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Review

Hydrobiome of Thermal Waters: Potential Use in Dermocosmetics

María Lourdes Mourelle [1,*], Carmen P. Gómez [2] and José L. Legido [1]

[1] FA2 Research Group, Department of Applied Physics, University of Vigo, Campus Lagoas-Marcosende s/n, 36310 Vigo, Spain; xllegido@uvigo.es
[2] CINBIO—Biomedical Research Centre, University of Vigo, Campus Universitario de Vigo, 36310 Vigo, Spain; carmengomez@uvigo.es
* Correspondence: lmourelle@uvigo.es

Abstract: Over the course of the last 20 years, numerous studies have identified the benefits of thermal waters on different skin conditions. Consequently, several investigations have been carried out on their effects on the skin, which are linked to their chemical composition, and, recently, scientists have turned their attention to the role of the thermal spring's microbiota, named "hydrobiome", regarding these therapeutic effects. At the same time, the development of cosmetics based on pre, pro, and postbiotics has reached great relevance and research is increasing every day. This review gathers information on the biological diversity of thermal spring waters and their potential use in obtaining biological compounds, metabolites, or bacterial extracts for use in dermocosmetics as active ingredients. These bioactive compounds are able to improve dermatological diseases such as atopic dermatitis or rosacea and ameliorate pruritus and xerosis; moreover, they can increase protection against UV exposure, strengthen barrier function, maintain good homeostasis of skin defenses, repair damaged skin, promote wound healing, improve skin condition, reduce uneven skin pigmentation, and prevent skin aging. From a future perspective, fruitful cooperation among researchers, hydrologists, thermal spa centers, and cosmetic industries will drive this sector toward a better understanding of the role of the hydrobiome of thermal spring waters on healthy skin and dermatological diseases and consider the inclusion of derivatives of this hydrobiome (in the form of fermenters, lysates, extracts, etc.) in dermocosmetic formulations. Therefore, and being aware of the potential of the hydrobiome in dermatological and skin care applications, the future prospects for the use of bioactive substances derived from it in dermocosmetic formulations are promising.

Keywords: hydrobiome; skin microbiome; thermal water; cosmeceuticals

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1. Introduction

Thermal spring waters have been used to treat different ailments, mainly rheumatic and dermatologic diseases since ancient times. Thermal spring waters are effective in the treatment of several dermatological conditions, applied topically, both in the form of baths, sprays, or compresses. The mechanisms by which the thermal water acts, in spa therapy, involve chemical, thermal, mechanical, and immunological effects on different dermatologic conditions, such as atopic dermatitis, seborrhea, seborrheic dermatitis, psoriasis, and ichthyoses.

Cosmetic formulations are "any substance or mixture intended to be placed in contact with the external parts of the human body (epidermis, hair system, nails, lips, and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odors" (EU Regulation 1223/2009, Article 2.1.a).

Cosmetics are made from several active ingredients and an excipient; water is the main excipient in most formulas (lotions, creams, etc.); thus, mineral/thermal spring water can be used both as an active ingredient or as a part of the excipient. During the last decades,

cosmetic companies have launched products made with thermal water, mainly aimed at improving or relieving certain symptoms of skin affected by dermatological disorders and other skin conditions, such as dehydration, seborrhea, or acne.

There is a growing body of evidence that shows thermal spring waters are useful for the treatment of several skin diseases, and whose effects are linked to their chemical composition; however, recently, scientists have turned their attention to the role of the thermal spring's microbiota on these therapeutic effects.

On the other hand, research in recent years related to the link between the human microbiome and certain diseases, including dermatological disorders, has promoted the development of dermocosmetic products to alleviate or improve certain skin ailments, such as acne or atopic dermatitis, with the aim of repairing or balancing the microbiota, since it has been shown that the imbalance in skin microbiota is linked to some of these disorders. The active ingredients of these cosmetics include lysates, fermenters, or metabolites of microbial species related to the skin microbiota, and, in some cases, prebiotics, understood as nutrients for the skin-resident species.

Considering the great growth experienced by these types of cosmetics, the main companies that manufacture and market dermocosmetics whose main ingredient or excipient is thermal water have positioned their research toward extracts, lysates, or metabolites of the microbiota of these thermal waters, so that the efficacy of these ingredients can currently be evaluated.

The aim of this work is to revise the latest investigations that can shed light on this matter. For this review, Web of Science, SciFinder, and Scopus databases were reviewed up to March 2023. Search terms included "microbiome and thermal waters", "skin microbiome", "thermal spring waters and skin", combined with, for example, "cosmetics", "dermocosmetics", "cosmeceuticals", "probiotics", "postbiotics", "microalgae, and "cyanobacteria".

2. Human Microbiome and Health

The study of the human microbiome has aroused great interest in the last decade, evidencing its importance in human health. The interaction of the human being with the microorganisms that inhabit it is highly complex and encompasses different disciplines and specializations.

The Human Microbiome Project, of the National Institute of Health in the United States (Human Microbiome Project, NIH), arises as an initiative of this institution with the objective of identifying and characterizing the microorganisms that are associated with humans, both in health and in the disease, that is, of the human microbiome. It began in 2008 and lasted for five years, using techniques for the characterization of microbial communities, such as metagenomics and whole genome sequencing. Emphasis was placed on the microbiology of five locations in the body: oral, skin, vaginal, intestinal, and nasal/pulmonary, and since 2014, there have been numerous scientific publications that have shown that there are around 10 times more microbial cells than human cells in the human body [1]. Organized characterization of the human microbiome is also being carried out internationally under the auspices of the International Human Microbiome Consortium (www.human-microbiome.org; accessed on 20 March 2023).

The term "human microbiota" is the set of symbiotic microorganisms that coexist with the human organism without damaging it. The term "microbiome" refers to the entire microbiota habitat, including microorganisms, their genomes, and the surrounding environment.

The normal microbiota fulfills multiple functions, such as endocrine, neurological signaling, changes in bone mineral density, maturation of the immune system, inhibition of pathogens, the synthesis of vitamins (K, B_{12}, and folate), the metabolism of bile salts, and the modulation of some drugs [2].

There is a growing body of evidence that shows the relationship between microbiota and health. Disruption of the microbiome is associated with susceptibility to a range of diseases such as cancer, diabetes, allergy, obesity, and infection [3,4], and also in cancer, Alzheimer's disease [5], and inflammatory disease [6]. Other studies have suggested an association between the gut microbiome and the development of psoriasis [7], atopic dermatitis [8], hidradenitis suppurativa, acne, and rosacea [9].

Microbiota can also have an impact on ageing. Melby et al. [10] revised the role of the microbiome on aging. They postulated that longevity is inversely correlated with microbiota diversity and positively associated with an abundance of bacteria that metabolize fiber into short-chain fatty acids (SCFAs), which influence energy metabolism, homeostasis, and immunity in ways that promote healthy aging. Thus, the microbiome may play a role in the response to stressors and the degree to which hormetic versus detrimental responses are triggered, in turn, impacting aging.

Thus, in recent years, there has been a great development of pre, pro, and postbiotic products, both in the form of nutraceuticals for oral consumption and for topical application with the aim of repairing or balancing the microbiota.

The concept of probiotics was first coined by the Russian scientist Elie Metchnikoff in 1907 referring to microorganisms that are beneficial to health, based on the study of different fermented foods and observing that the microorganisms present in them could replace the harmful ones in the body [11].

Subsequently, the concept of prebiotics (nutrients for these probiotics) and the concept of synbiotics (a combination of probiotics and prebiotics and referring to the synergy between them) were developed [12]. The term microbiotics is also used to identify probiotics, and, more recently, the concept of postbiotics has emerged, referring to the use of dead or inactivated cells (non-viable microorganisms), cell extracts, or metabolites of these microorganisms that can provide favorable effects on human health, observing that the action of probiotics does not always depend on the organisms being alive, but of their metabolites [13]. The consensus definition proposed by the International Scientific Association of Probiotics and Prebiotics (ISAPP) in 2021 defines postbiotics as follows: "preparation of inanimate microorganisms and/or their components that confers a health benefit on the host" [14]. Later on, emerges the concept of paraprobiotics, which constitute inactivated/dead/non-viable microbial cells of probiotics as intact or ruptured, containing cell components of probiotic cells upon lysis [15]. Cuevas-González et al. [16] revised the health benefits, finding that some postbiotics and paraprobiotics exhibit bioactivities such as anti-inflammatory, immunomodulatory, anti-proliferative, antioxidant, and antimicrobial, and that these bioactivities are involved in the health-promoting effects observed in human and clinical trials. This review also mentioned that several technologies can be used for obtaining postbiotics and paraprobiotics, with a focus on inducing the loss of viability in the microorganism; the methods commonly used for these purposes include heat, high pressure, and sonication, among others.

Figure 1 summarizes the concept of prebiotic, probiotic, synbiotic and postbiotic.

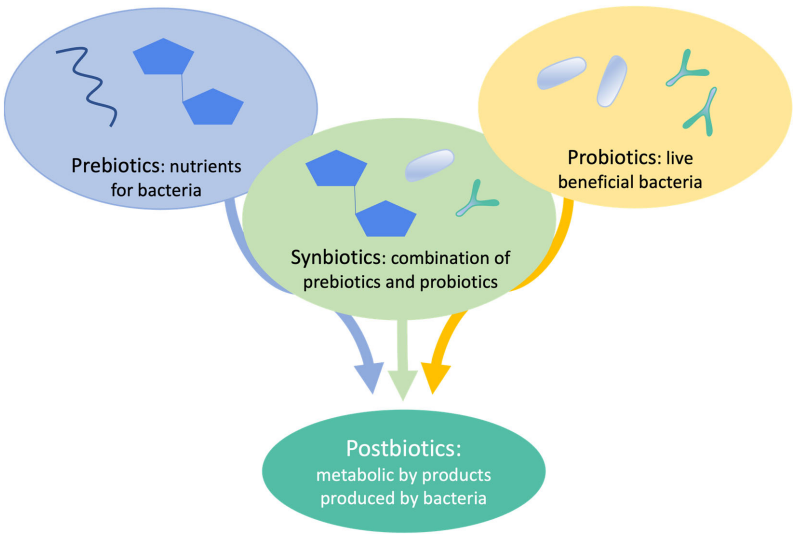

Figure 1. Concept of prebiotic, probiotic, synbiotic, and postbiotic (Adapted from Chaudhari and Dwivedi, 2022 [12]).

Postbiotic components include short-chain fatty acids, exopolysaccharides, vitamins, teichoic acids, bacteriocins, enzymes, and peptides in a non-purified inactivated cell preparation that may be of therapeutic interest, as there is increasing evidence that postbiotics have the potential to modulate human health. Specifically, several postbiotics have been shown to improve gut health by strengthening the gut barrier, reducing inflammation, and promoting antimicrobial activity against gut pathogens [17]. Postbiotics can be classified as the metabolites generated by the microbiota, such as short-chain fatty acids (SCFAs), exopolysaccharides, cell wall fragments, enzymes/proteins, and other metabolites, but also as structural, such as peptides, teichoic acids, and plasmalogens, or based on their elemental composition (carbohydrates, proteins, lipids, vitamins, etc.) [18].

3. Skin Microbiome

The skin is an environment with specific characteristics for microorganisms due to its acidic pH (approximately 5.5), the presence of a humid environment, and the hydrolipidic layer.

The set of microorganisms present on the skin is also called dermobiota [19–21]; they can be:

- Commensal and pathogenic microorganisms: a commensal microorganism can become a pathogen and cause pathology; for example, *Cutibacterium acnes* in the development of acne.
- Resident microbiota: it is permanent, stable, and diverse; and lives in symbiosis with skin cells. In addition, it exerts a protective function against other microorganisms, for example, *Sthaphyloccus epidermidis* and *Malasezzia*.
- Transient microbiota: varies throughout the day, depending on the activities carried out and environmental conditions; for example, *S. aureus* in atopic dermatitis.

An average of one billion microorganisms per cm^2 are found on the skin, of which 80 percent are aerobic without sporulation, such as cocci and bacilli. Deeper in the dermis and hair follicles (hypoxic environments) are less abundant but more diverse anaerobic and microaerophilic taxa that are potential reservoirs of pathogens in susceptible individuals. For example, *Cutibacterium acnes* is able to thrive in the anoxic sebaceous gland using proteases to release the amino acid arginine from skin proteins and lipases that degrade sebum triglycerides, releasing free fatty acids that promote bacterial adherence [22].

In the skin, as there are ridges, folds, holes, etc., and also secretions, there are different microenvironments that condition the types of microorganisms that inhabit them. Thus, they are distributed in moist microenvironments (armpit, antecubital fold, umbilicus, nasal vestibule, inguinal fold, intergluteal and popliteal folds, feet, and interdigital membrane) dominated by the genus *Corynebacterium*, and *Staphylococcus*, and the phylum Proteobacteria; dry (forearm and hand), where the bacterial flora is more diverse and consists mainly of *Corynebacterium*, Proteobacteria, and Bacteroidetes (flavobacteria); and sebaceous or seborrheic (head and back), dominated by lipophilic bacteria such as *Cutibacterium* and *Staphylococcus* [23].

The study of the scalp microbiome and its influence on certain disorders, such as alopecia areata, androgenetic alopecia, and cicatricial alopecia is a topic of great interest in the last decade. Actinobacteria, Firmicutes, and Proteobacteria predominate on the scalp surface, with the genus *Cutibacterium* spp. the most frequent (being *Cutibacterium acnes* the most prevalent bacteria) and *Staphylococcus* spp. (with a predominance of *Staphylococcus epidermidis*). Others equally present are *Corynebacterium* spp., *Streptococcus* spp., *Acinetobacter* spp., and *Prevotella* spp., among others. *Malassezia globosa* and *Malassezia restricta* species are also identified, being the most predominant fungal species. Likewise, the presence of *Demodex folliculorum* in the follicular infundibulum and *Demodex brevis* in sebaceous glands is known [24].

Another aspect that has gained great relevance in recent years is the relationship between the intestinal and skin microbiota. In fact, a new axis called the "gut–skin axis" has been described, finding associations between the intestinal microbiota and dermatological alterations such as acne, atopic dermatitis, rosacea, and psoriasis, and, for this reason, treatments have been developed with pre and postbiotics for the improvement of certain dermatological disorders [25].

The skin microbiome is individual and its interaction with the environment puts down colonies on all contact surfaces, called the bacterial profile. It is relatively stable, but it adapts daily to the environment, varying according to skin topography, age, gender, ethnicity, etc., environmental factors (humidity, temperature), diet, stress, hygiene routines, etc. [26,27].

