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Review

Bioengineered Skin Microbiome: The Next Frontier in Personalized Cosmetics

Cherelle Atallah [1,†], Ayline El Abiad [1,†], Marita El Abiad [1,†], Mantoura Nakad [2,*] and Jean Claude Assaf [1,*]

[1] Department of Chemical Engineering, Faculty of Engineering, University of Balamand, P.O. Box 100, Tripoli 1300, Lebanon; cherelle.atallah@std.balamand.edu.lb (C.A.); ayline.elabiad@std.balamand.edu.lb (A.E.A.); marita.elabiad@std.balamand.edu.lb (M.E.A.)
[2] Department of Sustainability in Engineering, Faculty of Engineering, University of Balamand, Koura Campus, Kelhat P.O. Box 100, Lebanon
* Correspondence: mantoura.nakad@balamand.edu.lb (M.N.); jeanclaude.assaf@balamand.edu.lb (J.C.A.)
† These authors contributed equally to this work.

Abstract

Human skin microbiome plays a fundamental role in maintaining skin health, immunity, and appearance. While current microbiome-friendly cosmetics emphasize the use of probiotics and prebiotics, recent advances in bioengineering are paving the way for a new generation of personalized and sustainable skincare solutions. This evolution is increasingly necessary given the limitations of conventional dermatological treatments in addressing individual variability. Emerging technologies such as artificial intelligence (AI), synthetic biology, and high-throughput microbiome sequencing now enable precise skin analysis and the development of tailored, more effective cosmetic formulations. This review critically examines these technological breakthroughs, including genetic modification of microbial strains, engineered delivery systems, and quorum sensing modulation, with a focus on their cosmetic and therapeutic applications. These innovations not only facilitate product customization but also reduce environmental impact by minimizing resource use, synthetic chemicals, and testing burdens aligning with sustainability goals. Several structured tables synthesize the latest findings on microbial targets, bioengineered ingredients, delivery platforms, and mechanistic pathways, providing a practical reference for researchers and product developers. Additionally, this review addresses key regulatory and safety considerations, particularly those associated with genetically modified organisms (GMOs) in cosmetic products. It highlights the need for region-specific clinical trials, toxicity assessments, and microbial safety screening to ensure consumer protection. While current frameworks offer a foundation, further ethical and environmental guidelines may be necessary as synthetic biology advances. Thus, AI-integrated synthetic biology and microbiome transplantation emerge as transformative pathways for advancing sustainable, personalized skincare innovation.

Keywords: microbiome; bioengineering; synthetic biology; cosmetics; personalized skin care; sustainability

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1. Introduction

The human skin microbiome is an ecosystem of bacteria, fungi and viruses which plays a crucial role in maintaining skin health. This ecosystem protects the skin barrier against infections and pathogenic invaders [1–3]. Thus, it also helps moderate and regulate the immune system in order to prevent inflammation and skin disorders that result from

overreactions of the immune system [2,4]. Furthermore, the skin microbiome ensures a balanced microbial environment, therefore maintaining homeostasis which is essential for the body to function properly [2,4,5]. Sustaining and supporting the natural balance of the skin's microbiome is crucial for skin health which is a main goal of microbiome-friendly cosmetics [6,7]. These microbiome-friendly products can be used as anti-aging products, treatments for skin conditions such as acne and eczema, and even as moisturizing products that enhance skin hydration [8]. The beneficial impacts of these products are a result of the application of prebiotics, probiotics, and natural antimicrobial agents which compose the main ingredients of microbiome-friendly cosmetics [7,8]. These ingredients help in nurturing beneficial bacteria while controlling harmful ones, thus upholding skin balance and preventing risks of allergic reactions that result from chemical-based cosmetics [9].

In parallel to these products, research proved that synthetic biology has the potential to efficiently contribute to dermatology by developing innovative systems and devices that help better understand disease mechanisms. Hence, it led to the production of advanced, rapid and accurate diagnostic tools for skin infections [10]. Synthetic biology can also provide novel strategies and tools to improve existing treatments of various skin conditions through tissue engineering [11], developing skin substitutes [12,13], wound healing and infection control [14]. Synthetic biology has the potential to revolutionize dermatology by offering therapeutic strategies, solutions for skin tissue regeneration, and treating dermatological conditions. Additionally, it is critical to address the current challenges in skin health. For instance, wound healing through traditional and current treatments can lead to severe skin scarring [15]. Similarly, treating burns and chronic ulcers can lead to functional and aesthetic skin issues [16]. Bioengineered skin is being integrated in dermatology due to its high potential in addressing skin conditions [17]. By manipulating and using cells and scaffolds, skin substitutes—with similar structure and function to natural skin—have been developed [15]. However, their effectiveness is limited to repairing the skin rather than regenerating it [16]. Moreover, it varies with individuals which prompts the need for bioengineered solutions for personalized skincare [17,18].

Personalized skincare tailored to individual needs is essential for maintaining skin microbial balance and overall skin health. This review first outlines current knowledge of the skin microbiome in cosmetics, emphasizing how microbial balance affects skin conditions and how these conditions are influenced by environmental interactions. Indeed, it highlights the benefits and current use of probiotic-based skincare products. Furthermore, this review explores emerging technologies in personalized skincare, particularly the potential of synthetic biology in addressing skin issues. Hence, it underscores the role of artificial intelligence (AI) through existing AI-driven approaches. Thus, the current applications, regulatory challenges, sustainability considerations, and future directions in bioengineered skin microbiome research were also examined.

2. The Current Understanding of Skin Microbiome in Cosmetics

Skin microbiome plays a crucial role in maintaining skin health and creates the need to implement microbiome-friendly ingredients in cosmetic products. Hence, it is therefore essential to understand the role of natural skin bacteria in maintaining skin health and contributing to cosmetic efficacy. This section will develop the importance of skin bacteria and provide information on commercial probiotics and prebiotics in skincare, highlighting their key role in enhancing the skin microbiome.

