45(8):1617-22. https://doi.org/10.1023/A:1005577330695

128. Shen Q, Zhang B, Xu R, Wang Y, Ding H, Zhou P. Antioxidant activity in vitro of selenium-containing protein from the Se-enriched *Bifidobacterium animalis* 01. Anaerobe. 2010; 16(4):380-6. https://doi.org/10.1016/j.anaerobe.2010.06.006
129. Terahara M, Kurama S, Takemoto N. Prevention by lactic acid bacteria of low-density lipoprotein oxidation and its antiatherogenic effect in rabbits. Biosci Biotechnol Biochem. 2001; 65(8):1864-8. https://doi.org/10.1271/bbb.65.1864
130. Kang YM, Hong CH, Kang SH, Seo DS, Kim SO, Lee HY, *et al.* Anti-photoaging effect of plant extract fermented with *Lactobacillus buchneri* on CCD-986sk fibroblasts and HaCaT keratinocytes. J Funct Biomater. 2020; 11(1):3. https://doi.org/10.3390/jfb11010003
131. Rong J, Shan C, Liu S, Zheng H, Liu C, Liu M, *et al.* Skin resistance to UVB-induced oxidative stress and hyperpigmentation by the topical use of *Lactobacillus helveticus* NS8-fermented milk supernatant. J Appl Microbiol. 2017; 123(2):511-23. https://doi.org/10.1111/jam.13506
132. Feingold KR. The role of epidermal lipids in cutaneous permeability barrier homeostasis. J Lipid Res. 2007; 48(12):2531-46. https://doi.org/10.1194/jlr.R700013-JLR200
133. Farmer S, inventor. Topical compositions containing probiotic Bacillus bacteria, spores, and extracellular products and uses thereof. United States patent US 6,905,692 B2. 2005 Jun 14.
134. Yadav H, Jain S, Sinha PR. Production of free fatty acids and conjugated linoleic acid in probiotic dahi containing *Lactobacillus acidophilus* and *Lactobacillus casei* during fermentation and storage. Int Dairy J. 2007; 17(8):1006-10. https://doi.org/10.1016/j.idairyj.2006.12.003
135. Fahlén A, Engstrand L, Baker BS, Powles A, Fry L. Comparison of bacterial microbiota in skin biopsies from normal and psoriatic skin. Arch Dermatol Res. 2012; 304(1):15-22. https://doi.org/10.1007/s00403-011-1189-x
136. Gao Z, Tseng CH, Strober BE, Pei Z, Blaser MJ. Substantial alterations of the cutaneous bacterial biota in psoriatic skin. PLoS One. 2008; 3(7):e2719. https://doi.org/10.1371/journal.pone.0002719
137. Reygagne P, Bastien P, Cauavoux MP, Philippe D, Benyacoub J, Guéniche A, *et al.* The positive benefit of *Lactobacillus paracasei* NCC2461 ST11 in a dandruff and sensitive scalp condition. Benef Microbes. 2017; 8(5):671-80. https://doi.org/10.3920/BM2016.0144
138. Groeger D, O'Mahony L, Murphy EF, Bourke JF, Dinan TG, Kiely B, *et al. Bifidobacterium infantis* 35624 modulates host inflammatory processes beyond the gut. Gut Microbes. 2013; 4(4):325-39. https://doi.org/10.4161/gmic.25487
139. Chiba K. Development of functional cosmetic ingredients using lactic acid bacteria in Japan. Jpn J Lactic Acid Bact. 2007; 18(3):105-12. https://doi.org/10.4109/jslab.18.105
140. Lieurey S, Watkins K, inventors. Use of fermented milk product for skin treatment. United States patent US 2008/0252812 A1. 2008 Oct 16.