Changes in the skin microbiota are linked to:

- Nutrients: Skin bacteria depend on available nutrients and enzymes produced by the host, such as phosphatases (7–8% acid and 12–13% alkaline) that allow them to utilize soluble organic phosphorus components. In the skin, some amino acids are produced by the host such as lactate, pyruvate, formiate, caprate, and valerate, together with others by the same bacteria such as succinate (a fermentation product of *S. epidermidis*). Sebum and stratum corneum lipids are used by *Malassezia* and *Corynebacterium* since they cannot produce their own lipids. *Corynebacterium* spp. use lipids to generate corynemycolic acids that coat their cell surface. For their part, *Staphylococcus* spp. have developed strategies to survive on the skin: they are halotolerant (they resist the high salt content of sweat), they use sweat urea as a nitrogen source, and they produce proteases that release nutrients from the stratum corneum [28].
- Genetics: Ethnic origin and pigmentation condition differences in the microbiota; it is thought that there are microbial interactions with melanocytes, whose metabolic activity changes in response to UVR exposure, hormonal stimuli, or inflammation [29].
- Diet and obesity: It has been observed that high-fat diets favor the growth of *Corynebacterium*, considering that it promotes skin inflammation through the expression of mycolic acid. It has also been observed that the relationship between Firmicutes and Bacteroidetes in obese people is altered, and weight loss induces changes in the composition of the microbiota, increasing Bacteroidetes and decreasing Firmicutes [30].
- Primary immunodeficiencies: Clostridials (*Anaerococcus* and *Peptoniphilus*) increase in the skin of patients with primary immunodeficiencies and may act as opportunistic pathogens [28].

Regarding hygiene routines, it should be remembered that excessive use of detergent or alcohol products, which are excessively lipid-reducing, alters the skin barrier, eliminating the hydrolipid layer and the natural dermobiota. UVR has also a great influence on the composition of the skin microbiome, and it has been shown to increase in the phylum Cyanobacteria and to decrease in the families Lactobacillaceae and Pseudomonadaceae [31].

3.1. Skin Microbiota throughout Life

Some skin changes are associated with age, since bacterial communities change with the stages of life and sexual maturity. For example, Staphylococcus-associated atopic dermatitis subsides in most children before puberty, whereas Malassezia-associated tinea versicolor is more common in adults [32].

In intra-uterus, several bacterial species have been detected in the placentas of healthy mothers, in the amniotic fluid of premature newborns, and in umbilical cord blood [30]. The microbiome in neonates resembles maternal vaginal communities if delivered vaginally (*Lactobacillus* and *Prevotella* spp.), or maternal skin communities if delivered by cesarean section (*Staphylococcus*, *Streptococcus*, *Corynebacterium*, and *Propionibacterium* spp.). Vernix caseosa, rich in lipids, prevents water loss, regulates temperature, and plays a key role in the development of early cutaneous innate immunity; contains IL-37, lysozyme, lactoferrin, alpha-defensins, and other antimicrobial peptides, thus inhibiting *Klebsiella*, *Bacillus megaterium*, *Listeria monocytogenes*, group B *Streptococcus*, and *Candida albicans*. *Staphylococcus*, *Corynebacterium*, and *Prevotella* abound in preterm infants, while *Brevundimonas*, *Flavobacterium*, and *Sphingobacterium* predominate in full-term infants. [33,34]. During childhood, the microbiome is acquired from close contacts, evolves throughout childhood, and its intervention could prevent diseases. In infants, Firmicutes (*Staphylococcus* and *Streptococcus*) predominate on the skin, followed by Actinobacteria, Proteobacteria, and Bacteroidetes [33]. The skin microbiota changes with puberty; Firmicutes (*Streptococcus* spp.), Bacteroidetes, and Proteobacteria abound at this stage, while the fungal community becomes more diverse [34]. In the post-puberal stage, hormones stimulate the seba-

ceous glands, which produce a greater amount of sebum, favoring the expansion of lipophilic microorganisms, such as *Propionibacterium* spp., *Corynebacterium* spp., and *Malassezia* spp. [34]. At the adult stage, *Corynebacterium*, *Propionibacterium*, *Streptococcus*, and *Staphylococcus* predominate [32], and, at the senile stage, there is a decrease in the production of antimicrobial peptides, increasing susceptibility to bacterial infections [33].

3.2. Skin Microbiome Functions

A "healthy microbiome" involves three main functions [20]:

- Maintenance of the microbial community itself: through the cleaning and decomposition of natural products, the production of energy, and the generation of metabolites.
- Development and maintenance of the immune response: through interactions with the host.
- Specialized functions: pH regulation, lipid degradation to contribute to the formation of the hydrolipidic barrier, and protection against immunosuppression caused by ultraviolet light, among others.

Additionally, it suppresses genes related to virulence and promotes genes associated with commensalism, influencing adnexal development, lipid metabolism, aging, sensory nerve function, tumorigenesis, and the innate immune system [29].

The close interaction between the skin microbiota and the immune system has been known in recent years. Before describing these interactions, it should be remembered that keratinocytes express pattern recognition receptors (RRP) and toll-like receptors (TLRs), which respond to pathogenic stimuli by producing antimicrobial peptides (AMP) and cytokines that inhibit the growth of pathogens. For their part, T lymphocytes, together with skin-resident macrophages and Langerhans cells, initiate and maintain the immune response by detecting and presenting microbial skin antigens [9].

Microorganisms residing on the skin also play a determining role in the immune response, since they occupy a niche competing for nutrients and space, produce antimicrobial substances, and induce the immune response by inhibiting the growth of pathogenic germs, promoting immune tolerance, and maintaining an immune circuit feedback that modulates and maintains the innate and adaptive immune response, maintaining homeostasis. Some of them have an important role, e.g., *Staphylococcus epidermidis* and *Cutibacterium acnes* [35,36].

Staphylococcus epidermidis (˜90% of the resident aerobic microbiota) plays several roles in the skin: it prevents the formation of biofilms through serine proteases; inhibits the colonization of potentially pathogenic strains of *S. aureus*, through the production of antibacterial peptides (bacteriocins); inhibits the growth of *Cutibacterium acnes* through fermentation products, such as succinic acid; and participates in immunomodulation, through the production of IL-10, anti-inflammatory cytokines, and lipoteichoic acid, and the inhibition of the production of inflammatory cytokines through the activation of TLR receptors in keratinocytes and antigen-presenting cells (APCs) [32,37,38].

Cutibacterium acnes breaks down sebaceous lipids into free fatty acids, inhibiting the colonization of opportunistic pathogens, which contributes to the maintenance of the acid pH of the skin, although, in some cases, if they are produced in excess, these free fatty acids can be irritating to the skin [21].

The different roles played by the skin microbiota in skin defenses can be summarized as follows [20]:

- Infections: The skin microbiota prevents the proliferation of pathogenic germs. Even so, some of them, such as *S. epidermidis*, can be opportunistic pathogens, producing nocosomial infections in immunocompromised patients.
- Inflammation: The skin microbiota plays a role in the control of local inflammation and the function of resident T lymphocytes. Alterations in the composition of the skin microbiome (dysbiosis) can change the reactivity of the immune system, causing the development of inflammatory diseases or protecting the host from an aberrant inflammatory response.

- Wound repair: When the skin barrier is broken, commensal microorganisms can behave as pathogens or generate microbial metabolites that further damage host tissues. Healing is accelerated in sterile environments, but at the same time, the commensal microbiota can produce AMP that inhibit invasion by pathogens. For example, *S. epidermidis* inhibits wound-associated inflammation by inhibiting cytokine release from keratinocytes.

4. Thermal Spring Waters Microbiome

Thermal spring waters have been traditionally used for their medicinal and well-being benefits. They have been reported to benefit a variety of diseases across rheumatology, gastroenterology, pulmonology, and dermatology. Caccipuoti et al. [39] described recent evidence of major dermatologic diseases that are frequently treated by balneotherapy with a remarkable rate of success. They also discussed the potential role of balneotherapy either alone or as a complement to conventional medical treatments, and suggested that balneotherapy offers several advantages, as this approach needs no chemicals or potentially harmful drugs; there are almost no side effects during and after treatment, and there is a low risk to the patient's general health and well-being.

The chemical and immunological basis of the therapeutic effects of thermal waters on chronic inflammatory skin diseases are quite well studied, but there is a lack of information about how the hydrobiome of thermal waters can play a role in recovering the skin.

The hydrobiome can be defined as the "natural microbial community present in waters". There is abundant scientific literature regarding the microbiological diversity of thermal springs waters, especially in extreme environments, such as hot spring waters, although other extremophile environments such as saline and acidic ones have also been investigated.

The most studied area is Yellowstone Park hot springs, and it was found that the dissolved nutrients and minerals have a great influence on microbial diversity, and the Microaerophilic genera of the *Aquificales* predominated in many of the planktonic communities. In contrast, taxa capable of mineral-based metabolism such as S(o) oxidation/reduction or Fe-oxide reduction predominated in sediment communities [40].

Microbial biodiversity has also been investigated in several thermal springs in Italy [41–45], France [46], Iceland [47,48], Hungary [49], Czech Republic [50], Croatia [51], Turkey [52], Armenia [53], and Russia [54,55]. In the eastern countries, other geothermal aquifers have been studied: Trans-Himalayan plateau [56], Pakistan [57,58], Tibet [59], China [60], India [61], Thailand [62], and Japan [63,64]. In the Latin-American countries, the most studied are Copahue in Argentina [65] and other thermal springs in Mexico, Perú, Colombia, and the Caribbean Island of Montserrat [66–69], and also, on the African continent, in Tunisia [70] and South Africa [71]. Some examples are described below.

Valeriani et al. [41] investigated the microbiome profile of several thermal springs in the Lazio region (Italy), finding a total of 12 main bacterial phyla, and demonstrating that waters did not show significant variations with most of the sequences assigned to *Proteobacteria* (82.3–98.6%) and *Firmicutes* (0.6–5.6%) phyla. They further hypothesized that some chemical characteristics are closely related to the prevalent microflora and biodiversity composition, as phylogenic grouping showed a clear separation between sulfurous and non-sulfurous waters. The same research group studied the bacterial biodiversity in Bullicame hot springs (sulfate-bicarbonate spring water) finding that, in the water, the main phyla were *Proteobacteria* (91%), *Firmicutes* (5%), *Chloroflexi* (1%), and other categories (<1%) including *Thermi*, *Bacteroidetes*, *Chlorobia*, *Actinobacteria*, and unclassified phyla (2%); the authors suggested that the high concentration of sulfur species and HCO_3 can be linked to create a selective environment where pioneer communities are able to live and shape the ecosystem [42]. Similar data were obtained by Paduano et al. [44] in Sirmione thermal spring, where the four dominant phyla were *Proteobacteria*, *Thermi*, *Thermodesulfobacteria*, and *Firmicutes*.

These results are in concordance with the studies performed in other areas. For example, in hot spring waters (over 40 °C) in Pakistan, the bacterial phyla *Proteobacteria*

and *Chloroflexi* are dominant [58], and the predominant genera are *Thiobacillus*, followed by *Sphingobium* and *Agrobacterium*. *Sulfuricurvum* was also found, which indicates the presence of sulfur oxidizers [72].

Skirnisdottir et al. [47] studied the microbial diversity of Iceland hot springs; the molecular diversity analysis showed that *Chloroflexus* was the dominant mat organism in the low-sulfide spring below 70 °C, whereas *Aquificales* was dominant in the high-sulfide spring (and similar to other hot springs in the world). The authors also found that a comparison with other published data indicated that there is a relationship between the mat type and composition of *Aquificales* on the one hand and the temperature and sulfide concentration on the other hand. Later on, a *Leptolyngbya*-like cyanobacterium was isolated from the warm saline waters of the Blue Lagoon, which is capable to grow well in warm (45–54 °C) waters at high salinities [48].

The Gellért Bath hot springs in Budapest (sulfate-bicarbonate spring water, 36 °C) were also investigated, in which the *Alphaproteobacteria* was characteristic in all spring waters; members of *Actinobacteria*, *Firmicutes*, *Beta-* and *Gammaproteobacteria*, *Deinococcus–Thermus*, and *Bacteroidetes* were also identified. Many of the detected taxa in well water are able to fix nitrogen, e.g., *Pseudomonas azotiofingens*, *Rhizobium alkalisoli*, *Rhizobium straminoryzae*, and also *Hartmannibacter diazotrophicus*; and the largest bacterial groups in the pool water belonged to the genera *Tistrella* and *Chelatococcus* [49].

Pedron et al. [73] studied the Comano thermal spring water (spring, well, storage tank, and bath tube), a bicarbonate-calcium spring water, which emerges at 27 °C, finding that the composition of the microbiome is dominated by *Proteobacteria* and *Nitrospirae* and family *Methylocystaceae* (*alpha-Proteobacteria*) was among the major components of the well microbiome, whereas in spring, storage tank, and bathtub, its abundance was much lower. They also found an unclassified genus of the thermophilic family methanocaldococcaceae.

Other recent studies were carried out in Australia. Aburto-Medina et al. [72] studied the geothermal spring waters of an Australian natural hot spring bathing facility comparing the "bathing microbiome" before and after bathing, finding that *Thiobacillus*, *Sphingobium*, and *Agrobacterium* were the predominant genera in samples collected from the borehole. The predominant genera changed to *Sphingobium*, *Parvibaculum*, and *Achromobacter* following chloride treatment and *Azospira* replaced the *Achromobacter* once the water reached ambient temperature and was stored ready to be used by bathers. The microbial community changed again following use by bathers, dominated by *Pseudomonas*, although *Sphingobium* persisted.

Extremely acid hydrothermal systems were also investigated. Crognale et al. [74] studied the thermal waters of Pisciarelli Spring (Campi Flegrei area, southern Italy), characterized by high levels of reduced gaseous species (e.g., H_2S, H_2, CH_4, and CO) and very low pH values (<2.3), showing that the microbiome in this extreme environment was mainly constituted by chemoautotrophic microorganisms that were likely involved in N-, S-, and Fe-bearing species transformations (e.g., *Acidianus infernus*, *Ferroplasma acidarmanus*, *Acidithiobacillus*, *Sulfobacillus*, and *Thaumarchaeota*).

Hypersaline environments are a great source of halophilic bacteria and derivatives. The Dead Sea is the most studied extreme hypersaline environment, as it is a very popular destination for thermal cures, and these waters are also used to prepare cosmetic formulations [75]. Over years and different studies, several halophilic bacteria have been found: *Haloarcula marismortui* (Volcani) [76]; *Bacillus persicus*, which showed antimicrobial activity [77]; and *Bacillus* species with antibacterial and antifungal activity [78].

Gosh et al. [79] revised the potential biotechnological applications of halophilic microorganisms, considering that these microorganisms can produce bioactive molecules such as enzymes, antibiotics, osmolytes, and polymers, with possible applications in bioremediation, enzyme industry, drug development, biofuels, and bioplastics, among others. Giordano et al. [80] also revised the potential of extreme ecosystems such as hydrothermal vents, marine areas of high pressure, and high salinity in which organisms have adopted a huge variety of strategies to cope with such harsh conditions, such as the production of

bioactive molecules potentially valuable for biotechnological applications and for pharmaceutical, nutraceutical, and cosmeceutical sectors.

Sorokin et al. [81] studied the sediments and brines from 12 hypersaline lakes (Russia, Mongolia, and North America) that have been isolated, enriched, and cultivated with different polysaccharides with the aim of studying them as a source of extremely halo(alkali)stable extracellular hydrolases, which have important application potential in the production of biofuel from lignocellulosic wastes [81].