2.1. Role of Natural Skin Bacteria in Beauty and Skin Health

Exceeding human cells by more than tenfold, commensal bacteria are diverse and abundant microorganisms forming an ecosystem that inhabits mucosal and epidermal

surfaces [19,20]. Fungi are also part of the human ecosystem and play a significant role in the skin microbiome as they are diverse and can be found on dry, moist and oily skin environments [21]. They can contribute to the skin's protective immunity as they affect the composition of bacterial communities [22,23]. However, skin disorders can be associated with imbalances in fungal populations, such as infections and non-infectious conditions like psoriasis and atopic dermatitis [23,24]. Another major component of the skin microbiome is viruses and eukaryotic viruses that can modulate the composition of the bacterial community and influence the functions of host cells through genetic exchange [25,26]. The composition of commensal bacteria varies between individuals depending on one's health, diet, living conditions, and the status of the host immune system [19]. These bacteria are responsible of modulating adaptive and innate immune interactions through signaling to the skin via the TLR2/TLR1 pathway, unlike non-commensal bacteria which signal via TLR2/TLR6 which triggers a stronger immune response [27]. Toll-like receptors (TLRs) are essential for recognizing microbial components and initiating immune responses [28]. Indeed, the TLR2/TLR1 pathway is more associated with a balanced immune response to commensal bacteria, while the TLR2/TLR6 pathway triggers a stronger response to pathogenic bacteria, shedding light on the versatility and specificity of TLR-mediated immune regulation [29–31]. By blocking pathogen adhesion, they reduce their impact through the synthesis of immunological substances and the production of antimicrobial products, contributing to pathogen colonization prevention [32–34]. Highlighting the importance and contribution of commensal bacteria is their ability to protect the skin barrier from dehydration and aging [35]. A common commensal bacterium is *Staphylococcus epidermidis* which aids in producing ceramide, thus maintaining the skin barrier's integrity [35]. In addition, *Cutibacterieum acnes* is known for its ability to form biofilms [36,37]. These biofilms are implemented in post-surgical infections, especially those involving the implementation of medical devices [38]. Commensal bacteria also prevent skin inflammation by maintaining a balanced and healthy microbiome which is crucial in preventing skin conditions [39]. For instance, disturbance in microbial balance, particularly involving *Cutibacterieum acnes*, can lead to acne development [40]. Additionally, severe eczema is a result of imbalanced *Staphylococcus aureus* [41,42].

In parallel, this disbalance can accelerate aging due to an increase in systemic inflammation [43]. The interaction between the skin microbiome and its environment is key in affecting microbial balance [44]. First, toxic pollutants such as heavy metals can induce inflammation and oxidative stress by increasing pathogenic bacteria such as *Staphylococcus aureus* and decreasing beneficial bacteria like *Corynebacterium* and *Propionibacterium* [44,45]. Therefore, Lam et al. (2022) and Reztsova et al. (2020) warn that the skin microbiome produces metabolites that can protect the skin as desired or contribute to inflammation, depending on the microbial balance [38,41]. Another factor that may impact the skin's ability to defend itself against infections is exposure to UV radiation [44]. This UVB radiation (290–320 nm) is the most harmful, it increases the risk of skin infections and sunburns, damaging the skin barrier [45]. This damage is primarily due to the disruption of the epidermal barrier, oxidative stress, and inflammation caused by UVB exposure [46,47]. The skin's defense mechanism against such threats is enhancing its immune response [39,42]. UV radiation can suppress the immune system by inhibiting antigen presentation, stimulating the release of immunosuppressive cytokines, and inducing the generation of regulatory lymphocytes [48]. In addition, silver nanoparticles (AgNPs) have the potential to enhance the absorption of UV radiation due to their unique optical properties. The comparative analysis conducted by Khatoon et al. showcases a peak in the UV-Vis spectra, known as Surface Plasmon Resonance (SPR) [49]. This peak occurs around 395 nm to 440 nm which suggests remarkable absorption of UV [50]. Also, AgNPs can be synthesized using

UV light, thus improving their absorption properties [51]. Furthermore, chemical-based products, unlike microbiome-friendly products, can cause harm to the skin barrier leading to irritations and allergic reactions [9,41]. Using therapeutic targets such as *Cutibacterieum acnes* and *Staphylococcus aureus* along with probiotics and postbiotics support the skin when faced with conditions such as eczema, aging and acne [52]. Table 1 provides insight into these therapeutic targets.

Table 1. Skin Microbiome Therapeutic Targets.

Condition	Therapeutic Target	Key Information	Efficiency	References
Acne	*Cutibacterium acnes* (*C. acnes*).	- Dysbiosis involving *C. acnes* is linked to acne. - Targeting specific strains of *C. acnes* may be necessary.	Colonization rate: 96% of patients	[52,53]
Eczema	*Staphylococcus aureus* (*S. aureus*).	- Increased colonization by *S. aureus* is associated with eczema severity. - Loss of bacterial diversity is a key factor.	Lesional Skin: 70.2% colonized, with 47.3% being *S. aureus*. Non-lesional Skin: 32.7% colonized, with 27.9% being *S. aureus*	[54,55]
Aging	General microbial balance (Usage of probiotics and prebiotics).	- Microbial imbalance can accelerate skin aging. - Probiotics and prebiotics reduce signs of aging and maintain skin health.	Bifidobacteria increase was observed during synbiotic supplementation and Reduction in Inflammatory Markers: Enhanced IL-10 production and decreased TNF-α.	[56,57]

2.2. Commercial Probiotics and Prebiotics in Skincare

Probiotic-based skincare products are becoming more mainstream due to their potential in improving skin health [58]. These products benefit the skin through multiple mechanisms; starting with maintaining a healthy and balanced skin microbiome by controlling harmful bacteria and boosting the growth of beneficial ones [58–61]. Additionally, probiotics such as *Lactobacillus rhamnosus* and *Lactobacillus reuteri* DSM 17938 contribute to enhanced skin health by their production of antimicrobial substances that target the elimination of pathogenic bacteria [58,62]. These skincare products manage skin inflammation by stimulating the immune system which is essential for healthy skin [58,60,62]. Thus, probiotic-based products keep the skin hydrated, reduce wrinkle depth and minimize pore size [59,63,64]. Probiotic-based skincare are currently used as anti-aging, moisturizing and skin disorders preventing products [59]. Key probiotic ingredients such as *Lactobacillus plantarum* and *Bifidobacterium lactis* are used in moisturizers, *Micrococcus luteus* is commonly found in serums aimed at reducing pores and wrinkles, and *Bacillus coagulans* is utilized in anti-aging creams due to significantly increasing skin hydration by up to 101% [62,65]. Hence, several skincare brands are shifting towards developing their products using microbiome-friendly ingredients, thus avoiding the use of alcohols and fragrances. The table below (Table 2) summarizes the main ingredients of commercial microbiome-friendly products.