141. Di Marzio L, Cinque B, De Simone C, Cifone MG. Effect of the lactic acid bacterium *Streptococcus thermophilus* on ceramide levels in human keratinocytes *in vitro* and stratum corneum *in vivo*. J Invest Dermatol. 1999; 113(1):98-106. https://doi.org/10.1046/j.1523-1747.1999.00633.x
142. Miyazaki K, Hanamizu T, Iizuka R, Chiba K. Bifidobacterium-fermented soy milk extract stimulates hyaluronic acid production in human skin cells and skin. Skin Pharmacol Physiol. 2003; 16(2):108-16. https://doi.org/10.1159/000069031
143. Izawa N, Hanamizu T, Sone T, Chiba K. Effects of fermentation product of soybean by *Streptococcus thermophilus* YIT 2084 on hyaluronic acid production in human skin cells. J Biosci Bioeng. 2010; 109(4):356-60. https://doi.org/10.1016/j.jbiosc.2009.10.011
144. Cavaliere V, De Simone C, inventors. Sphingomyelinase compositions and use thereof. United States patent US 6,258,355 B1. 2001 Jul 10.
145. Weill FS, Cela EM, Paz ML, Ferrari A, Leoni J, Maglio DHG. Lipoteichoic acid from *Lactobacillus rhamnosus* GG as an oral photoprotective agent against UV-induced carcinogenesis. Br J Nutr. 2013; 109(3):457-66. https://doi.org/10.1017/S0007114512001225
146. Nakatsuji T, Chen TH, Butcher AM, Trzoss LL, Nam SJ, Shirakawa KT, *et al.* A commensal strain of *Staphylococcus epidermidis* protects against skin neoplasia by producing 6-N-hydroxyaminopurine. Sci Adv. 2018; 4(2): eaao4502. https://doi.org/10.1126/sciadv.aao4502
147. Zommiti M, Feuilloley MGJ, Connil N. Update of probiotics in the human world: a nonstop source of benefactions till the end of time. Microorganisms. 2020; 8(12):1907. https://doi.org/10.3390/microorganisms8121907
148. Lee GR, Maarouf M, Hendricks AJ, Lee DE, Shi VY. Topical probiotics: the unknowns behind their rising popularity. Dermatol Online J. 2019; 25(5):13030/qt6h00v76r. https://doi.org/10.5070/D3255044062
149. Habeebuddin M, Karnati RK, Shiroorkar PN, Nagaraja S, Asdaq SMB, Anwer MK, *et al.* Topical probiotics: more than a skin deep. Pharmaceutics. 2022; 14(3):557. https://doi.org/10.3390/pharmaceutics14030557
150. Puebla-Barragan S, Reid G. Probiotics in cosmetic and personal care products: trends and challenges. Molecules. 2021; 26(5):1249. https://doi.org/10.3390/molecules26051249
151. Patel A, Shah N, Prajapati JB. Clinical application of probiotics in the treatment of Helicobacter pylori infection—a brief review. J Microbiol Immunol Infect. 2014; 47(5):429-37. https://doi.org/10.1016/j.jmii.2013.03.010
152. Snydman, DR. The safety of probiotics. Clin Infect Dis. 2008; 46(Suppl 2): S104-11. https://doi.org/10.1086/523331

153. Shanahan F. A commentary on the safety of probiotics. Gastroenterol Clin North Am. 2012; 41(4):869-76. https://doi.org/10.1016/j.gtc.2012.08.006
154. Fedorak RN, Madsen KL. Probiotics and prebiotics in gastrointestinal disorders. Curr Opin Gastroenterol. 2004; 20(2):146-55. https://doi.org/10.1097/00001574-200403000-00017
155. Bull M, Plummer S, Marchesi J, Mahenthiralingam E. The life history of *Lactobacillus acidophilus* as a probiotic: a tale of revisionary taxonomy, misidentification and commercial success. FEMS Microbiol Lett. 2013; 349(2):77-87. https://doi.org/10.1111/1574-6968.12293