As the microbiome contributes to multiple ecosystem functions and services through its interactions with a complex environment and other organisms, Zhu et al. [82] proposed establishing a new framework for microbiome study called "Ecosystem Microbiome Science" to study microbiomes of ecosystems as a whole, applying molecular and genomic technologies, together with data science and modeling [82]. This may lead to a greater understanding of the hydrobiome and its role in the broader context of the ecosystem microbiome.

Finally, it is worth mentioning that, according to Valeriani et al. [43], the microbiota of thermal waters changes dramatically after a seismic event, and persists for several months, so the authors proposed that microbiota could be used as a biomarker for the surveillance of spring waters.

Thermal spring waters have been demonstrated to improve dermatological diseases, but biological properties may not be entirely explained by their mineral composition only; therefore, the interactions between the biological fraction of thermal waters and the skin are an area of research of growing interest.

As has been previously mentioned, there is scarce information about the role of the hydrobiome in thermal cures, but some recent studies try to elucidate how certain microorganisms, traditionally known as "non-pathogenic flora", can contribute to the effects of water, together with the other very well-known mechanisms (thermal, chemical, and neuro-immune–endocrine). The physico-chemical profile of the thermal waters varies from Bicarbonate, Sulfate, Chloride, and Sulfide, as main anions, or Calcium, Sodium, and Magnesium as main cations; the genus and strains are also diverse, but there is a lack of studies that link the microbiota of thermal waters to their effects on the skin. Some examples are listed in Table 1.

Table 1. Thermal spring waters microbiome and skin interactions.

Thermal Spring Water	Main Composition	Microorganisms (Phyla/Genus/Strain)	Key Findings	References
Avène	Bicarbonate Calcium Magnesium	*Nitrospirae*	Decrease *S. aureus* Improve SCORAD index	[83,84]
Comano	Bicarbonate Sulphate	*Aeromonas hydrophila*, *Brevundimonas vesicularis*, *Chromobacterium violaceum*, *Citrobacter youngae*, *Empedobacter brevis*, *Pantoea agglomerans*, *Pseudomonas putida*, *Pseudomonas stutzeri*, and *Streptococcus mitis*.	Skin regeneration	[85,86]
La Roche-Posay	Bicarbonate Calcium Silica	*Xantomonadaceae* (*Proteobacteria*)	Psoriasis: Improve PASI index	[87]
			Atopic dermatitis: Improve SCORAD index	[88]
			Atopic dermatitis: Improve SCORAD index. Improve gut microbiota	[89]

Nevertheless, some research links thermal spring bathing with changes in the skin microbiota, which raises the question: What degree of influence does the microbiota of the

thermal springs have on the balance of the skin microbiota? Therefore, more studies are needed in this regard.

Despite there being only scant data on changes in the microbiome system of the skin during balneotherapy, some examples can shed light on this matter.

Dead Sea bathing is very well-known to improve psoriasis and other dermatological diseases; the bacterial and fungal microbiota of the skin were examined on healthy volunteers after a Dead Sea climatotherapy treatment, showing that the diversity of the bacterial community remained the same before and after the treatment, while the fungal diversity significantly decreased after the treatment; the authors suggested a restorative property of Dead Sea climatotherapy on the healthy skin mycobiota [90].

Recently, Bender et al. [91] compared the effects of Lakitelek thermal water and tap water on the skin's microbiome in healthy volunteers, showing that there is a difference between both waters. After balneotherapy in mineral water containing sodium hydrogen carbonate, the number of certain inflammatory infectious agents decreased (for example, *Pseudomonas*), and other more beneficial ones increased. For example, the *Deinococcus* genus increased, and knowing that may play an important role in inhibiting *Staphylococcus aureus* infection, this can be considered a positive effect. Moreover, the same happened with *Rothia mucilaginosa*, which is able to secrete anti-inflammatory mediators.

Bourrain et al. [84] studied the structure of skin microbiome in patients with atopic dermatitis and its changes during an 18-day course of hydrotherapy with Avène spring water, finding that the number of lesional sites colonized by *S. aureus*, and the SCORAD index were significantly reduced, mainly in inflammatory and moist areas, promoting the emergence of a diversified microflora [83]. Later on, the same research group studied the microbial diversity of this thermal spring water and concluded that bacteria were distributed into 39 phyla, with Nitrospirae and Proteobacteria as the most prevalent.

In previous studies, Comano spring water was able to improve skin regeneration in an animal experimental model, not only by increasing keratinocyte proliferation and migration, but also by modulating the regenerated collagen and elastic fibers in the dermis [85]. Therefore, Comano spring water was investigated in order to identify any possible correlation between these bacterial populations and the demonstrated biological properties of this water. A total of nine different strains were isolated: *Aeromonas hydrophila*, *Brevundimonas vesicularis*, *Chromobacterium violaceum*, *Citrobacter youngae*, *Empedobacter brevis*, *Pantoea agglomerans*, *Pseudomonas putida*, *Pseudomonas stutzeri*, and *Streptococcus mitis*. The authors found a favorable action of the native microbiota in Comano spring water on human fibroblast proliferation, and this regenerative effect might not be associated only with the well-known anti-inflammatory action of spring water. Therefore, a combination of biological properties of several bacterial species within this spring water might be responsible for its regenerative effects on human skin [86].

In an open-label study conducted by Martin et al. [87], microbial communities of patients with psoriasis vulgaris were characterized prior to and post a 3-week selenium-rich water balneotherapy treatment at the thermal care center La Roche-Posay (La Roche-Posay, France). Balneotherapy consisted of high-pressure filiform showers, baths, facial, and body spray treatments as well as La Roche-Posay thermal spring water (LRP-TSW) consumption. Results showed that the treatment with LRP-TSW significantly increased the level of the *Xanthomonas* genus and, to a lesser extent, the *Corynebacterium* genus. *Xanthomonas* is known to be keratolytic; therefore, authors associated the clinical improvement observed after a 3-week balneotherapy treatment with the increasing of this genus, possibly due to the effect of selenium-rich LRP-TSW.

Zeichner and Seite [88] revised the effects of La Roche-Posay thermal spring water (LRP-TSW) on the skin microbiome, concluding that clinical studies showed that topical treatment with LRP-TSW increases Gram-negative bacteria, with a reduction in Gram-positive bacteria, and improvements in skin microbial diversity. At the same time, skin condition in atopic dermatitis, psoriasis, and general dryness in otherwise healthy skin, has been shown to improve.

Recently, Thirion et al. [89], investigated the changes in gut microbiota of patients with Atopic Dermatitis (AD) after a 3-week balneotherapy treatment. The results showed a SCORAD reduction occurring during balneotherapy that was also associated with the gut microbiota. The authors postulated that the gut–brain–skin axis via a neurotransmitter such as GABA should be further studied in diseases such as AD.

5. Probiotics and Postbiotics in Dermocosmetics and Cosmeceuticals

As described in the previous paragraphs, the skin microbiome comprises several species of microorganisms; any imbalance in these microorganisms results in skin disorders. Acne, atopic dermatitis, psoriasis, and rosacea are some common skin conditions that arise due to an imbalance in the existing skin microbiome [92]. This is why, in recent years, cosmetic products have been developed that include prebiotics, probiotics, and/or postbiotics in their composition. The topical application of dermocosmetic and cosmeceutical products with probiotics can promote a positive balance of the skin in favor of beneficial bacteria, reducing and eliminating pathogens, especially in those pathologies associated with skin dysbiosis, which is responsible for immune dysfunction and disrupting the skin barrier. The effects of improving skin health by topical probiotics are considered mainly based on three elements: to antagonize pathogens, improve immunotolerance, and induce anti-inflammatory effects; to release bioactive molecules such as bacteriocins, modulins, antimicrobial peptides, and propionic acid; and to inhibit the growth of pathogens and recover skin barrier function [93]. Although the precise mechanisms by which probiotics improve skin health are not yet known, the literature and patents related to the application of topical probiotics for the treatment of various skin disorders continue to grow [94].

Puebla-Barragan and Reid [95] explored the existing research on probiotics for potential cosmetic and personal care applications, and also searched the websites of two major retailers of cosmetics in North America, revealing that at least 50 products are already being commercialized with a claim to contain "probiotics", whose most common claims are geared toward "balancing" the skin microbiome, improving the skin barrier, and enhancing the skin's overall appearance. The authors considered that a product claiming to "balance" the microbiome should have been studied, and the cosmetic industry needs to be consistent and transparent in its labeling practices and direct efforts to generate more scientific evidence before making such claims.

Habbedbuddin et al. [93] compiled the patents that include probiotics for skin care (20 patents) and summarized the probiotic microorganisms useful in the management of various skin disorders. In acne, topical probiotics improved the skin barrier and produced a secondary increase in antimicrobial peptides; the probiotic strains were *Streptococcus thermophiles*, *Enterococcus faecalis*, and *Streptococcus salivarius*. In atopic dermatitis, ointments comprising probiotics inhibited the growth of *S. aureus* and reduced symptoms; the probiotics strains were *Vitreoscilla filiformis*, *Streptococcus thermophiles*, *Lactobacillus johnsonii*, and *Roseomonas mucosa*. For dandruff and seborrheic dermatitis, *Vitreoscilla filiformis* was used, showing a reduction in erythema, scaling, and pruritis; and *Lactiplantibacillus plantarum*, *Lactobacillus fermentum*, and *Saccharomyces cerevisiae* were useful in wound healing.

Di Marzio et al. [96] investigated the effects of the topical treatment containing a sonicated preparation of the lactic acid bacterium *Streptococcus thermophilus* on ceramide levels of stratum corneum of healthy elderly women, finding a relevant increase in stratum corneum ceramide levels, and also the hydration values of the treated forearm of each subject were significantly higher than control sites.

Gueniche et al. [97], using a probiotic lysate from *Bifidobacterium longum* sp., demonstrated (in vitro, and in a clinical trial) that this non-replicating bacteria form applied to the skin was able to improve sensitive skin.

Ashoori et al. [98] developed three formulations from nanogel consisting of probiotic supernatant (*Lactobacillus reuteri*, *Lactobacillus fermentum*, and *Bacillus subtilis* sp. *natto*)-loaded chitosan nanogels, showing that all of them were able to improve wound healing. The same research group investigated, also in rats, the wound healing effect of three

cold creams formulated with the same probiotic supernatants, showing that all of them significantly accelerated the wound healing process, but *Bacillus subtilis* natto cold cream manifested a better wound healing property [99].

Rong et al. [100] investigated the preventive properties of the supernatant of *Lactobacillus helveticus* NS8-fermented milk against UV light-induced skin oxidative damage and hyperpigmentation in hairless mice, demonstrating the potential of these cell-free fermented products of lactic acid bacteria in topical photoprotection [100].

Furthermore, Notay et al. [101] investigated the effect of two different concentrations of aerosolized live *Nitrosomonas eutropha* in a buffer (lower concentration 1×10^9 cells/mL; and high concentration 8×10^9 cells/mL) in skin ageing. The results showed a significant difference in wrinkle depth and severity in the high-concentration probiotic group, and there was also a statistically significant improvement in pigmentation of the forehead and glabella in the higher-concentration group.

Postbiotics are also useful in the management of skin disorders and ageing. Postbiotic preparations of *Lactococcus chungangensis* induced the expression of wound-healing-promoting cytokines, growth factors, and chemokines [102]. Kim et al. [103] investigated the anti-aging effect of an *Epidermidibacterium keratini* ferment filtrate showing that it contained the metabolite called orotic acid, which can ameliorate the skin microbiota linked with the aging phenotype of the skin.

Duarte et al. [104] investigated the market of postbiotics, finding that they are mainly derived from lactic acid bacteria and *S. cerevisiae*. Postbiotics are able to restore/improve the skin barrier integrity, may have antioxidant activity, and can improve UV protection, delaying the ageing process of skin cells. Some of these postbiotics have also been shown to inhibit certain enzymes associated with extracellular matrix disintegration, or up/downregulate some genes to potentially reduce inflammatory response. Furthermore, some of these molecules also demonstrated antimicrobial activity with the potential to fight some skin conditions where microbiota influence has been hypothesized (e.g., acne vulgaris, scalp infectious diseases). When compared to probiotics, postbiotics have a longer shelf life and greater safety and do not require viability in topical formulations, which turns them into an innovative approach within the cosmetic ingredients market.

A study conducted by Iglesia et al. [105] investigated the effects on the dermal–epidermal junction of an anti-aging facial moisturizer formulated at a skin neutral pH with a prebiotic (alpha glucan-oligosaccharide) and a post-biotic (*Pseudoalteromonas* ferment extract), finding that they can be effective in improving the diversity and balance of the facial microbiome at the species level while providing anti-aging benefits.

Finally, it is worth mentioning the investigation related to spermidine and ageing. Kim et al. [106] investigated the secretions of some species of *Streptococcus* in in vitro and clinical studies and found that secretions of *S. pneumoniae* and *S. infantis* induced the expression of genes associated with the formation of skin structure and the skin barrier function in human skin cells. Furthermore, Streptococcus-secreted spermidine contributed to the recovery of skin structure and barrier function through the upregulation of collagen and lipid synthesis in aged cells. The authors suggested that skin microbiome could play a role in anti-aging and clinical applications.

Oral prebiotics and probiotics for skin care also should be taken into consideration, as several studies have demonstrated an improvement in skin hydration, skin gloss, elasticity, and resistance to UVA light, as well as wrinkles reduction [107].

6. Dermocosmetics and Hydrobiome from Thermal Spring Waters

Thermal spring waters have been shown to have an impact on membrane fluidity, skin barrier repair, anti-radical, antioxidant, anti-inflammatory, and immunomodulatory properties, along with proliferative activity and the regulation of processes involved in ageing and moisturizing [108]. The main companies that elaborate and sell dermocosmetics whose main ingredient or excipient is thermal water have positioned their research toward

extracts, lysates, or metabolites of the microbiota of these thermal waters, and therefore, currently, the efficacy of these ingredients can be evaluated.

From the analysis of scientific articles, only six companies that developed dermocosmetic products linked to the hydrobiome of thermal spring waters were found (Avène, Blue Lagoon, Comano, La Roche-Posay, Uriage, and Vichy). The active ingredients range from extracts to exopolysaccharides, peptides, and lipids (Table 2). In all of them, previous in vitro and ex vivo studies were carried out to evaluate their potential therapeutic and cosmetic activity, which are described below. Some cosmetic companies have also developed patents (which are listed in the next section).

Table 2. Active ingredients derived from the hydrobiome of thermal spring waters for dermocosmetic uses.