Table 2. Comparison of microbiome-friendly cosmetics and their ingredients.

Category	Description	Examples	Composition	Effects on Microbiome	Efficiency	References
Probiotics	Beneficial bacteria used in cosmetics to promote healthy skin microbiome.	*Micrococcus luteus Q24.*	*Lactobacillus* and *Bifidobacterium.*	Hydrates the skin, reduces pores, wrinkles, spots and impurities.	45–80% reduction in skin impurities and 83.1 ± 6.1% encapsulation efficiency.	[61]
Prebiotics	Non-digestible ingredients that support the growth of beneficial bacteria on the skin to enhance its natural defenses.	Prebiotic formulations such as serums and face creams.	Inulin, fructo-oligosaccharides, and other oligosaccharides.	Strengthens skin's proteome, and stimulates beneficial microbiota.	Reduces the severity of atopic dermatitis (AD) and xerosis, improves skin barrier properties, and provides itch relief within 4 weeks.	[10]
Natural Antimicrobial Agents	Ingredients derived from natural sources that control harmful bacteria without altering beneficial microbiota.	Plant extracts, essential oils, phenolic compounds, alkaloids, and polyphenols.	Tea tree oil, neem oil, and other plant-derived antimicrobial compounds such as antibiotics, antifungals, antivirals and antiprotozoals.	Helps maintain microbiome balance and provides antimicrobial benefits.	35% reduction in burn wound infection.	[10,66]
Bio-surfactants	Eco-friendly alternatives to synthetic surfactants, naturally produced by bacteria such as *Pseudomonas aeruginosa* and *Bacillus* species.	Bacterial bio-surfactants.	Sophorolipids, rhamnolipids and lipopeptides.	Biodegradable, non-toxic, and compatible with skin microbiome.	Not specifically mentioned.	[67,68]
Fermented ingredients	Ingredients obtained through fermentation processes; often contain beneficial microbial metabolites.	Ferments of rice and soy. Fermented oils such as *F-Shiunko*, *F-Artemisia* and *F-Glycyrrhiza.*	Fermented rice extract, fermented soy extract, and other fermented botanicals which includes plant-derived products.	Have varying effects on skin microbiota with properties like skin moisturizing, antioxidant, and skin-whitening.	Improved skin condition and gut microbiota.	[69]
Microbial Polysaccharide Gums	Polysaccharides produced by microbes, used for their functional properties in cosmetics.	Various microbial polysaccharide gums.	Xanthan gum, gellan gum, and other polysaccharides derived from microbial fermentation.	Have functions like emulsion stabilization and skin conditioning which provides safe use in cosmetics.	Not specifically mentioned.	[70]

In parallel, Figure 1 illustrates real life applications of probiotic ingredients in commercial cosmetics. These ingredients are key factors in enhancing skin health and in optimizing the efficacy of skincare products.

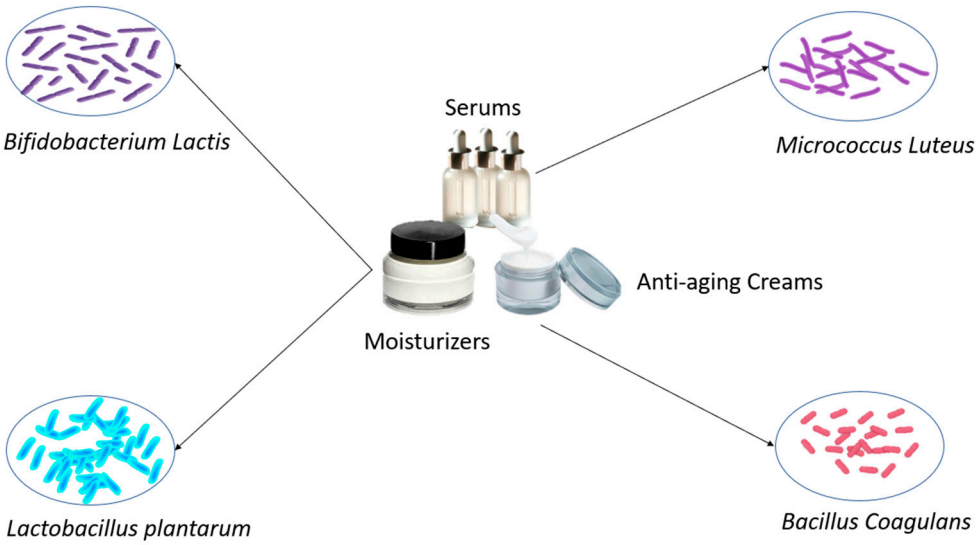


Figure 1. Probiotic ingredients used in cosmetic formulations.

3. Bioengineering and Synthetic Biology for Skincare

Synthetic biology is being recognized for its beneficial impact on skin health and on skin microbiome balance [71]. Thus, it contributes to the advancement of technologies aiming to provide treatments to skin disorders [71]. This section provides an insight

into current advances in genetically modified bacteria. It also focuses on the importance of engineered microbes in cosmetics and it highlights the potential of synthetic biology in dermatology. Figure 2 illustrates the mechanisms by which bioengineered bacteria contribute to skin health, including biofilm production, antimicrobial peptide secretion, gene delivery, inflammation suppression, and competitive inhibition of harmful pathogens.

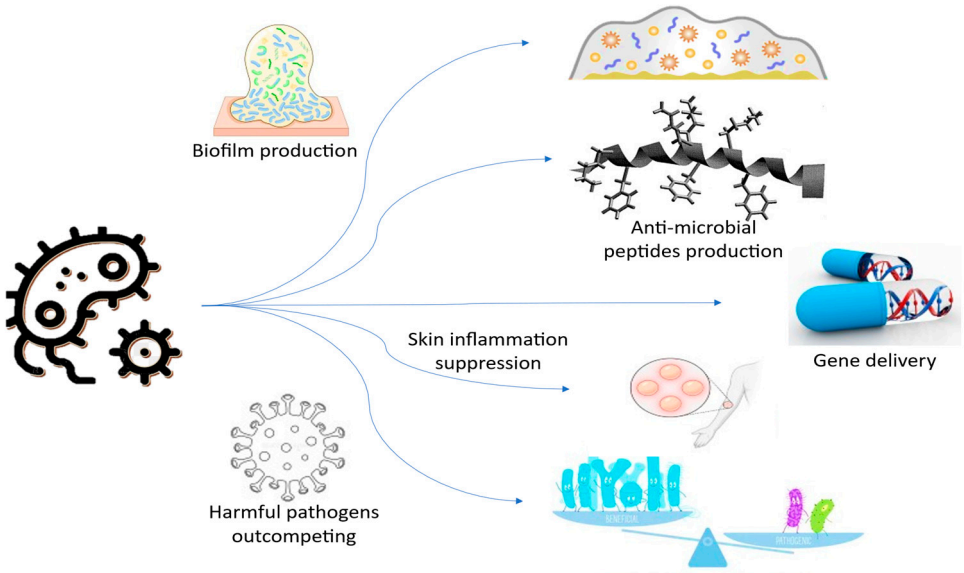


Figure 2. Key interactions between bioengineered bacteria and skin cells.