156. Dinleyici EC, Kara A, Ozen M, Vandenplas Y. Saccharomyces boulardii CNCM I-745 in different clinical conditions. Expert Opin Biol Ther. 2014; 14(11):1593-609. https://doi.org/10.1517/14712598.2014.937419
157. Champagne CP. Some technological challenges in the addition of probiotic bacteria to foods. In: Charalampopoulos D, Rastall RA, editors. Prebiotics and probiotics: science and technology. New York: Springer; 2009. p. 761-804. https://doi.org/10.1007/978-0-387-79058-9_19
158. Lahtinen S, Ouwehand AC, Salminen S, von Wright A, editors. Lactic acid bacteria: microbiological and functional aspects. 4th ed. Boca Raton: CRC Press; 2011. https://doi.org/10.1201/b11503
159. Pineiro M, Stanton C. Probiotic bacteria: legislative framework—requirements to evidence-based. J Nutr. 2007; 137(3 Suppl 2):850S-3S. https://doi.org/10.1093/jn/137.3.850S
160. Kolacek S, Hojsak I, Berni Canani R, Guarino A, Indrio F, Pot B, *et al.* Commercial probiotic products: a call for improved quality control. A position paper by the ESPGHAN Working Group for Probiotics and Prebiotics. J Pediatr Gastroenterol Nutr. 2017; 65(1):117-24. https://doi.org/10.1097/MPG.0000000000001603
161. Liang B, Xing D. The current and future perspectives of postbiotics. Probiotics Antimicrob Proteins. 2023; 15(6):1626-43. https://doi.org/10.1007/s12602-023-10045-x
162. Degnan FH. The US Food and Drug Administration and probiotics: regulatory categorisation. Clin Infect Dis. 2008; 46(Suppl 2): S133-6. https://doi.org/10.1086/523324
163. Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, *et al.* Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the scope and appropriate use of the term probiotic. Nat Rev Gastroenterol Hepatol. 2014; 11(8):506-14. https://doi.org/10.1038/nrgastro.2014.66
164. Salvetti E, O'Toole PW. When regulation challenges innovation: the case of the genus *Lactobacillus*. Trends Food Sci Technol. 2017; 66:187-94. https://doi.org/10.1016/j.tifs.2017.05.009
165. Foligné B, Daniel C, Pot B. Probiotics from research to market: the possibilities, risks and challenges. Curr Opin Microbiol. 2013; 16(3):284-92. https://doi.org/10.1016/j.mib.2013.06.008
166. Arora M, Baldi A. Regulatory categories of probiotics across the globe: a review representing existing and recommended categorisation. Indian J Med Microbiol. 2015; 33(Suppl):S2-10. https://doi.org/10.4103/0255-0857.150868
167. Amagase H. Current marketplace for probiotics: a Japanese perspective. Clin Infect Dis. 2008; 46(Suppl 2): S73-5. https://doi.org/10.1086/523338
168. Kumar H, Salminen S, Verhagen H, Rowland I, Heimbach J, Bañares S, *et al.* Novel probiotics and prebiotics: road to the market. Curr Opin Biotechnol. 2015; 32:99-103. https://doi.org/10.1016/j.copbio.2014.11.021
169. Tiwari G, Tiwari R, Pandey S, Pandey P. Promising future of probiotics for human health: current scenario. Chron Young Sci. 2012; 3(1):17-28. https://doi.org/10.4103/2229-5186.94308
170. Chen T, Wu Q, Li S, Xiong S, Jiang S, Tan Q, *et al.* Microbiological quality and characteristics of probiotic products in China. J Sci Food Agric. 2014; 94(1):131-8. https://doi.org/10.1002/jsfa.6221
171. Chen T, Wu Q, Zhou H, Deng K, Wang X, Meng F, *et al.* Assessment of commercial probiotic products in China for labelling accuracy and probiotic characterisation of selected isolates. Int J Dairy Technol. 2017; 70(1):119-26. https://doi.org/10.1111/1471-0307.12331