Thermal Spring Water	Composition *	Microorganism Pre/Pro/Pos-Biotic	Type of Study	Dermocosmetic Formulation/Active Ingredient	Effects on the Skin	References
Avène (ATW)	Bicarbonate Calcium Magnesium Silica Sulfate Chloride Potassium Sodium	*Aquaphilus dolomiae* extract	In vitro	-	Inhibition expression of the inflammatory mediators	[109]
		Aquaphilus dolomiae extract	Ex vivo	-	Inhibition of SP-stimulated release of IL-8 and histamine (92% and 112%, respectively)	[110]
		Aquaphilus dolomiae aqueous protein extract	In vitro	-	Counteracting the mitogenic effect of a *S. aureus* secretome on CD4.T cells	[111]
		Aquaphilus dolomiae proteins and lipopolysaccharides extract (I-modulia)	In vitro	-	Immunomodulatory, anti-inflammatory, and antipruritic activity in AD pharmacological model	[112]
		Aquaphilus dolomiae extract (ADE-G1)	Ex vivo	-	Modulate the inflammatory response Increasing antimicrobial activities Strengthening barrier function, by restoring filaggrin expression	[113]
		Aquaphilus dolomiae extract (AEG-3)	In vitro Ex vivo	-	Inhibition of SP-stimulated release of inflammatory cytokines (IL-1b and TNF-a) Inhibit IL-8 with inhibition of histamine	[114]
		Aquaphilus dolomiae extract (AEG-2)	In vivo Ex vivo	-	Increasing fibroblast proliferation and keratinocyte migration Induction re-epithelialization of wounded skin	[115]
		Aquaphilus dolomiae extract	Open-label, real-world study	Emollient cream	Improvement of symptoms of xerosis and pruritus by more than 50%	[116]
		Aquaphilus dolomiae extract	Real-world, prospective, observational, multicenter study	Emollient balm	Reduction in xerosis severity in cancer patients (objective clinical signs, 67.7%; subjective clinical signs, 57.4%)	[117]

Table 2. *Cont.*

Thermal Spring Water	Composition *	Microorganism Pre/Pro/Pos-Biotic	Type of Study	Dermocosmetic Formulation/Active Ingredient	Effects on the Skin	References
Blue Lagoon (BL)	Chloride Sodium Potassium Calcium Silica	Blue Lagoon filamentous algae extract Blue Lagoon coccoid algae extract + solution from silica mud	In vitro In vivo	- Galenic formulation	Reduction in TEWL (by increasing mRNA expression for involucrin, filaggrin, and transglutaminase-1) Protection from UV radiation (UV-induced gene expression was reduced) Reduction in TEWL	[118]
		Cyanobacterium aponinum extract	In vitro	-	Stimulation of human dendritic cells (DCs) to produce immuno-suppressive cytokine IL-10	[119]
		Cyanobacterium aponinum extract	In vitro		Decreasing number of pigment spots Diminution uneven skin pigmentation	[120]
Comano (CTW)	Bicarbonate Calcium Sulphate Magnesium	*Rudaea cellulosilytica*, *Mesorhizobium erdmanii*, *Herbiconiux ginsengi*, *Fictibacillus phosphorivorans* lysates	In vitro	–	Human fibroblast stimulation	[121]
La Roche-Posay (LRP)	Bicarbonate Calcium Silica Magnesium Strontium Selenium	*Vitreoscilla filiformis* (Biomass fraction obtained by fermentation)	In vitro		Endogenous antioxidant defenses stimulation	[122]
		Vitreoscilla filiformis extract	Randomized, double-blind, vehicle-controlled trial	Ointment	Improvement of AD skin symptoms	[123]
		Culture of *V. filiformis* in La Roche-Posay thermal water	Monocenter, intra-individual, left–right comparison study	Cream	Improvement of AD skin symptoms	[124]
		Culture of *V. filiformis* in La Roche-Posay thermal water	Randomized, double-blind, vehicle-controlled, and parallel-group comparison study	Lotion	Reduction pruritus of seborrheic dermatitis	[125]
		Vitreoscilla filiformis lysate	Prospective, double-blind, placebo-controlled clinical study	Cream	Decreasing SCORAD levels and pruritus Decreasing loss of sleepReduction in *Staphylococcus aureus* colonization Skin barrier improvement	[126]
		Vitreoscilla filiformis lysate	In vitro In vivo	-	Reduction in inflammation of AD	[127]
		Vitreoscilla filiformis	Double-blind, randomized, comparative study	Emollient cream	Normalizing skin microbiota Reduction number and severity of flare-ups	[128]
Uriage (UTW)	Sulphate Chloride Sodium Bicarbonate Calcium Magnesium	Unknown (PS291®, a rhamnose-rich polysaccharide obtained by fermentation)	In vitro	Emollient cream (UTW + PS291®)	Reduction in biomass of *Cutibacterium acnes* Staphylococcus aureus final biomass decreased Antibiofilm activity	[129]

Table 2. *Cont.*

Thermal Spring Water	Composition *	Microorganism Pre/Pro/Pos-Biotic	Type of Study	Dermocosmetic Formulation/Active Ingredient	Effects on the Skin	References
Vichy (VTW)	Magnesium Potassium Calcium Sulphate Sodium	*Vitreoscilla filiformis* lysate	Randomized, split-face study	Dermocosmetic formulation (M89PF) Containing Vichy mineral water, *V. filiformis* lysate, niacinamide, hyaluronic acid, and vitamin E	Skin erythema, tightness, dryness, hydration, and TEWL improvement	[130]

* Taken from [108]. AD: Atopic Dermatitis; TEWL: Transepidermal Water Loss.

Despite not being cosmetic, it is worth mentioning the richness in microalgae and cyanobacteria of the dermocosmetic and dermatological peloids (mud from thermal springs waters) as both seem to exert a great influence on their therapeutic and cosmetic properties, since they have been proven to generate biologically active substances (especially during the maturation process), which, in turn, are responsible for the beneficial effects and actions on the skin. Mourelle et al. [131] revised the biological composition of several peloids, finding that the biological communities were diverse, and highlighting those from Euganea basin muds in the Spa area of Abano Terme (Italy), where strains of the *Phormidium* genus, and also new species such as *Cyanobacterium aponinum* or *Anoxybacillus thermarum*, were found. In other Italian thermal spas, species of *Chlorella* sp., *Coccomyxa* sp., *Scenedesmus* sp., *Leptolyngbya* sp., and *Anabaena* sp. were identified, along with the genera *Pelobacter*, *Desulfomonile*, and *Thiobacillus*. In France, nine cyanobacterial were isolated from the Thermes de Balaruc-Les-Bains muds, belonging to the orders Chroococcales, and in Dead Sea mud, *Bacillus persicusi* was identified, which is known to be responsible for antimicrobial activity.

6.1. Aquaphilus Dolomiae Extracts

Several studies investigated the effects of three different *Aquaphilus dolomiae* extracts, obtained from the aquifer of Avène thermal spring water, Cévennes mountains, France, by downstream extraction methods.

Aries et al. [109] investigated the effects that an *Aquaphilus dolomiae* extract (ADE-G1) containing periplasmic and membrane proteins, peptides, lipopolysaccharides, and exopolysaccharide had on atopic dermatitis cell models. The effects of the extract on pruritus and inflammatory mediators and immune mechanisms were evaluated, finding that, in a keratinocyte model, the extract inhibited the expression of inflammatory mediators, thymic stromal lymphopoietin, interleukin (IL)-18, IL-4R, IL-8, monocyte chemoattractant protein-3, macrophage inflammatory protein-3a, and macrophage-derived chemokine and induced the expression of involucrin. They also found that the extract inhibited protease-activated receptor-2 activation in HaCaT human keratinocytes stimulated by the stratum corneum tryptic enzyme and T helper type (Th) 1, Th2, and Th17 cytokine production in Staphylococcal enterotoxin B–stimulated CD4+ lymphocytes. Additionally, the extract was able to activate the innate immunity through toll-like receptor (TLR) 2, TLR4, and TLR5 activation (in recombinant human embryonic kidney 293 cells) and through antimicrobial peptide induction (psoriasin, human beta-defensin-2, and cathelicidin), mainly through TLR5 activation (in normal human keratinocytes). The authors concluded that, taking into consideration the effect on inflammatory and immune responses, the *A. dolomiae* extract may be of value by virtue of its potential as an adjunctive treatment of atopic dermatitis inflammatory and pruritic lesions [109].

Later on, using the same *A. dolomiae* extract (ADE-G1), Nguyen et al. [110] investigated the inhibition of human mast cell degranulation in vitro and its effect on substance P-induced neurogenic inflammation on ex vivo human skin explants. The results showed that ADE-G1 topically applied (1%) inhibited the SP-stimulated release of IL-8 and histamine by 92% and 112%, respectively.

Further studies showed that an aqueous protein extract of *Aquaphilus dolomiae* counteracted the mitogenic effect of a *S. aureus* secretome on CD4.T cells, through the activation of resident immune cells producing anti-inflammatory cytokines such as IL-10, suggesting a new therapeutic approach for the treatment of atopic dermatitis [111]. Similarly, an extract of *A. dolomiae* (called I-modulia), containing proteins and lipopolysaccharides, showed immunomodulatory, anti-inflammatory, and antipruritic activity in an atopic dermatitis pharmacological model [112].

Galliano et al. [113] investigated the protective effect of *Aquaphilus dolomiae* extract (ADE-G1) on tight junction barrier function in a *Staphylococcus aureus*-infected atopic dermatitis model. Results showed that ADE-G1 strongly increased transepithelial electrical resistance in non-infected cells and provided protection against infection by overcoming the decrease in transepithelial electrical resistance induced by the infection with *S. aureus*. In infected cells exposed to a pro-inflammatory environment—depicting atopic dermatitis-like conditions—transepithelial electrical resistance protection by ADE-G1 was still observed. Furthermore, gene expression analysis of infected and pro-inflammatory stimulated cells indicated that *A. dolomiae* extract modulated the inflammatory response (induced IL-8 and attenuated CCL20 expression), increased antimicrobial activities, and strengthened barrier function, by restoring filaggrin expression.

Lestienne et al. [114] evaluated the global protective properties of *Aquaphilus dolomiae* extract (AEG-3) using neuro-inflammatory in vitro models, focusing on the role of substance P (SP) as an inflammatory mediator in cutaneous neurogenic inflammation. The results showed that *A. dolomiae* extract significantly inhibited the SP-stimulated release of inflammatory cytokines (IL-1b and TNF-a) from normal human keratinocytes; and, significantly and dose-dependently, inhibited SP-stimulated activation of human mast cells. Additionally, it significantly inhibited the veratridine-stimulated release of SP from human sensory neurons, and, when applied topically to an ex vivo human explant model, significantly inhibited IL-8 with the inhibition of histamine.

Similar investigations were carried out with another *Aquaphilus dolomiae* extract (AEG-2) evaluating the wound-healing effects using in vitro and ex vivo models of injured skin. Results showed that ADE-G2 increased fibroblast proliferation and keratinocyte migration, as well as the re-epithelialization of wounded ex vivo skin. ADE-G2 was able to induce the expression of all AMP genes analyzed in keratinocytes, as well as stimulate the release into the medium of the hBD2 peptide, encoded by DEFB4A/B. The authors concluded that *A. dolomiae* extract is a promising component for use in formulations for repairing damaged skin and to promote wound healing [115].

In an open-label, real-world study that involved 5910 patients from 33 European, South American, Asian, and North and South African countries, Delauran et al. [116] investigated the effects of an emollient containing an extract of *Aquaphilus dolomiae* (7-day routine, twice daily on the face and body), finding that this 7-day regimen was a universally effective treatment for pruritus and xerosis, regardless of the underlying pathology, reducing the severity by more than 50%.

Recently, Vendedry et al. [117] studied the effects of an extract of *Aquaphilus dolomiae* (AEG-2) in acute xerosis. In a real-world, prospective, observational, multicenter study, which involved 319 xerotic cancer patients, an emollient containing AEG-2 was applied daily for 4 weeks. The xerosis severity was reduced in 62.7% of patients; the mean total severity scores for objective and subjective clinical signs were reduced by 67.7% and 57.4%, respectively; and the mean Dermatology Life Quality Index (DLQI) score also significantly improved at the end of follow up (−56.6%). Additionally, the product was rated as "effective" or "very effective" by the physician for over 80% of patients.

6.2. *Cyanobacterium aponinum* and Other Blue Lagoon Algae Extracts

The microalgae of Blue Lagoon geothermal water have been extensively investigated over the last 15 years. *Cyanobacterium aponinum* is the dominant member of the Blue Lagoon's microbial ecosystem.

Grether-Beck et al. [118] studied the effects of two microalgae extracts: Blue Lagoon filamentous algae extract and Blue Lagoon coccoid algae extract, and also a solution from Blue Lagoon silica mud. In an in vitro study, the extract from silica mud and both extract algae induced involucrin, loricrin, transglutaminase-1, and filaggrin gene expression in primary human epidermal keratinocytes. Extracts from silica mud and coccoid algae type inhibited the UVA radiation-induced upregulation of matrix metalloproteinase-1 expression and both algae, as well as the silica mud extracts, induced collagen 1A1 and 1A2 gene expression in this cell type. Additionally, in an in vivo study, a galenic formulation containing all three extracts induced identical gene regulatory effects, which were associated with a significant reduction in transepidermal water loss [118].

In an in vitro study, Gudmundsdottir et al. [119] investigated the immunomodulatory effects of exopolysaccharides (EPSs) secreted by *C. aponinum*, showing that these EPSs are able to stimulate human dendritic cells (DCs) to produce vast amounts of the immunosuppressive cytokine IL-10. These DCs induced differentiation of allogeneic CD4+T cells with increased T regulatory cells but decreased Th17 phenotype. The authors suggested that exopolysaccharides may be involved in the therapeutic results observed in psoriasis patients following a treatment in the Blue Lagoon [119]. Later studies suggested that exopolysaccharides may induce a regulatory phenotype of DCs, T cells that are less active/inflammatory and less prone to being retained in the skin, and keratinocytes that induce less recruitment of inflammatory cells to the skin, and these effects may be mediated by the effects of EPSs on C-type lectin domain family 7 member A (CLEC7A) and Spleen tyrosine kinase (SYK), involved in inflammation, autoimmunity, and allergy [132].

Further studies on normal human epidermal melanocytes, which had been treated with nontoxic concentrations of Blue Lagoon algae extract (*Cyanobacterium aponinum*), showed a significantly reduced expression of the α melanocyte-stimulating hormone-induced expression of genes important for melanin synthesis, such as tyrosinase, tyrosinase-related protein 1, dopachrome tautomerase, melan A protein, and pre-melanosome protein. Additionally, a randomized, double-blind, intra-individual, comparative split-face in vivo study was performed; 60 volunteers, suffering from pigment spots were treated twice daily, for 12 weeks, with a serum containing Blue Lagoon algae or a vehicle control. Using digital photography under cross-polarized lighting and RBX technology (VISIA CR), the results revealed that the number of pigment spots in the serum-treated face decreased significantly compared to the vehicle-treated side, so Blue Lagoon algae could be useful in reducing uneven skin pigmentation [120].

6.3. Comano Thermal Spring Microflora

In previous studies, Comano spring water was able to improve skin regeneration in an animal experimental model, not only by increasing keratinocyte proliferation and migration, but also by modulating the regenerated collagen and elastic fibers in the dermis; therefore, non-pathogenic bacteria were investigated in order to identify any possible correlation between these bacterial populations and the demonstrated biological properties of the Comano water. A total of nine different strains were isolated from the Comano spring water: *Aeromonas hydrophila*, *Brevundimonas vesicularis*, *Chromobacterium violaceum*, *Citrobacter youngae*, *Empedobacter brevis*, *Pantoea agglomerans*, *Pseudomonas putida*, *Pseudomonas stutzeri*, and *Streptococcus mitis*. Considering that the correlation between the well-known beneficial effects on the skin and the resident non-pathogen bacterial populations was demonstrated in certain spring waters, the authors concluded that the non-pathogenic bacterial populations of the Comano spring water are likely to be credited for its demonstrated regenerative properties [86].