3.1. Advances in Genetically Modified Bacteria for Dermatology

Treating acne has always been the center of research aiming to improve skin health, resulting in several medications against acne [72]. Bioengineered strains created a new pathway to cure and treat acne through the production of antimicrobial peptides (AMPs) [72]. Due to their ability to effectively reduce acne (68–83% reduction in bacterial activity), AMPs became promising alternatives to traditional antibiotics. Bioengineering techniques have been employed to optimize the stability, selectivity and production efficiency of AMPs [73,74]. Two main production methods are used in this process: recombinant production and synthetic production [74,75]. The former is effective for large-scale productions while being cost-effective and scalable [74]. However, it faces challenges in managing peptide toxicity, thus requiring the implementation of fusion proteins and inclusion bodies [74]. Whereas, the latter, synthetic production, is based on a chemical process which creates an efficient way of controlling peptides structures and modifications, improving their activity [73,75]. Another branch of dermatology is the production of anti-inflammatory compounds to reduce infections and itching [76]. Research proved that *Staphylococcus epidermidis* is able to reduce inflammation and promote a healthy skin through various approaches [76]. This bacterium produces anti-inflammatory metabolites and lipoteichoic acid which promotes collagen synthesis and can diminish UV radiation damage to the skin barrier [76]. Moreover, its interaction with host cells like keratinocytes, increases the production of antimicrobial peptides such as human β-defensin 2 (hBD2) and hBD3 in keratinocytes which are effective against infections as Lai et al. state in their study [77]. *Staphylococcus epidermidis* has also been subjected to genetic engineering, expressing tumor antigens (like Carcinoembryonic Antigen) which has the potential to elicit anti-inflammatory responses [78].

3.2. Engineering Skin-Friendly Microbes for Cosmetic Applications

The development of bacteria that produce anti-aging peptides has great potential in various applications. Thus, among the most well-known ribosomally synthesized antimicrobial peptides are bacteriocins, primarily produced by lactic acid bacteria [79,80]. Several complex pathways exist for the production of bacteriocins, including quorum sensing [81,82]. This technique starts by producing signal molecule production, also known as autoinducers, with an increase in concentration with bacterial population growth [83]. Reaching a critical threshold, these autoinducers bind to specific bacterial cells which alters gene expression by initiating a signal transduction cascade [83,84]. This binding results in gene regulation which is essential in order to ensure a production of bacteriocins solely when the bacterial population is effectively dense [84,85]. Furthermore, anti-aging peptides are applied in skin health due to their antimicrobial and antioxidant properties [86,87]. For example, the fermentation of silk peptides by thermophilus plays a huge role in reducing inflammation, enhancing skin barrier and promoting collagen synthesis since it reduces the expression of IL-1β, IL-6, and AGEs, and promotes the expression of FLG, AQP3, SOD, and COL-1 [86]. In addition, producing procollagen by bacteriochlorophyll α demonstrated significant anti-aging effects [87].

Maintaining healthy skin also involves an even skin tone which requires melanin production [88]. Several generic modifications were developed to enhance melanin production through the melanogenesis process [89]. This process takes place in melanocytes, cells located in hair follicles and in the basal layer of epidermis [89,90]. First, during embryonic development, melanoblasts mitigate from the neural crest to the epidermis [88]. Then, tyrosinase, the essential enzyme for melanin biosynthesis, catalyzes the initial hydroxylation of L-tyrosine to L-DOPA and its subsequent oxidation to DOPA-quinone [90,91]. Finally, melanin is synthesized within melanosomes which regulates skin pigmentation [90,92,93]. In order to increase melanin production, several generic modifications have been implemented into this process. First, compounds that can increase tyrosinase activity have been identified such as a methanol extract of *Ardisia crenata* with a concentrations of 10, 20, and 40 μg/mL which led to a concentration-dependent increase in melanin levels [92]. Moreover, regulating tyrosinase expression by MITF (Microphthalmia-Associated Transcription Factor) influences melanin production [94]. In addition, suppressing certain pathways such as ERK and Akt pathways promotes melanogenesis [95].

Certain microorganisms have shown the potential to protect the skin against these harmful radiation through the production of UV antioxidants and protectants [96,97]. For example, *Cyanobacteria* and fungi can lead to the production of mycosporine-like amino acids, UV protectants, which transform UV-A and UV-B into harmless heat [96,98,99]. As another defense mechanism, microalgae and extremophiles produce carotenoids as antioxidants [97,100,101]. The inclusion of these techniques creates an opportunity to enhance skincare and cosmetics products.

3.3. Potential of CRISPR and Synthetic Biology in Beauty Industry

Clustered Regularly Interspaced Short Palindromic Repeat (CRISPR) technology, along with synthetic biology, holds immense potential to revolutionize the beauty industry by enabling the creation of novel biological systems and facilitating precise genetic modifications [102,103]. CRISPR is a gene-editing technology that can make precise modifications to the genetic material of living organisms [104]. Thus, it resembles an adaptive immune system in bacteria that defends against viral DNA by the recognition and removal of foreign genetic elements [105,106]. The CRISPR system primarily consists of two components, the Cas9 enzyme that acts as molecular scissors that will cut the DNA at specific locations, and a guide RNA (gRNA) which directs Cas9 to the target DNA sequence, ensuring precise

editing [106,107]. Moreover, CRISPR technology offers efficient methods to edit microbial genes which can be leveraged for many cosmetic applications such as the production of cosmetics ingredients such as astaxanthin and citric acid [108]. For instance, CRISPR is able to optimize the metabolic pathways in *Cyanobacteria* for enhanced hyaluronic acid (HA) production. HA is widely used in cosmetics because it has moisturizing properties [109]. By repressing specific genes such as TP53 (86% repression), CRISPR achieved significant increases in the production of HA resulting in higher yields in cosmetic applications [110]. In addition, CRISPR enhances the production of terpenoids, which have therapeutic properties and good fragrance by editing microbial hosts such as *Escherichia coli* and *Saccharomyces cerevisiae* [110]. Furthermore, CRISPR presents many advantages in cosmetics applications such as increased precision and efficiency [111]. Thus, CRISPR allows for precise targeting and modification of specific genes, which is crucial for optimizing the production of cosmetic ingredients such as Violaceins and Red Pigments [112]. There are two types of targeted genes which are knockout and knock-in genes. Knockout genes are disrupted by CRISPR by introducing mutations, a useful approach for observing phenotypic effects of gene loss [113]. Knock-in genes have modified specific sequences including epitope tags, green fluorescent protein, and protein tags that allow for studying gene function with beneficial traits [114]. Also, this technology can be applied to a wide range of microorganisms, including fungi, bacteria and archaea, presenting the opportunity of producing diverse cosmetic compounds and allowing significant implications in biotechnology [114]. Finally, it is cost-effective compared to other genetic modification methods that are more expensive and time consuming, making it more suitable for large-scale industrial applications [112,115]. Advances in synthetic biology platforms allow for safe and stable microbial applications. In fact, recent developments that focus on engineering microbial consortia involve multiple interaction microbial species [116]. These consortia are designed for various applications like bioproduction, bioremediation, and therapeutic interventions [117]. Therefore, it is crucial to maintain the ability to control intercellular interactions and maintain stability and robustness in these communities [118]. Engineering microbes are developed as biosensors to monitor the environment and diagnose diseases [119]. Advances in circuit design, biocontainment, and machine learning are optimizing the performance and safety of these microbial sensors [119]. Biocontainment is a robust strategy that also ensures the safety of engineered microbes by designing genetic circuits that prevent the escape of engineered traits into the environment [120]. Metabolic engineering of microbes like *Corynebacterium glutamicum* and *Saccharomyces cerevisiae* has significantly improved due to synthetic biology [120]. These advances include optimizing metabolic pathways and enhancing the stability of engineered strains (L-Isoleucine production increased by 13.01%) [121]. According to Wan et al. (2021) and Brooks et al. (2021), the future of engineered microbiome-based beauty products is promising knowing that it is driven by advancements in synthetic biology and microbiome research [120,121]. Technological advancements include synthetic biology and AI innovations that enable precise manipulation of microbial communities for various skincare applications [121]. Indeed, these technologies aid in the development of probiotics or other microbiome-friendly ingredients that improve skin health and appearance [121]. Postbiotics, derived from probiotics, also offer advantages like longer shelf life and greater safety, making them suitable for cosmetic formulations [122]. Regulation (EC) No 1223/2009 addresses the minimum durability of products in Article 19, section c, specifying that products with a minimum durability of 30 months or less must display a "best before" date on the packaging [123]. The future of engineered microbiome-based beauty products is bright, with ongoing research and technological advancements paving the way for innovative and effective skincare solutions. It is important to note that ensuring the safety of microbiome-based beauty products is as crucial as ensuring the efficiency

of the products which will be discussed later on. The table below (Table 3) summarizes different bioengineering techniques and explains their role in the cosmetic field.

Table 3. Bioengineering techniques and their cosmetic applications.

Bioengineering Technique	Cosmetic Application	Description	References
Recombinant DNA Technology	Production of bioactive molecules such as vitamins and oils, peptides and proteins, amino acids like serine, alanine and threonine, and biotechnologically derived compounds.	Used for large-scale production of ingredients like epidermal growth factor, botulinum toxin, collagen, ceramide, and kojic acid. These ingredients are used for skin and hair care, replacing harmful synthetic compounds.	[124]
Cell Culture Techniques	Creation of cosmetic ingredients like plant cell culture-derived ingredients and microbial and fermentation-derived ingredients.	Ingredients are created in sterile fermentation reactors, avoiding the need for growing, harvesting, and extracting. This leads to safer and more effective products.	[125]
Biorefinery and Bioconversion	Purification of bioactive molecules.	Enables the addition of pure phytochemicals in cosmetic formulations, eliminating the need for crude plant extracts and reducing side effects.	[124]
Synthetic Biology	Development of cosmetic ingredients such as hyaluronic acid, kojic acid, collagen, resveratrol, peptides, ceramides, Epidermal Growth Factor (EGF), Botulinum Toxin and polyphenols and terpenes.	Focuses on creating effective, safe, and environmentally friendly ingredients.	
Phage Display	Skin infection and acne treatment.	Bacteriophages are used as nanomaterials, delivery vectors, and growth factor alternatives.	
Engineered Skin Tissue	Cosmetic testing and toxicological evaluation.	Used for in vitro testing of cosmetic products, providing a scientific method for safety assessment.	[126]
Algal Biotechnology	Production of active ingredients, such as brown macroalgae, green macroalgae and red macroalgae.	Extracts from algae are used for anti-aging, moisturizing, whitening, UV protection and anti-cellulite care.	[127]
Bioengineering of Volatile Carboxylic Acids (VCAs)	Ingredient production.	VCAs are used in various cosmetic formulations, with advanced techniques for their efficient separation and collection.	[128]
Freeze-dried Aloe Vera Extract	Skin hydration.	Used in moisturizing formulations to improve skin hydration.	[129]

It is important to highlight that genetically modified microbes are employed to produce bioactive compounds, while nanocarriers such as liposomes and nanoparticles encapsulate and transport these actives across the skin barrier [124]. Thus, this combined approach enhances ingredient stability, bioavailability, and targeted delivery in personalized cosmetic applications. The below figure (Figure 3) represents this bioengineered approach.