Later on, four lysates obtained from Comano microflora were investigated with the aim of studying their regenerative properties. Human fibroblasts were cultured with *Rudaea cellulosilytica* (L1), *Mesorhizobium erdmanii* (L2), *Herbiconiux ginseng* (L3), and *Fictibacillus phosphorivorans* (L4) lysates, and cell proliferation was evaluated by spectrophotometric absorbance analysis after the XTT-Microculture Tetrazolium Assay. Results showed that, among the four bacterial species, stimulation of cell proliferation was observed only after

the addition of Firmicutes-derived bacterial lysates (L4) to the culture medium. L1 showed weak inhibitory power on fibroblast growth throughout the observation time; L2 and L3 showed enhancement of cell proliferation, followed by a decrease in the rate of proliferation by 72 hours, with an eventual cell proliferation rate that was lower than that of the control. The authors concluded that there is a favorable action of the native microbiota in Comano spring water on human fibroblast proliferation, and this regenerative effect might not be associated solely with the well-known anti-inflammatory action of spring water. Therefore, a combination of biological properties of several bacterial species within this spring water might be responsible for its regenerative effects on human skin [121].

6.4. *Vitreoscilla filiformis*

Vitreoscilla filiformis is a non-photosynthetic, nonfruiting, filamentous, bacterium belonging to the Beggiatoales order; it was named based on its colorless gliding filamentous morphology. In the Pyrénées mountains, *V. filiformis* was spotted in spa muds used for skin cures and subsequently fermented at an industrial scale for more than 20 years to generate a bacterial lysate to add to emollients [133,134].

The vast majority of studies on *V. filiformis* extracts and lysates are restricted to the skin care of atopic dermatitis [123–128], but also in sensitive skin [135], and even in healthy skin, they have been able to strengthen the skin physical barrier function and maintain good homeostasis of skin defenses [122].

Mahe et al. [122] investigated, in vitro, a biomass fraction obtained by the fermentation of *V. filiformis*. Using normal human keratinocytes and normal human fibroblasts demonstrated that *V. filiformis* stimulated endogenous antioxidant defenses by stimulating mitochondrial manganese superoxide dismutase 2 (MnSOD2) activity at both the mRNA and protein levels. The authors suggested that *V. filiformis* could induce skin cells to produce their own endogenous environmental stressors such as UV irradiation as well as to combat endogenous sources of deleterious free radicals involved in skin ageing. Additionally, in an in vivo study, *V. filiformis* was found to significantly inhibit the appearance of sunburn cells in UVB-exposed areas, a signature of skin alteration that may be linked to a defect in MnSOD protective activity.

Gueniche et al. [123–126] conducted four studies mainly focused on atopic dermatitis. In 2006, this research group investigated the efficacy and safety of a 5% *V. filiformis* extract-containing ointment on mild to moderate AD in a randomized, double-blind, vehicle-controlled trial. Results showed that, after 28 days of treatment with the ointment, the AD skin symptoms significantly improved, and the beneficial effects were observed after two weeks of treatment and increased thereafter [123].

In 2008, Gueniche et al. [124] reported, in a monocenter, intra-individual, left–right comparison study, that a cream containing 5% biomass, from a culture of *V. filiformis* in La Roche-Posay thermal water, was able to improve Atopic Dermatitis symptoms to a greater extent than that of a standard cream formulated with LRP water (referred to as the control).

The same lotion (5% LRP-biomass lotion) was able to reduce pruritus of seborrheic dermatitis. A total of 60 patients with moderate scalp seborrheic dermatitis were included in a randomized, double-blind, vehicle-controlled, and parallel-group comparison study. The total clinical score (sum of erythema and scaling subscores) showed a high improvement (62.7% decrease) in the group treated with the test lotion (5% LRP-biomass lotion) once daily for 4 weeks compared to the vehicle-treated group [125].

Later on, the same research group performed a prospective, double-blind, placebo-controlled clinical study with a cream containing a 5% lysate of the nonpathogenic bacteria *Vitreoscilla filiformis*. Efficacy was evaluated by the SCORe of Atopic Dermatitis (SCORAD), transepidermal water loss (TEWL), assessment of microflora, and the patient's assessment of itch and loss of sleep. Authors found that, compared with the placebo, *V. filiformis* lysate significantly decreased SCORAD levels and pruritus; significantly decreased loss of sleep from day 0 to day 29; and a qualitative and quantitative assessment of cutaneous microbial colonization revealed that *V. filiformis* lysate reduced *Staphylococcus aureus* colonization of

the skin. Furthermore, the skin barrier as determined by TEWL also improved significantly with the cream alone [126].

Further studies in vitro and in vivo showed that *V. filiformis* lysate could be useful in the treatment of atopic dermatitis and inflammatory diseases as it was found that cells exposed to *V. filiformis* lysate caused induction of IL-10 + T helper cells to become regulatory Tr1 (type 1 regulatory T) cells that suppress T effector cells and reduce inflammation [127].

Seite et al. [128] evaluated the efficacy of an emollient supplemented with a biomass of *Vitreoscilla filiformis*—grown in a medium containing La Roche-Posay thermal spring water—in a double-blind, randomized, comparative study with 60 patients with moderate atopic dermatitis. The study demonstrated that a specific emollient containing *V. filiformis* biomass was able to normalize skin microbiota and significantly reduce the number and severity of flare-ups compared with another emollient.

Other studies focused on the effects of a mixture of *V. filiformis* extracts with Vichy volcanic thermal water. The procedure to obtain the *V. filiformis* lysate is described in Gueniche et al. [136].

Gueniche et al. [137] revised in vivo and ex vivo studies with a dermocosmetic formulation (M89PF) containing 80% Vichy mineral water, 5% of a *V. filiformis* lysate (cultured in Vichy mineral water), 4% niacinamide (vitamin B3), 0.4% hyaluronic acid, and 0.2% vitamin E, to evaluate the clinical efficacy in preventing and repairing stressed skin. Results showed that the M89PF dermocosmetic formulation significantly accelerated skin renewal compared to untreated skin. Skin antioxidant defense activity of the formulation was shown after exposure to stress from UVA plus cigarette smoke aggression. Furthermore, skin microbiome recovery after acute stress from a harsh cleanser was significantly better in M89PF-treated skin compared to bare skin. Additionally, clinical benefits of M89PF on correcting clinical signs of stressed skin were shown in both Caucasian and Asian women exposed to a stressful lifestyle and various external (pollution, tobacco smoking, and solar radiation) and internal (poor sleep, stressful work, unbalanced diet, and alcohol consumption) exposome factors. M89PF also showed depigmenting properties on dark spots in Asian women. Authors suggested that the studied dermocosmetic formulation could act as adjuvant care to prevent and repair skin barrier disruption and reinforce skin defenses in skin exposed to acute stresses [137].

Recently, Berardesca et al. [130] compared the above-mentioned dermocosmetic formulation M89PF to usual skin care in a randomized, split-face study, for 30 days in subjects with rosacea associated with erythema and sensitive skin. Products were to be applied twice daily for 30 days and evaluations were performed at day 15 (D15) and day 30 (D30). Clinical evaluations included erythema, desquamation, skin tightness, dryness, burning sensation, itching, stinging, stinging test, and local tolerability. Instrument evaluations were also used, including erythema, skin hydration, and TEWL; subject satisfaction was also assessed. The results showed that erythema significantly improved with M89PF at both time points: D15 and D30. Skin sensitivity assessed by the skin stinging test improved significantly with M89PF at D30, compared to baseline and usual skin care. Skin erythema, tightness, dryness, hydration, and TEWL significantly improved with M89PF, both at D15 and D30 versus control. Moreover, subjects were highly satisfied with M89PF and tolerance was very good in all subjects [130].

6.5. Nostoc Comune and Combination of Uriage Thermal Water and Fermented-Derived

Two more studies deserve attention as they could be the basis for developing new dermocosmetics derived from hydrobiome and thermal spring waters. Mijouin et al. [138] (2013) demonstrated the thermal water from Uriage-les-Bains and an artificial polysaccharide (Teflose®, obtained by bacterial fermentation) were capable to antagonize the effect of a skin neuropeptide substance P on bacterial virulence.

Gannesen et al. [129] investigated the effects of Uriage thermal water (UTW) and a rhamnose-rich polysaccharide (PS291®) on ribotype 4 (RT4) and ribotype 5 (RT5) acneic strains of *Cutibacterium acnes* and a cutaneous strain of *Staphylococcus aureus*. UTW affected

the growth kinetic of acneic *C. acnes* essentially by increasing its generation time and reducing its biomass, whereas only the *S. aureus* final biomass was decreased. PS291 had more marginal effects. Both compounds showed a marked antibiofilm activity on *C. acnes* and *S. aureus*.

Recently, Drouillard et al. [139] identified the structure of the polysaccharides of *Nostoc commune* (cyanobacterium living in various and extreme environments) harvested in Saint Martin de Uriage (France), which could be the starting point for the preparation of cosmetics with polysaccharides derived from this species.

7. Dermocosmetic Patents Based on Thermal Spring Waters Hydrobiome

As has been previously mentioned, in the last 20 years, many patents were launched based on the use the bacterial strains from the thermal/hot springs described in the previous section. For example, for *Vitreoscilla filiformis*, 440 patents were found, but only 10 of them included thermal spring water; 2 patents of *Aquaphilus dolomiae*, with 1 of them including thermal spring water; and 45 of *Cyanobacterium aponinum* can also be found, but in this last case, none of them included thermal spring water. There are also cosmetics that include prebiotics (e.g., Uriage thermal water containing "thermal biotic complex", with Inulin).

Table 3 lists several patents related to the application of thermal water and pro and postbiotics for dermocosmetic use.

Table 3. Several patents related to the application of thermal water and pro and postbiotics for dermocosmetic use.

Sr. No	Invention	Pro/Postbiotic Strain	Type of Cosmetic/Aim	Date of Publication	Patent Number
1	Cosmetic use of an extract from the bacteria *Vitreoscilla filiformis*, composition and procedure of cosmetic treatment no therapeutic *	*Vitreoscilla filiformis*	Prevention and/or treatment of dry skin	16 August 2016	PI 0802515-0 B1
2	Bacterial extracts cultured in thermal waters for reducing bags and/or dark circles around the eyes	*Vitreoscilla filiformis*	Eye contour care and/or makeup composition	19 July 2016	US9393266B2
3	Process for the preparation of active principles on thermal water and compositions comprising them	*Vitreoscilla filiformis*	Not explain: use in the cosmetics or pharmaceutical field	10 August 2017	US20170226470A1
4	Bacterial extracts cultured in thermal waters for treating sensitive skin, mucous membranes, and scalps	*Vitreoscilla filiformis*	Care of sensitive skin and/or scalps	8 September 2015	US9125934B2
5	Use of bacterial extracts cultivated on thermal water as an anti-redness agent	*Vitreoscilla filiformis*	Treatment of rosacea and sensitive skin	28 January 2009	EP2018891A1
6	Use of at least one bacterial extract cultivated on thermal water for the treatment of sensitive skin, mucosa, and scalps	*Vitreoscilla filiformis*	Care of sensitive skin and/or scalp	28 January 2009	EP2018893A1
7	Bacterial extracts cultured in thermal waters for the treatment of dry skin	*Vitreoscilla filiformis*	Care of dry skin	22 January 2009	US20090022819A1

Table 3. *Cont.*

Sr. No	Invention	Pro/Postbiotic Strain	Type of Cosmetic/Aim	Date of Publication	Patent Number
8	Use of an extract of non-photosynthetic and non-fruiting filamentous bacteria cultivated in a medium containing non-sulfurous mineral and/or thermal water, as agent to, e.g., prevent or limit hair loss and/or promote hair growth	*Vitreoscilla filiformis*	Field of hair growth	23 January 2009	FR2918887A1
9	Association of a Vichy thermal water and an extract of at least one bacterium from the species *Vitreoscilla filiformis* cultured on a medium comprising at least one Vichy thermal water	*Vitreoscilla filiformis*	Caring for and/or treating keratin materials, in particular, the skin	12 May 2022	WO2022096649A1
10	Composition comprising at least one monosaccharide and a filamentary bacterium extract	*Vitreoscilla filiformis*	Preventing and/or treating cutaneous dryness and skin-related disorders, dry and/or hypo-seborrheic.	26 July 2019	FR3016291A1
11	Skin treatment methods	*Aquaphilus dolomiae*	Treatment and/or prevention of a skin condition	19 August 2021	US 2021/0251869 A1

* In Portuguese: "Uso cosmético e uso de pelo menos um extrato de bacteria *Vitreoscilla filiformis*, composiçao e processo de tratamento cosmético nao-terapéutico".

8. Conclusions

Consumer demand is turning toward more effective products that are free of risks and possible toxicities, and therefore cosmetics that include thermal or natural spring water are increasingly in demand. Thermal spring water contains macro and microelements, as well as trace elements that have proven their effectiveness in skin care, but also in certain skin conditions. Additionally, the hydrobiome of the hot springs has been studied and its implications for the balance of the skin microbiome have been observed. Although more studies are needed, this review points to the potential of hydrobiome-derived compounds to be included in dermocosmetics as the bioactive ingredient. Bioactive compounds from the hydrobiome of thermal spring waters can improve dermatological diseases such as atopic dermatitis or rosacea and ameliorate pruritus and xerosis; and also increase protection against UV exposure, strengthened barrier function, maintain good homeostasis of skin defenses, repair damaged skin, promote wound healing, improve skin condition, reduce the uneven skin pigmentation, and prevent skin aging. Among them, it is worth mentioning the exopolysaccharides from bacteria of thermal spring waters, which, until now, have been poorly studied.

In view of the important role that dermocosmetics derived from thermal water can play in skin care and in the improvement of certain skin disorders, an effort is necessary to investigate the hydrobiome of thermal waters, its role in the treatment of dermatological diseases, the complete study of the hydrobiome of each spring of thermal water, and the methods for obtaining derivatives thereof for possible use in cosmeceuticals.

From a future perspective, fruitful cooperation among researchers, hydrologists, thermal spa centers, and cosmetic industries will drive this sector toward a better understanding of the role of the hydrobiome of thermal spring waters on skin and dermatological diseases and consider the inclusion of derivatives of this hydrobiome (in the form of fermenters, lysates, extracts, etc.) in dermocosmetic formulations. Therefore, and being aware of the potential of the hydrobiome in dermatological and skin care applications, the future prospects for the use of bioactive substances derived from it in dermocosmetic formulations are promising.