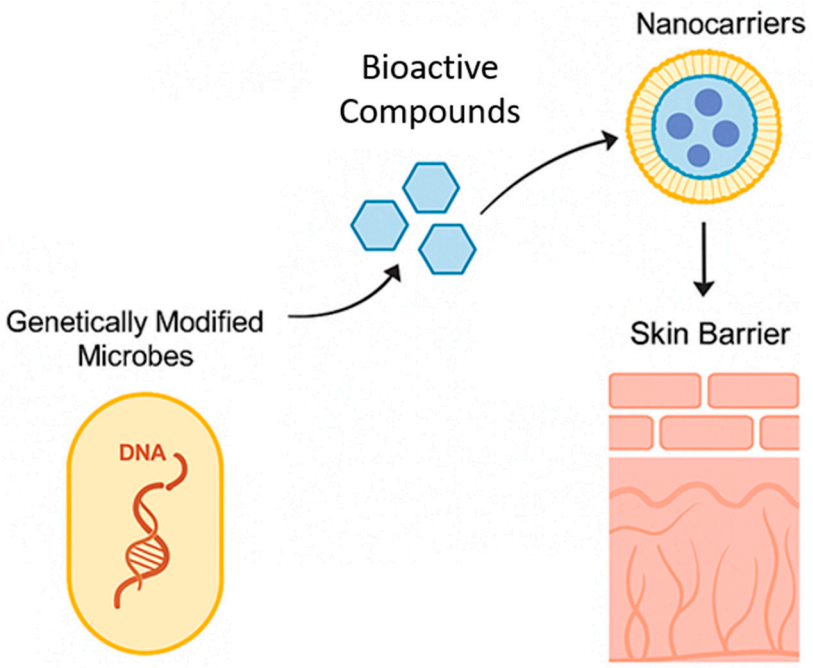


Figure 3. Schematic representation of bioengineered microbial strains and engineered delivery systems in cosmetic formulations.

4. Next-Generation Personalized Microbiome-Based Cosmetics

Advanced technologies such as microbiome sequencing can help formulate personalized skincare to satisfy an individual's needs for optimal skin health knowing that each microbiome is unique. This section explains how microbiome sequencing allows the customization of skincare as it is a transformative technology that offers genomic advancements. AI-driven microbiome analysis has also proved to be efficient for tailor-made cosmetics specific for each microbiome due to AI capabilities in diagnosing skin conditions.

4.1. Customizing Skincare Through Microbiome Sequencing

Microbiome sequencing, specifically next-generation sequencing (NGS), is a transformative technology [130]. Thus, it offers genomic advancements especially in the microbiome domain because it allows the rapid sequencing of millions of DNA fragments, thus providing insight into genome structure and genetic variations [130]. The microbiome requires comprehensive understanding and some NGS approaches include pathogen surveillance, functional dysbiosis, and therapeutic potential [130]. The latest next-generation sequencing is described as the third generation of sequencing technology, commonly used for metagenome projects [130]. One example is the Oxford Nanopore platform, which is a single-molecule and real-time technology that is cost-effective and presents valuable assets for sequencing [131]. Furthermore, NGS can characterize and identify bacterial genomes and complex microbiomes [131]. Some techniques include 16S rRNA gene sequencing, metagenomics, and meta-transcriptomics which are used to study the taxonomic composition and functional potential of microbiomes [132,133]. In addition to the identification of species, NGS enables the understanding of microbial activities, interactions and their roles in the health or disease of a host [134]. Some computational methods and genome-scale metabolic models can predict microbial interactions and metabolism, providing key information on potential therapeutic targets and contributing in metabolic pathways [135,136]. One of these methods include Flux Sampling (FS) that provides a range of fluxes within a microbial community that allows the evaluation of metabolic interactions [137]. Also, Gap-Filling Algorithms address metabolic gaps by adding biochemical reactions from

external databases [138]. Moreover, sophisticated bioinformatics tools and pipelines are developed to process the enormous amount of data generated by NGS, facilitating sequence processing, clustering, alignment, taxonomic annotation, and statistical analysis [139]. For instance, sequence alignment tools such as Bowtie are useful to read large datasets, and Burrows-Wheeler Aligner is widely known for aligning short sequencing reads due to its speed and accuracy [140]. Furthermore, personalized skincare formulations tailored to individual bacterial profiles are an emerging trend in dermatology [140]. Thus, it involves customizing products that suit a person's skin profile determined through skin measurements and algorithms [140–142]. Also, probiotics or Live Biotherapeutic Products (LBPs) are used in skincare to solve skin issues such as acne, atopic dermatitis and wound healing by modulating the skin's bacterial populations [142]. Indeed, they reduce skin inflammation by enhancing the skin's immune response and by modulating cytokine production [142]. Probiotics also improve the skin barrier function and maintain hydration in order to protect the skin from the environment [64,143]. Therefore, personalized formulations are critical to enhance compatibility with the skin's unique microenvironment [143]. Another benefit for personalized formulations is that they can influence the skin microbiome in a positive way knowing that the regular use of products can alter the skin microbiome in a healthy way by improving skin hydration and texture [144]. Indeed, personalized formulations include specific active ingredients tailored to individual skin needs such as vitamins, peptides and collagens [145]. In addition, the development of self-preserving skincare products tailored to an individual's bacterial profile aids in maintaining microbiological safety without conventional preservatives [145]. Alternative preservatives such as natural and physical preservation allows the creation of safe environments that promote microbial growth and thus supporting the microbiome [146].

Microbial therapy and the use of postbiotic bacteria is also being explored for its potential in improving skin microbiome homeostasis as these therapies can be incorporated into skincare products as active ingredients, providing antimicrobial, antioxidant, and anti-inflammatory benefits [147]. For instance, postbiotics promote the growth of beneficial bacteria and inhibit harmful bacteria in order to maintain a balanced and healthy skin microbiome by producing antimicrobial substances that eliminate pathogenic bacteria [58]. Emerging commercial platforms offer microbiome-based skincare diagnostics [148]. Hence, in vitro skin models incorporate microbiome components to develop drug and cosmetic tests by replicating the human skin [148]. Moreover, cell-free systems based on *Cutibacterium* acnes have been developed for the production of protein and genetic circuit prototyping, thus showing potential for cosmetic applications [149]. Finally, customizing skincare through microbiome sequencing is an emerging field that helps understand the skin microbial communities to develop personalized skincare solutions. The figure below (Figure 4) presents a workflow of personalized microbiome-based skincare.

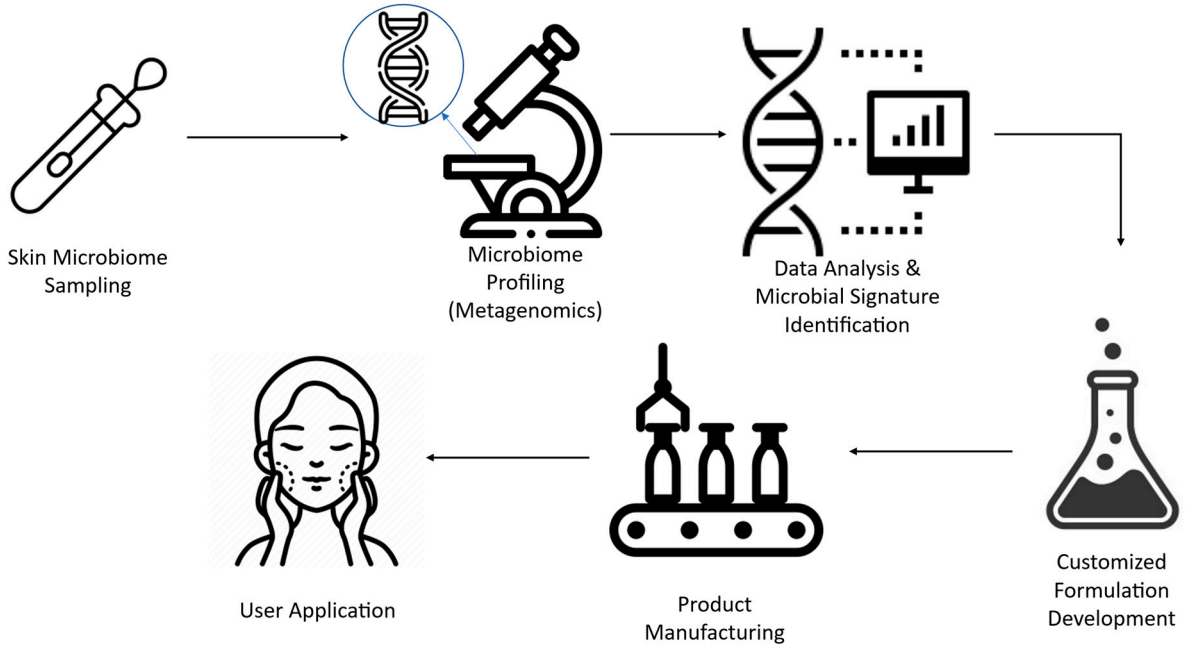


Figure 4. Workflow of personalized microbiome-based skincare.

4.2. AI-Driven Microbiome Analysis for Tailor-Made Cosmetics

The skincare industry has become so large that people encounter difficulties when trying to find suitable solutions for their specific skin needs. In fact, the wide diversity of products makes it hard for an individual to settle for a certain recommendation knowing that it may not be the best for their skin tone, type or color [150]. As a result, artificial intelligence proves to be an opportunity to enhance personalized skincare recommendations and thus provides better personal care [150]. AI models have the capability to identify and diagnose specific skin patterns in order to predict effective and efficient products for everyone [150]. The AI systems analyze skin type, acne count, UV exposure and oiliness level and other specific data to suggest tailored skincare products by using different techniques [150]. These techniques include K-Nearest Neighbors (KNN) and Natural Language Processing (NLP) that convert analyzed results into skincare regimens [150]. In addition to that, machine learning models are known to analyze molecular descriptors and solubility indices, optimizing the content of a product and its ingredients to enhance its performance [150]. AI can also simulate precise treatments to adjust real-time interventions which leads to satisfied patients and better outcomes due to skin health monitoring and proactive skincare interventions [150]. Furthermore, machine learning algorithms show potential in mapping interactions between the skin and its microbiome [151,152]. To note that, certain techniques have proven to be helpful in establishing skin age indices such as skin phenotype age (SPA), skin microbiota age (SMA), and skin integration age (SIA) [153]. These factors aid in understanding how the microbiome influences skin aging and appearance [154]. Microbiome also influences disease predictions, so some machine learning methods analyze the microbiome and can differentiate between healthy and diseased states of skin [155]. Indeed, learning algorithms succeed in investigating microbiome datasets to uncover complex patterns and come up with conclusions and solutions such as microbiome-based disease prediction and microbiome analysis [156]. Some of the most common machine learning algorithms include Support Vector Machine (SVM) which is effective for predicting health states based on microbiome data and Random Forest (RF) utilized for pattern recognition and classification, mapping microbiome interactions in high accuracy and precision [157,158]. In summary, machine learning methods analyze mi-

crobiome data by processing high-dimensional data, training predictive models, selecting relevant features and validating their performance [159].

While some studies support the effectiveness of artificial intelligence in evaluating the microbiome, others caution that errors may arise if machine learning models are not sufficiently advanced (5% error rate in disease prediction) [160,161]. With that being said, Chen et al. (2022) and Wu et al. (2021) revealed that microbiome data can be very dimensional and heterogeneous which requires machine learning models that are sophisticated enough to handle complex interactions and give accurate results that can be interpreted [160,161]. Thus, this may be due to the precision of the microbiome that should be taken into consideration while studying it [161]. In addition, the future of at-home microbiome analysis kits is promising due to the evolution of technology and its easier accessibility nowadays [162]. Growing interest in personalized health is driven by technological advancements, particularly in at-home testing kits and cost-effective sequencing for efficient microbiome analysis [162]. As a matter of fact, the rise in sequencing technologies significantly increased the efficiency of microbiome analysis while being cost effective [162]. For instance, the cost of sequencing a single bacterial genome has dropped from nearly $100,000 to less than $100, thus making large scale microbiome studies more accessible [163]. These technologies make large-scale sampling and sequencing more feasible [164].