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References

1. Proctor, L.; LoTempio, J.; Marquitz, A.; Daschner, P.; Xi, D.; Flores, R.; Brown, L.; Ranallo, R.; Maruvada, P.; Regan, K.; et al. A review of 10 years of human microbiome research activities at the US National Institutes of Health, Fiscal Years 2007–2016. *Microbiome* **2019**, *7*, 31. [CrossRef]
2. Lynch, S.V.; Pedersen, O. The Human Intestinal Microbiome in Health and Disease. *N. Engl. J. Med.* **2016**, *375*, 2369–2379. [CrossRef] [PubMed]
3. Alam, M.Z.; Maslanka, J.R.; Abt, M.C. Immunological consequences of microbiome-based therapeutics. *Front. Immunol.* **2023**, *13*, 1046472. [CrossRef]
4. Gopalakrishnan, V.; Helmink, B.A.; Spencer, C.N.; Reuben, A.; Wargo, J.A. The influence of the gut microbiome on cancer, immunity, and cancer immunotherapy. *Cancer Cell* **2018**, *33*, 570–580. [CrossRef] [PubMed]
5. Chen, C.; Liao, J.; Xia, Y.; Liu, X.; Jones, R.; Haran, J.; McCormick, B.; Sampson, T.R.; Alam, A.; Ye, K. Gut microbiota regulate Alzheimer's disease pathologies and cognitive disorders via PUFA-associated neuroinflammation. *Gut* **2022**, *71*, 2233–2252. [CrossRef] [PubMed]
6. Kamada, N.; Seo, S.U.; Chen, G.Y.; Núñez, G. Role of the gut microbiota in immunity and inflammatory disease. *Nat. Rev. Immunol.* **2013**, *13*, 321–335. [CrossRef] [PubMed]
7. Chen, L.; Li, J.; Zhu, W.; Kuang, Y.; Liu, T.; Zhang, W.; Chen, X.; Peng, C. Skin and Gut Microbiome in Psoriasis: Gaining Insight Into the Pathophysiology of It and Finding Novel Therapeutic Strategies. *Front. Microbiol.* **2020**, *11*, 589726. [CrossRef] [PubMed]
8. Mazur, M.; Tomczak, H.; Łodyga, M.; Plagens-Rotman, K.; Merks, P.; Czarnecka-Operacz, M. The Intestinal and Skin Microbiome in Patients with Atopic Dermatitis and Their Influence on the Course of the Disease: A Literature Review. *Healthcare* **2023**, *11*, 766. [CrossRef]
9. Nørreslet, L.B.; Agner, T.; Clausen, M.L. The Skin Microbiome in Inflammatory Skin Diseases. *Curr. Dermatol. Rep.* **2020**, *9*, 141–151. [CrossRef]
10. Melby, M.K.; Kansal, A.; Nichter, M. Biocultural Perspectives on Aging: Importance of the Microbiome. In *Anthropological Perspectives on Aging*, 1st ed.; Howell, B.M., Harrod, R.P., Eds.; University Press of Florida: Gainesville, FL, USA, 2023; pp. 46–76. [CrossRef]
11. Ozen, M.; Dinleyici, E.C. The history of probiotics: The untold story. *Benef. Microbes* **2015**, *6*, 159–165. [CrossRef] [PubMed]
12. Chaudhari, A.; Dwivedi, M.K. The concept of probiotics, prebiotics, postbiotics, synbiotics, nutribiotics, and pharmabiotics. In *Probiotics in the Prevention and Management of Human Diseases*; Dwivedi, M.K., Amaresan, N., Sankaranarayanan, A., Kemp, E.H., Eds.; Academic Press: Cambridge, MA, USA, 2022; pp. 1–11. [CrossRef]
13. Vallejo-Cordoba, B.; Castro-López, C.; García, H.S.; González-Córdova, A.F.; Hernández-Mendoza, A. Postbiotics and paraprobiotics: A review of current evidence and emerging trends. *Adv. Food Nutr. Res.* **2020**, *94*, 1–34. [CrossRef]
14. Salminen, S.; Collado, M.C.; Endo, A.; Hill, C.; Lebeer, S.; Quigley, E.M.M.; Sanders, M.E.; Shamir, R.; Swann, J.R.; Szajewska, H.; et al. The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. *Nat. Rev. Gastroenterol. Hepatol.* **2021**, *18*, 649–667. [CrossRef]
15. Nataraj, B.H.; Ali, S.A.; Behare, P.V.; Yadav, H. Postbiotics-parabiotics: The new horizons in microbial biotherapy and functional foods. *Microb. Cell Factories* **2020**, *19*, 168. [CrossRef] [PubMed]

16. Cuevas-Gonzalez, P.F.; Liceaga, A.M.; Aguilar-Toala, J.E. Postbiotics and paraprobiotics: From concepts to applications. *Food Res. Int.* **2020**, *136*, 109502. [CrossRef]
17. Scott, E.; De Paepe, K.; Van de Wiele, T. Postbiotics and Their Health Modulatory Biomolecules. *Biomolecules* **2022**, *12*, 1640. [CrossRef] [PubMed]
18. Thorakkattu, P.; Khanashyam, A.C.; Shah, K.; Babu, K.S.; Shanker Mundanat, A.; Deliephan, A.; Deokar, G.S.; Santivarangkna, C.; Nirmal, N.P. Postbiotics: Current Trends in Food and Pharmaceutical Industry. *Foods* **2022**, *11*, 3094. [CrossRef]
19. Emiola, A.; Zhou, W.; Oh, J. An enhanced characterization of the human skin microbiome: A new biodiversity of microbial interactions. *bioRxiv* **2020**. [CrossRef]
20. Mourelle, M.L.; Gómez, C.P.; Legido, J.L. *Nutraceuticals and Nutricosmetics*; Liberlibro.com AC: Albacete, Spain, 2023; pp. 77–79. (In Spanish)
21. Harris-Tryon, T.A.; Grice, E.A. Microbiota and maintenance of skin barrier function. *Science* **2022**, *376*, 940–945. [CrossRef]
22. McBain, A.J.; O'Neill, C.A.; Amezquita, A.; Price, L.J.; Faust, K.; Tett, A.; Segata, N.; Swann, J.R.; Smith, A.M.; Murphy, B.; et al. Consumer safety considerations of skin and oral microbiome perturbation. *Clin. Microbiol. Rev.* **2019**, *32*, e00051-19. [CrossRef] [PubMed]
23. Grice, E.A.; Segre, J.A. The skin microbiome. *Nat. Rev. Microbiol.* **2011**, *9*, 244–253. [CrossRef]
24. Polak-Witka, K.; Rudnicka, L.; Blume-Peytavi, U.; Vogt, A. The role of the microbiome in scalp hair follicle biology and disease. *Exp. Dermatol.* **2020**, *29*, 286–294. [CrossRef]
25. De Pessemier, B.; Grine, L.; Debaere, M.; Maes, A.; Paetzold, B.; Callewaert, C. Gut-Skin Axis: Current Knowledge of the Interrelationship between Microbial Dysbiosis and Skin Conditions. *Microorganisms* **2021**, *9*, 353. [CrossRef]
26. Costello, E.K.; Lauber, C.L.; Hamady, M.; Fierer, N.; Gordon, J.I.; Knight, R. Bacterial community variation in human body habitats across space and time. *Science* **2009**, *326*, 1694–1697. [CrossRef] [PubMed]
27. Paetzold, B.; Willis, J.R.; Pereira de Lima, J.; Knödlseder, N.; Brüggemann, H.; Quist, S.R.; Gabaldon, T.; Güell, M. Skin microbiome modulation induced by probiotic solutions. *Microbiome* **2019**, *7*, 95. [CrossRef]
28. Bewick, S.; Gurarie, E.; Weissman, J.L.; Beattie, J.; Davati, C.; Flint, R.; Thielen, P.; Breitwieser, F.; Karig, D.; Fagan, W.F. Trait-based analysis of the human skin microbiome. *Microbiome* **2019**, *7*, 101. [CrossRef]
29. Dimitriu, P.A.; Iker, B.; Malik, K.; Leung, H.; Mohn, W.W.; Hillebrand, G.G. New Insights into the Intrinsic and Extrinsic Factors That Shape the Human Skin Microbiome. *mBio* **2019**, *10*, e00839-19. [CrossRef] [PubMed]
30. Maruvada, P.; Leone, V.; Kaplan, L.M.; Chang, E.B. The Human Microbiome and Obesity: Moving beyond Associations. *Cell Host Microbe* **2017**, *22*, 589–599. [CrossRef] [PubMed]
31. Burns, E.M.; Ahmed, H.; Isedeh, P.N.; Kohli, I.; Van Der Pol, W.; Shaheen, A.; Muzaffar, A.F.; Al-Sadek, C.; Foy, T.M.; Abdelgawwad, M.S.; et al. Ultraviolet radiation, both UVA and UVB, influences the composition of the skin microbiome. *Exp. Dermatol.* **2019**, *28*, 136–141. [CrossRef]
32. Balato, A.; Cacciapuoti, S.; Di Caprio, R.; Marasca, C.; Masarà, A.; Raimondo, A.; Fabbrocini, G. Human Microbiome: Composition and Role in Inflammatory Skin Diseases. *Arch. Immunol. Ther. Exp.* **2019**, *67*, 1–18. [CrossRef]
33. Schoch, J.J.; Monir, R.L.; Satcher, K.G.; Harris, J.; Triplett, E.; Neu, J. The infantile cutaneous microbiome: A review. *Pediatr. Dermatol.* **2019**, *36*, 574–580. [CrossRef]
34. Byrd, A.; Belkaid, Y.; Segre, J. The human skin microbiome. *Nat. Rev. Microbiol.* **2018**, *16*, 143–155. [CrossRef]
35. Prajapati, D.P.; Dodiya, T.R. A review on skin microbiome: Novel strategy in cosmetics. *Int. J. Res. Ayurveda Pharm.* **2021**, *12*, 99–102. [CrossRef]
36. Brandwein, M.; Katz, I.; Katz, A.; Al-Ashhab, A.; Nejman, D.; Straussman, R.; Hodak, E.; Harari, M.; Steinberg, D.; Bentwich, Z.; et al. Beyond the gut: Skin microbiome compositional changes are associated with BMI. *Hum. Microbiome J.* **2019**, *13*, 100063. [CrossRef]
37. Chau, T.A.; McCully, M.L.; Brintnell, W.; Kasper, K.J.; Vinés, E.D.; Kubes, P.; Haeryfar, S.M.; McCormick, J.K.; Cairns, E.; Heinrichs, D.E.; et al. Toll-like receptor 2 ligands on the staphylococcal cell wall downregulate superantigen-induced T cell activation and prevent toxic shock syndrome. *Nat. Med.* **2009**, *15*, 641–648. [CrossRef] [PubMed]
38. Gallo, R.L.; Nakatsuji, T. Microbial symbiosis with the innate immune defense system of the skin. *J. Investig. Dermatol.* **2011**, *131*, 1974–1980. [CrossRef]
39. Cacciapuoti, S.; Luciano, M.A.; Megna, M.; Annunziata, M.C.; Napolitano, M.; Patruno, C.; Scala, E.; Colicchio, R.; Pagliuca, C.; Salvatore, P.; et al. The Role of Thermal Water in Chronic Skin Diseases Management: A Review of the Literature. *J. Clin. Med.* **2020**, *9*, 3047. [CrossRef]
40. Colman, D.R.; Feyhl-Buska, J.; Robinson, K.J.; Fecteau, K.M.; Xu, H.; Shock, E.L.; Boyd, E.S. Ecological diferentiation in planktonic and sediment-associated chemotrophic microbial populations in Yellowstone hot springs. *FEMS Microbiol. Ecol.* **2016**, *92*, fiw137. [CrossRef]
41. Valeriani, F.; Protano, C.; Gianfranceschi, G.; Leoni, E.; Galasso, V.; Mucci, N.; Vitali, M.; Romano-Spica, V. Microflora Thermarum Atlas project: Biodiversity in thermal spring waters and natural SPA pools. *Water Supply* **2018**, *18*, 1472–1483. [CrossRef]
42. Valeriani, F.; Crognale, S.; Protano, C.; Gianfranceschi, G.; Orsini, M.; Vitali, M.; Romano Spica, V.J. Metagenomic analysis of bacterial community in a travertine depositing hot spring. *New Microbiol.* **2018**, *41*, 126–135.
43. Valeriani, F.; Gianfranceschi, G.; Spica, V.R. The microbiota as a candidate biomarker for SPA pools and SPA thermal spring stability after seismic events. *Environ. Int.* **2020**, *137*, 105595. [CrossRef] [PubMed]

44. Paduano, S.; Valeriani, F.; Romano-Spica, V.; Bargellini, A.; Borella, P.; Marchesi, I. Microbial biodiversity of thermal water and mud in an Italian spa by metagenomics: A pilot study. *Water Supply* **2017**, *18*, 1456–1465. [CrossRef]
45. Corniello, A.; Guida, M.; Stellato, L.; Trifuoggi, M.; Carraturo, F.; Del Gaudio, E.; Del Giudice, C.; Forte, G.; Giarra, A.; Iorio, M.; et al. Hydrochemical, isotopic and microbiota characterization of telese mineral waters (Southern Italy). *Environ. Geochem. Health* **2022**, *44*, 1949–1970. [CrossRef] [PubMed]
46. Hilaire, P.; Contreras, S.; Blanquart-Goudezeune, H.; Verbeke, J.; Delépine, B.; Marmiesse, L.; Peyraud, R.; Morand, S.C. Complete genome sequence of Sphingobium xenophagum PH3-15, isolated from La Roche-Posay thermal water sources. *Microbiol. Resour. Announc.* **2021**, *10*, e00700-21. [CrossRef]
47. Skirnisdottir, S.; Hreggvidsson, G.O.; Hjörleifsdottir, S.; Marteinsson, V.; Petursdottir, S.K.; Holst, O.; Kristjansson, J.K.; Hjörleifsdottir, S. Influence of Sulfide and Temperature on Species Composition and Community Structure of Hot Spring Microbial Mats. *Appl. Environ. Microbiol.* **2000**, *66*, 2835–2841. [CrossRef]
48. Banerjee, M.; Everroad, R.C.; Castenholz, R.W. An unusual cyanobacterium from saline thermal waters with relatives from unexpected habitats. *Extremophiles* **2009**, *13*, 707–716. [CrossRef] [PubMed]
49. Szuróczki, S.; Kéki, Z.; Káli, S.; Lippai, A.; Márialigeti, K.; Tóth, E. Microbiological investigations on the water of a thermal bath at Budapest. *Acta Microbiol. Immunol. Hung.* **2016**, *63*, 229–241. [CrossRef] [PubMed]
50. Smrhova, T.; Jani, K.; Pajer, P.; Kapinusova, G.; Vylita, T.; Suman, J.; Strejcek, M.; Uhlik, O. Prokaryotes of renowned Karlovy Vary (Carlsbad) thermal springs: Phylogenetic and cultivation analysis. *Environ. Microbiome* **2022**, *17*, 48. [CrossRef]
51. Mitrović, M.; Kostešić, E.; Marković, T.; Selak, L.; Hausmann, B.; Pjevac, P.; Orlić, S. Microbial community composition and hydrochemistry of underexplored geothermal waters in Croatia. *Syst. Appl. Microbiol.* **2022**, *45*, 126359. [CrossRef]
52. Çelik, I.; Keskin, E. Revealing the Microbiome of Four Different Thermal Springs in Turkey with Environmental DNA Metabarcoding. *Biology* **2022**, *11*, 998. [CrossRef]
53. Hedlund, B.P.; Dodsworth, J.A.; Cole, J.K.; Panosyan, H. An integrated study reveals diverse methanogens, Thaumarchaeota, and yet-uncultivated archaeal lineages in Armenian hot springs. *Antonie van Leeuwenhoek* **2013**, *104*, 71–82. [CrossRef]
54. Kublanov, I.; Perevalova, A.A.; Slobodkina, G.B.; Lebedinsky, A.V.; Bidzhieva, S.K.; Kolganova, T.V.; Kaliberda, E.N.; Rumsh, L.D.; Haertlï, T.; Bonch-Osmolovskaya, E.A. Biodiversity of Thermophilic Prokaryotes with Hydrolytic Activities in Hot Springs of Uzon Caldera, Kamchatka (Russia). *Appl. Environ. Microbiol.* **2008**, *75*, 286–291. [CrossRef]
55. Reigstad, L.J.; Jorgensen, S.L.; Schleper, C. Diversity and abundance of Korarchaeota in terrestrial hot springs of Iceland and Kamchatka. *ISME J.* **2010**, *4*, 346–356. [CrossRef]
56. Roy, C.; Rameez, M.J.; Haldar, P.K.; Peketi, A.; Mondal, N.; Bakshi, U.; Mapder, T.; Pyne, P.; Fernandes, S.; Bhattacharya, S.; et al. Microbiome and ecology of a hot spring-microbialite system on the Trans-Himalayan Plateau. *Sci. Rep.* **2020**, *10*, 5917. [CrossRef]
57. Ghalib, A.K.; Yasin, M.; Faisal, M. Characterization and Metal Detoxification Potential of Moderately Thermophilic *Bacillus cereus* from Geothermal Springs of Himalaya. *Braz. Arch. Biol. Technol.* **2014**, *57*, 554–560. [CrossRef]
58. Amin, A.; Ahmed, I.; Salam, N.; Kim, B.-Y.; Singh, D.; Zhi, X.-Y.; Xiao, M.; Li, W.-J. Diversity and Distribution of Thermophilic Bacteria in Hot Springs of Pakistan. *Microb. Ecol.* **2017**, *74*, 116–127. [CrossRef]
59. Lau, M.C.Y.; Aitchison, J.C.; Pointing, S.B. Bacterial community composition in thermophilic microbial mats from five hot springs in central Tibet. *Extremophiles* **2009**, *13*, 139–149. [CrossRef]
60. Li, J.; Peng, X.; Zhang, L.; Jiang, L.; Chen, S. Linking microbial community structure to S, N and Fe biogeochemical cycling in the hot springs at the Tengchong geothermal fields, Southwest China. *Geomicrobiol. J.* **2015**, *33*, 135–150. [CrossRef]
61. Sahoo, R.K.; Gaur, M.; Das, A.; Singh, A.; Kumar, M.; Subudhi, E. Comparative analysis of 16S rRNA gene Illumina sequence for microbial community structure in diverse unexplored hot springs of Odisha, India. *Geomicrobiol. J.* **2016**, *34*, 567–576. [CrossRef]
62. Kanokratana, P.; Chanapan, S.; Pootanakit, K.; Eurwilaichitr, L. Diversity and abundance of Bacteria and Archaea in the Bor Khlueng Hot Spring in Thailand. *J. Basic Microbiol.* **2004**, *44*, 430–444. [CrossRef]
63. Nakagawa, T.; Fukui, M. Molecular Characterization of Community Structures and Sulfur Metabolism within Microbial Streamers in Japanese Hot Springs. *Appl. Environ. Microbiol.* **2003**, *69*, 7044–7057. [CrossRef]
64. Everroad, R.C.; Otaki, H.; Matsuura, K.; Haruta, S. Diversification of bacterial community composition along a temperature gradient at a thermal spring. *Microbes Environ.* **2012**, *27*, 374–381. [CrossRef] [PubMed]
65. Urbieta, M.S.; Gonzalez-Toril, E.; Bazán, A.A.; Giaveno, M.A.; Donati, E. Comparison of the microbial communities of hot springs waters and the microbial biofilms in the acidic geothermal area of Copahue (Neuquén, Argentina). *Extremophiles* **2015**, *19*, 437–450. [CrossRef] [PubMed]
66. Brito, E.M.S.; Villegas-Negrete, N.; Sotelo-González, I.A.; Caretta, C.A.; Goñi-Urriza, M.; Gassie, C.; Hakil, F.; Colin, Y.; Duran, R.; Gutierrez-Corona, F.; et al. Microbial diversity in Los Azufres geothermal field (Michoacán, Mexico) and isolation of representative sulfate and sulfur reducers. *Extremophiles* **2014**, *18*, 385–398. [CrossRef]
67. Paul, S.; Cortez, Y.; Vera, N.; Villena, G.K.; Gutierrez-Correa, M. Metagenomic Analysis of Microbial Communities in the Soil-mousse Surrounding of an Amazonian Geothermal Spring in Peru. *Br. Biotechnol. J.* **2016**, *15*, 1–11. [CrossRef]
68. Rubiano-Labrador, C.; Díaz-Cárdenas, C.; López, G.; Gómez, J.; Baena, S. Colombian Andean thermal springs: Reservoir of thermophilic anaerobic bacteria producing hydrolytic enzymes. *Extremophiles* **2019**, *23*, 793–808. [CrossRef]
69. Burton, N.P.; Norris, P.R. Microbiology of acidic, geothermal springs of Montserrat: Environmental rDNA analysis. *Extremophiles* **2000**, *4*, 315–320. [CrossRef]

70. Sayeh, R.; Birrien, J.L.; Alain, K.; Barbier, G.; Hamdi, M.; Prieur, D. Microbial diversity in Tunisian geothermal springs as detected by molecular and culture-based approaches. *Extremophiles* **2010**, *14*, 501–514. [CrossRef]
71. Tekere, M. Metagenomic analysis of bacterial diversity of Siloam hot water spring, Limpopo, South Africa. *Afr. J. Biotechnol.* **2011**, *10*, 18005–18012. [CrossRef]
72. Aburto-Medina, A.; Shahsavari, E.; Cohen, M.; Mantri, N.; Ball, A.S. Analysis of the Microbiome (Bathing Biome) in Geothermal Waters from an Australian Balneotherapy Centre. *Water* **2020**, *12*, 1705. [CrossRef]
73. Pedron, R.; Esposito, A.; Bianconi, I.; Pasolli, E.; Tett, A.; Asnicar, F.; Cristofolini, M.; Segata, N.; Jousson, O. Genomic and metagenomic insights into the microbial community of a thermal spring. *Microbiome* **2019**, *7*, 8. [CrossRef]
74. Crognale, S.; Venturi, S.; Tassi, F.; Rossetti, S.; Cabassi, J.; Capecchiacci, F.; Bicocchi, G.; Vaselli, O.; Morrison, H.G.; Sogin, M.L.; et al. Geochemical and microbiological profiles in hydrothermal extreme acidic environments (Pisciarelli Spring, Campi Flegrei, Italy). *FEMS Microbiol. Ecol.* **2022**, *98*, fiac088. [CrossRef] [PubMed]
75. Dai, D.; Ma, X.; Yan, X.; Bao, X. The Biological Role of Dead Sea Water in Skin Health: A Review. *Cosmetics* **2023**, *10*, 21. [CrossRef]
76. Oren, A.; Ginzburg, M.; Ginzburg, B.Z.; Hochstein, L.I.; Volcani, B.E. *Haloarcula marismortui* (Volcani) sp. nov., nom. rev., an extremely halophilic bacterium from the Dead Sea. *Int. J. Syst. Bacteriol.* **1990**, *40*, 209–210. [CrossRef] [PubMed]
77. Al-Karablieh, N. Antimicrobial Activity of *Bacillus Persicus* 24-DSM Isolated from Dead Sea Mud. *Open Microbiol. J.* **2017**, *11*, 372–383. [CrossRef] [PubMed]
78. Obeidat, M. Isolation and characterization of extremely halotolerant *Bacillus* species from Dead Sea black mud and determination of their antimicrobial and hydrolytic activities. *Afr. J. Microbiol. Res.* **2017**, *11*, 1303–1314. [CrossRef]
79. Ghosh, S.; Kumar, S.; Khare, S.K. Microbial diversity of saline habitats: An overview of biotechnological applications. In *Microorganisms in Saline Environments: Strategies and Functions*; Bhoopander, G., Varma, A., Eds.; Springer: Berlin/Heidelberg, Germany, 2019; pp. 65–92.
80. Giordano, D. Bioactive Molecules from Extreme Environments. *Mar. Drugs* **2020**, *18*, 640. [CrossRef]
81. Sorokin, D.Y.; Elcheninov, A.G.; Khijniak, T.V.; Kolganova, T.V.; Kublanov, I.V. Selective enrichment on a wide polysaccharide spectrum allowed isolation of novel metabolic and taxonomic groups of haloarchaea from hypersaline lakes. *Front. Microbiol.* **2020**, *13*, 1059347. [CrossRef]
82. Zhu, Y.-G.; Zhu, D.; Rillig, M.C.; Yang, Y.; Chu, H.; Chen, Q.-L.; Penuelas, J.; Cui, H.-L.; Gillings, M. Ecosystem Microbiome Science. *mLife* **2023**, *2*, 2–10. [CrossRef]
83. Bourrain, M.; Ribet, V.; Calvez, A.; Lebaron, P.; Schmitt, A.M. Balance between beneficial microflora and *Staphylococcus aureus* colonisation: In vivo evaluation in patients with atopic dermatitis during hydrotherapy. *Eur. J. Dermatol.* **2013**, *23*, 786–794. [CrossRef]
84. Bourrain, M.; Suzuki, M.T.; Calvez, A.; West, N.J.; Lions, J.; Lebaron, P. In-depth prospection of Avène Thermal Spring Water reveals an uncommon and stable microbial community. *J. Eur. Acad. Dermatol. Venereol.* **2020**, *34*, 8–14. [CrossRef]
85. Faga, A.; Nicoletti, G.; Gregotti, C.; Finotti, V.; Nitto, A.; Gioglio, L. Effects of thermal water on skin regeneration. *Int. J. Mol. Med.* **2012**, *29*, 732–740. [CrossRef] [PubMed]
86. Nicoletti, G.; Corbella, M.; Jaber, O.; Marone, P.; Scevola, D.; Faga, A. Non-pathogenic microflora of a spring water with regenerative properties. *Biomed. Rep.* **2015**, *3*, 758–762. [CrossRef]
87. Martin, R.; Henley, J.B.; Sarrazin, P.; Seité, S. Skin Microbiome in Patients with Psoriasis Before and After Balneotherapy at the Thermal Care Center of La Roche-Posay. *J. Drugs Dermatol.* **2015**, *14*, 1400–1405.
88. Zeichner, J.; Seite, S. From Probiotic to Prebiotic Using Thermal Spring Water. *J. Drugs Dermatol.* **2018**, *17*, 657–662.
89. Thirion, F.; Guilly, S.; Fromentin, S.; Plaza Oñate, F.; Alvarez, A.S.; Le Chatelier, E.; Pons, N.; Levenez, F.; Quinquis, B.; Ehrlich, S.; et al. Changes in Gut Microbiota of Patients with Atopic Dermatitis During Balneotherapy. *Clin. Cosmet. Investig. Dermatol.* **2022**, *15*, 163–176. [CrossRef]
90. Brandwein, M.; Fuks, G.; Israel, A.; Al-Ashhab, A.; Nejman, D.; Straussman, R.; Hodak, E.; Harari, M.; Steinberg, D.; Bentwich, Z.; et al. Temporal Stability of the Healthy Human Skin Microbiome Following Dead Sea Climatotherapy. *Acta Derm. Venereol.* **2018**, *98*, 256–261. [CrossRef]
91. Bender, T.; Kalics, G.; Árvai, K.; Illés, A.; Kósa, J.P.; Tobias, B.; Lakatos, P.; Papp, M.; Nemes, K. The Effects of Lakitelek Thermal Water and Tap Water on Skin Microbiome, a Randomized Control Pilot Study. *Life* **2023**, *13*, 746. [CrossRef]
92. Navarro-López, V.; Núñez-Delegido, E.; Ruzafa-Costas, B.; Sánchez-Pellicer, P.; Agüera-Santos, J.; Navarro-Moratalla, L. Probiotics in the Therapeutic Arsenal of Dermatologists. *Microorganisms* **2021**, *9*, 1513. [CrossRef]
93. Habeebuddin, M.; Karnati, R.K.; Shiroorkar, P.N.; Nagaraja, S.; Asdaq, S.M.B.; Khalid Anwer, M.; Fattepur, S. Topical Probiotics: More Than a Skin Deep. *Pharmaceutics* **2022**, *14*, 557. [CrossRef]
94. Lombardi, F.; Augello, F.R.; Artone, S.; Bahiti, B.; Sheldon, J.M.; Giuliani, M.; Cifone, M.G.; Palumbo, P.; Cinque, B. Efficacy of probiotic *Streptococcus thermophilus* in counteracting TGF-β1-induced fibrotic response in normal human dermal fibroblasts. *J. Inflamm.* **2022**, *19*, 27. [CrossRef]
95. Puebla-Barragan, S.; Reid, G. Probiotics in Cosmetic and Personal Care Products: Trends and Challenges. *Molecules* **2021**, *26*, 1249. [CrossRef]
96. Di Marzio, L.; Cinque, B.; Cupelli, F.; De Simone, C.; Cifone, M.G.; Giuliani, M. Increase of skin-ceramide levels in aged subjects following a short-term topical application of bacterial sphingomyelinase from Streptococcus thermophilus. *Int. J. Immunopathol. Pharmacol.* **2008**, *21*, 137–143. [CrossRef] [PubMed]

97. Gueniche, A.; Benyacoub, J.; Philippe, D.; Bastien, P.; Kusy, N.; Breton, L.; Blum, S.; Castiel-Higounenc, I. *Lactobacillus paracasei* CNCM I-2116 (ST11) inhibits substance P-induced skin inflammation and accelerates skin barrier function recovery in vitro. *Eur. J. Dermatol.* **2010**, *20*, 731–737.
98. Ashoori, Y.; Mohkam, M.; Heidari, R.; Abootalebi, S.N.; Mousavi, S.M.; Hashemi, S.A.; Golkar, N.; Gholami, A. Development and In Vivo Characterization of Probiotic Lysate-Treated Chitosan Nanogel as a Novel Biocompatible Formulation for Wound Healing. *Biomed. Res. Int.* **2020**, *2020*, 8868618. [CrossRef]
99. Golkar, N.; Ashoori, Y.; Heidari, R.; Omidifar, N.; Abootalebi, S.N.; Mohkam, M.; Gholami, A. A Novel Effective Formulation of Bioactive Compounds for Wound Healing: Preparation, In Vivo Characterization, and Comparison of Various Postbiotics Cold Creams in a Rat Model. *J. Evid. Based Complement. Alternat. Med.* **2021**, *2021*, 8577116. [CrossRef] [PubMed]
100. Rong, J.; Shan, C.; Liu, S.; Zheng, H.; Liu, C.; Liu, M.; Jin, F.; Wang, L. 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*, 511–523. [CrossRef]
101. Notay, M.; Saric-Bosanac, S.; Vaughn, A.R.; Dhaliwal, S.; Trivedi, M.; Reiter, P.N.; Rybak, I.; Li, C.C.; Weiss, L.B.; Ambrogio, L.; et al. The use of topical *Nitrosomonas eutropha* for cosmetic improvement of facial wrinkles. *J. Cosmet. Dermatol.* **2020**, *19*, 689–693. [CrossRef]
102. Nam, Y.; Kim, J.; Baek, J.; Kim, W. Improvement of Cutaneous Wound Healing via Topical Application of Heat-Killed *Lactococcus chungangensis* CAU 1447 on Diabetic Mice. *Nutrients* **2021**, *13*, 2666. [CrossRef] [PubMed]
103. Kim, J.; Lee, Y.I.; Mun, S.; Jeong, J.; Lee, D.-G.; Kim, M.; Jo, H.; Lee, S.; Han, K.; Lee, J.H. Efficacy and Safety of *Epidermidibacterium Keratini* EPI-7 Derived Postbiotics in Skin Aging: A Prospective Clinical Study. *Int. J. Mol. Sci.* **2023**, *24*, 4634. [CrossRef]
104. Duarte, M.; Oliveira, A.L.; Oliveira, C.; Pintado, M.; Amaro, A.; Madureira, A.R. Current postbiotics in the cosmetic market—An update and development opportunities. *Appl. Microbiol. Biotechnol.* **2022**, *106*, 5879–5891. [CrossRef]
105. Iglesia, S.; Kononov, T.; Zahr, A.S. A multi-functional anti-aging moisturizer maintains a diverse and balanced facial skin microbiome. *J. Appl. Microbiol.* **2022**, *133*, 1791–1799. [CrossRef] [PubMed]
106. Kim, G.; Kim, M.; Kim, M.; Park, C.; Yoon, Y.; Lim, D.H.; Yeo, H.; Kang, S.; Lee, Y.G.; Beak, N.I.; et al. Spermidine-induced recovery of human dermal structure and barrier function by skin microbiome. *Commun. Biol.* **2021**, *4*, 231. [CrossRef]
107. Woolery-Lloyd, H.; Andriessen, A.; Day, D.; Gonzalez, N.; Green, L.; Grice, E.; Henry, M. Review of the microbiome in skin aging and the effect of a topical prebiotic containing thermal spring water. *J. Cosmet. Dermatol.* **2023**, *22*, 96–102. [CrossRef]
108. Figueiredo, A.C.; Rodrigues, M.; Mourelle, M.L.; Araujo, A.R.T.S. Thermal Spring Waters as an Active Ingredient in Cosmetic Formulations. *Cosmetics* **2023**, *10*, 27. [CrossRef]
109. Aries, M.F.; Hernandez-Pigeon, H.; Vaissière, C.; Delga, H.; Caruana, A.; Lévêque, M.; Bourrain, M.; Ravard-Helffer, K.; Chol, B.; Nguyen, T.; et al. Anti-inflammatory and immunomodulatory effects of *Aquaphilus dolomiae* extract on in vitro models. *Clin. Cosmet. Investig. Dermatol.* **2016**, *9*, 421–434. [CrossRef]
110. Nguyen, T.; Chol, B.; Maitre, M.; Ravard-Helffer, K.; Farinole, F.; Lestienne, F.; Castex-Rizzi, N. Additional pharmacological activity of I-modulia and generation of two newly designed extracts of *Aquaphilus dolomiae* culture for dermocosmetic actives. *J. Eur. Acad. Dermatol. Venereol.* **2020**, *34*, 27–29. [CrossRef]
111. Martin, H.; Laborel-Préneron, E.; Fraysse, F.; Nguyen, T.; Schmitt, A.M.; Redoulès, D.; Davrinche, C. *Aquaphilus dolomiae* extract counteracts the effects of cutaneous *S. aureus* secretome isolated from atopic children on $CD4^+$ T cell activation. *Pharm. Biol.* **2016**, *54*, 2782–2785. [CrossRef] [PubMed]
112. Nguyen, T.; Castex-Rizzi, N.; Redoulès, D. Immunomodulatory, anti-inflammatory, anti-pruritus and tolerogenic activities induced by I-modulia®, an Aquaphilus dolomiae culture extract, in atopic dermatitis pharmacology models. *Ann. Dermatol. Venereol.* **2017**, *144*, 2782–2785. [CrossRef]
113. Galliano, M.F.; Bäsler, K.; Caruana, A.; Mias, C.; Bessou-Touya, S.; Brandner, J.M.; Duplan, H. Protective effect of *Aquaphilus dolomiae* extract-G1, ADE-G1, on tight junction barrier function in a *Staphylococcus aureus*-infected atopic dermatitis model. *J. Eur. Acad. Dermatol. Venereol.* **2020**, *34*, 30–36. [CrossRef] [PubMed]
114. Lestienne, F.; Viodé, C.; Ceruti, I.; Carrere, S.; Bessou-Touya, S.; Duplan, H.; Castex-Rizzi, N. Cutaneous sensitivity modulation by *Aquaphilus dolomiae* extract-G3 on in vitro models of neuro-inflammation. *J. Eur. Acad. Dermatol. Venereol.* **2020**, *34*, 43–48. [CrossRef]
115. Noizet, M.; Bianchi, P.; Galliano, M.F.; Caruana, A.; Brandner, J.M.; Bessou-Touya, S.; Duplan, H. Broad spectrum repairing properties of an extract of *Aquaphilus dolomiae* on in vitro and ex vivo models of injured skin. *J. Eur. Acad. Dermatol. Venereol.* **2020**, *34*, 37–42. [CrossRef] [PubMed]
116. Deleuran, M.; Georgescu, V.; Jean-Decoster, C. An Emollient Containing Aquaphilus dolomiae Extract is Effective in the Management of Xerosis and Pruritus: An International, Real-World Study. *Dermatol. Ther.* **2020**, *10*, 1013–1029. [CrossRef]
117. Vendrely, V.; Mayor-Ibarguren, A.; Stennevin, A.; Ortiz-Brugués, A. An Emollient PLUS Balm Is Useful for the Management of Xerosis in Patients Treated for Cancer: A Real-World, Prospective, Observational, Multicenter Study. *Dermatol. Ther.* **2022**, *12*, 683–699. [CrossRef] [PubMed]
118. Grether-Beck, S.; Mühlberg, K.; Brenden, H.; Felsner, I.; Brynjólfsdóttir, A.; Einarsson, S.; Krutmann, J. Bioactive molecules from the Blue Lagoon: In vitro and in vivo assessment of silica mud and microalgae extracts for their effects on skin barrier function and prevention of skin ageing. *Exp. Dermatol.* **2008**, *17*, 771–779. [CrossRef] [PubMed]

119. Gudmundsdottir, A.B.; Omarsdottir, S.; Brynjolfsdottir, A.; Paulsen, B.S.; Olafsdottir, E.S.; Freysdottir, J. Exopolysaccharides from *Cyanobacterium aponinum* from the Blue Lagoon in Iceland increase IL-10 secretion by human dendritic cells and their ability to reduce the IL-17^{+}RORγt^{+}/IL-10^{+}FoxP3^{+} ratio in CD4^{+} T cells. *Immunol. Lett.* **2015**, *163*, 157–162. [CrossRef]
120. Grether-Beck, S.; Marini, A.; Jaenicke, T.; Brenden, H.; Felsner, I.; Aue, N.; Brynjolfsdottir, A.; Krutmann, J. Blue Lagoon Algae Improve Uneven Skin Pigmentation: Results from in vitro Studies and from a Monocentric, Randomized, Double-Blind, Vehicle-Controlled, Split-Face Study. *Skin Pharmacol. Physiol.* **2022**, *35*, 77–86. [CrossRef]
121. Nicoletti, G.; Saler, M.; Tresoldi, M.M.; Faga, A.; Benedet, M.; Cristofolini, M. Regenerative effects of spring water-derived bacterial lysates on human skin fibroblast in in vitro culture: Preliminary results. *J. Int. Med. Res.* **2019**, *47*, 5777–5786. [CrossRef]
122. Mahé, Y.F.; Martin, R.; Aubert, L.; Billoni, N.; Collin, C.; Pruche, F.; Bastien, P.; Drost, S.S.; Lane, A.T.; Meybeck, A. Induction of the skin endogenous protective mitochondrial MnSOD by *Vitreoscilla filiformis* extract. *Int. J. Cosmet. Sci.* **2006**, *28*, 277–287. [CrossRef]
123. Guéniche, A.; Hennino, A.; Goujon, C.; Dahel, K.; Bastien, P.; Martin, R.; Jourdain, R.; Breton, L. Improvement of atopic dermatitis skin symptoms by *Vitreoscilla filiformis* bacterial extract. *Eur. J. Dermatol.* **2006**, *16*, 380–384.
124. Guéniche, A.; Dahel, K.; Bastien, P.; Martin, R.; Nicolas, J.F.; Breton, L. *Vitreoscilla filiformis* bacterial extract to improve the efficacy of emollient used in atopic dermatitis symptoms. *J. Eur. Acad. Dermatol. Venereol.* **2008**, *22*, 746–747. [CrossRef]
125. Guéniche, A.; Cathelineau, A.C.; Bastien, P.; Esdaile, J.; Martin, R.; Queille-Roussel, C.; Breton, L. *Vitreoscilla filiformis* biomass improves seborrheic dermatitis. *J. Eur. Acad. Dermatol. Venereol.* **2008**, *22*, 1014–1105. [CrossRef]
126. Guéniche, A.; Knaudt, B.; Schuck, E.; Volz, T.; Bastien, P.; Martin, R.; Röcken, M.; Breton, L.; Biedermann, T. Effects of nonpathogenic gram-negative bacterium *Vitreoscilla filiformis* lysate on atopic dermatitis: A prospective, randomized, double-blind, placebo-controlled clinical study. *Br. J. Dermatol.* **2008**, *159*, 1357–1363. [CrossRef]
127. Volz, T.; Skabytska, Y.; Guenova, E.; Chen, K.M.; Frick, J.S.; Kirschning, C.J.; Kaesler, S.; Röcken, M.; Biedermann, T. Nonpathogenic bacteria alleviating atopic dermatitis inflammation induce IL-10-producing dendritic cells and regulatory Tr1 cells. *J. Investig. Dermatol.* **2014**, *134*, 96–104. [CrossRef]
128. Seité, S.; Zelenkova, H.; Martin, R. Clinical efficacy of emollients in atopic dermatitis patients-relationship with the skin microbiota modification. *Clin. Cosmet. Investig. Dermatol.* **2017**, *10*, 25–33. [CrossRef]
129. Gannesen, A.V.; Borrel, V.; Lefeuvre, L.; Netrusov, A.I.; Plakunov, V.K.; Feuilloley, M.G.J. Effect of two cosmetic compounds on the growth, biofilm formation activity, and surface properties of acneic strains of *Cutibacterium acnes* and *Staphylococcus aureus*. *MicrobiologyOpen* **2019**, *8*, 2045–8827. [CrossRef] [PubMed]
130. Berardesca, E.; Bonfigli, A.; Cartigliani, C.; Kerob, D.; Tan, J. A Randomized, Controlled Clinical Trial of a Dermocosmetic Containing Vichy Volcanic Mineralizing Water and Probiotic Fractions in Subjects with Rosacea Associated with Erythema and Sensitive Skin and Wearing Protective Masks. *Clin. Cosmet. Investig. Dermatol.* **2023**, *11*, 71–77. [CrossRef] [PubMed]
131. Mourelle, M.L.; Gómez, C.P.; Legido, J.L. Microalgal Peloids for Cosmetic and Wellness Uses. *Mar. Drugs* **2021**, *19*, 666. [CrossRef]
132. Gudmundsdottir, A.B.; Brynjolfsdottir, A.; Olafsdottir, E.S.; Hardardottir, I.; Freysdottir, J. Exopolysaccharides from *Cyanobacterium aponinum* induce a regulatory dendritic cell phenotype and inhibit SYK and CLEC7A expression in dendritic cells, T cells and keratinocytes. *Int. Immunopharmacol.* **2019**, *69*, 328–336. [CrossRef] [PubMed]
133. Strohl, W.R.; Schmidt, T.M.; Lawry, N.H.; Mezzino, M.J.; Larkin, J.M. Characterization of *Vitreoscilla beggiatoides* and *Vitreoscilla filiformis* sp. nov., nom. rev., and comparison with *Vitreoscilla stercoraria* and *Beggiatoa alba*. *Int. J. Syst. Bacteriol.* **1986**, *36*, 302–313. [CrossRef]
134. Contreras, S.; Sagory-Zalkind, P.; Blanquart, H.; Iltis, A.; Morand, S. Complete genome sequence of *Vitreoscilla filiformis* (ATCC 15551), used as a cosmetic ingredient. *Genome. Announc.* **2017**, *5*, e00913-17. [CrossRef]
135. Li, L.; Jun, H.; Dawei, Z.; Jammayrac, O.; Bastien, P.; Carpentier, M.; Aubert, L. Evaluation of the Efficacy and Skin Tolerance of a Cream Containing 1% *Vitreoscilla filiformis* Extract Applied on Chinese Women with Sensitive Skin. *Chin. J. Med. Aesthet. Cosmetol.* **2006**, *12*, 195–197. [CrossRef]
136. Guéniche, A.; Valois, A.; Kerob, D.; Rasmont, V.; Nielsen, M. A combination of *Vitreoscilla filiformis* extract and Vichy volcanic mineralizing water strengthens the skin defenses and skin barrier. *J. Eur. Acad. Dermatol. Venereol.* **2022**, *36*, 16–25. [CrossRef]
137. Gueniche, A.; Valois, A.; Salomao-Calixto, L.; Sanchez-Hevia, O.; Labatut, F.; Kerob, D.; Nielsen, M. A dermocosmetic formulation containing Vichy volcanic mineralizing water, *Vitreoscilla filiformis* extract, niacinamide, hyaluronic acid, and vitamin E regenerates and repairs acutely stressed skin. *J. Eur. Acad. Dermatol. Venereol.* **2022**, *36*, 26–34. [CrossRef] [PubMed]
138. Mijouin, L.; Hillion, M.; Ramdani, Y.; Jaouen, T.; Duclairoir-Poc, C.; Follet-Gueye, M.L.; Lati, E.; Yvergnaux, F.; Driouich, A.; Lefeuvre, L.; et al. Effects of a skin neuropeptide (substance P) on cutaneous microflora. *PLoS ONE* **2013**, *8*, e78773. [CrossRef]
139. Drouillard, S.; Poulet, L.; Marechal, E.; Amato, A.; Buon, L.; Loiodice, M.; Helbert, W. Structure and enzymatic degradation of the polysaccharide secreted by *Nostoc commune*. *Carbohydr. Res.* **2022**, *515*, 108544. [CrossRef] [PubMed]