The integration of automated technologies like microfluidic PCR enhanced the reproducibility and comparability of data [164,165]. In particular, a centrifugal microfluidic platform for qPCR showed high reproducibility with a linearity R^2 between 98.1% and 99.8% in standard curves [166]. Moreover, microfluidic PCR systems can handle small volumes that range from 100 nL to 5 µL and thus achieve amplification speeds between 100 and 400 s [167]. Another thing to consider is developing collection kits that are user-friendly, low-cost and with low-resource settings [168]. Some of these kits are available for less than 100$ if negotiated correctly, and offer user-friendly designs that do not require prior training or extensive knowledge [169–171]. Indeed, these kits are also suitable for low-resource settings due to reconfigurability, allowing them to adapt to different uses while improving supply chain responsiveness [169–171]. Furthermore, smartphone-based platforms and sensing technologies provide scalable solutions for microbiome analysis at home, thus making them far more accessible [172]. The smartphone-based systems can be operated by individuals with no special training and have the ability to provide real-life monitoring, thus allowing immediate feedback [172]. Also, these platforms can be used for health monitoring, including microbiome analysis which is crucial for understanding microbiota and health outcomes [173–175]. Thus, the integration of artificial intelligence is a crucial tool that can assist in selecting and optimizing ingredients that are favorable to an individual's skin microbiome by ensuring the selection of safe and efficient cosmetic products that do not harm the skin microbiome [173–175]. Indeed, AI-based imaging and predictive tools enable accurate treatment protocols and diagnostics that enhance the cosmetic dermatology field and improve patient satisfaction. The following table (Table 4) provides a structured overview of various techniques and their applications in microbiome research while highlighting the role of AI.

Table 4. Microbiome sequencing and AI-driven personalization.

Technique/Method	Description	Applications/ Examples	Key Points	References
High-Throughput Sequencing	Rapid sequencing of DNA/RNA to study microbial communities.	Analyzing prokaryotes in various niches.	Improved quality, speed, and cost.	[176]
16S rRNA Sequencing	Sequencing of the 16S ribosomal RNA gene to identify bacteria.	Taxonomic identification of microbiomes related to food.	Helps in understanding taxonomic composition.	[177]
Metagenomics	Sequencing of DNA from environmental samples to study microbial communities.	Studying human microbiome.	Offers species-level characterization.	[178]
Meta-transcriptomics	Sequencing of RNA to study gene expression in microbial communities.	Functional characterization of microbial interactions.	Provides insights into microbial functions.	[177]
Synthetic Biology	Engineering microbial communities for specific purposes.	Enhancing food safety and quality.	Food production processes revolution.	[179]
Artificial Intelligence (AI)	Analysing and interpreting complex microbiome data.	Personalized nutrition programs.	Dietary recommendations and health improvements.	[180]
Machine Learning (ML)	Applying algorithms to predict and analyse microbiome data.	Predicting clinical outcomes in obesity and cancer.	Identifying biomarkers and developing personalized therapies.	[181]
PCR (Polymerase Chain Reaction)	Amplifying DNA sequences to identify specific microbes.	Identification of bacteria, fungi, algae, and actinomycetes.	Isolating and characterizing microbial species.	[182]
Bioinformatics Tools	Software and algorithms to analyse sequencing data.	Analysing amplicon sequences, metagenome shotgun sequences.	Essential for processing and interpreting large datasets.	[176]
Microbial Culture	Growing microbes in controlled environments to study their properties.	Measuring functional capacity of individual microbes.	Provides detailed study of microbial traits and interactions.	[183]
Metabolomics	Study of metabolites produced by microbial communities.	Identifying gut microbiota's role in health and disease.	Offers insights into metabolic interactions and processes.	[184]
Proteomics	Study of proteins expressed by microbial communities.	Identifying functional proteins in microbiomes.	Understanding protein functions and interactions.	[183]
AI-Driven Biomarker Discovery	Identifying key microbial markers for health and disease by using AI.	Identifying biomarkers for treatments and diagnostics.	Accelerates the discovery of important microbial indicators.	[185]
Next Generation Sequencing (NGS)	Advanced sequencing technologies for detailed microbial analysis.	Investigating microbiomes of fermented and non-fermented foods.	Deep understanding of microbial communities.	[177]
Deep Learning (DL)	Advanced ML techniques for analysing complex microbiome data.	Predicting microbial interactions and health outcomes.	Uncovers complex patterns within microbiome data.	[184]
AI in Microbial Diagnostics	Using AI to enhance the accuracy and speed of microbial diagnostics.	Rapid diagnosis of microbial infections.	Improves workflow speed and accuracy in clinical settings.	[186]
Microbiome Engineering	Modifying microbial communities to improve food quality and safety.	Extending shelf life and enhancing food production.	Requires robust public engagement and standardized frameworks.	[179]
AI in Precision Nutrition	Tailoring dietary recommendations based on individual microbiome data.	Managing conditions like obesity and diabetes.	Potential in improving personalized dietary recommendations.	[187]
Microbial Interaction Networks	Discovering the relationships between different microbial species.	Understanding ecological dynamics and biotechnological applications.	Constructing and deciphering complex microbial networks.	[188]

5. Regulatory and Ethical Considerations

The development and application of bioengineered skin microbiome technologies raise essential regulatory and ethical considerations [189]. Ensuring the safety, stability, and non-pathogenicity of engineered strains is critical before their incorporation into cosmetic products [189]. These concerns are amplified by the potential risks associated with genetically modified organisms (GMOs), such as allergenicity, toxicity, and ecological impact [189]. Consequently, bioengineered formulations require rigorous risk assessments,

clinical evaluations, and regulatory compliance across different global jurisdictions [190]. This section addresses the key regulatory frameworks, safety evaluations, and ethical challenges associated with microbiome engineering in cosmetics, while also considering future pathways to ensure public trust and sustainable innovation.

5.1. Safety of Engineered Microbes in Cosmetics

Genetically modified organisms (GMOs) are organisms whose genetic characteristics have been altered in an artificial way [189]. In fact, introducing a single gene can affect the overall pattern of gene expression and result in many outcomes, thus the need to assess risks and concerns related to this technology usage is critical [189]. Several human health risks are associated with the use of GMOs in products, notably allergic reactions in certain individuals that can be triggered due to protein modifications such as oligomerization and tyrosine nitration [190]. Moreover, toxicity is an additional concern as high levels of heavy metals including lead and mercury and toxic substances such as glyphosate and dichlorvos can be found in GMOs, leading to harmful consequences when absorbed by the skin on a regular basis [191]. As for long term health effects, they are not yet fully understood but some studies suggest unforeseen health issues and GMOs' abilities to disrupt natural biological processes [191,192]. On the other hand, environmental risks associated with GMOs include gene flow, where modified genes are transferred to non-target species, and products that may wash off to the environment could lead to negative ecological consequences [193]. Additionally, the development of resistance in pests and pathogens through the use of GMOs could affect the ecosystems and reduce biodiversity by outcompeting natural species [193]. As a result, regulatory and safety measures are applied to ensure risk assessment [194,195]. For example, regulatory bodies such as the European Union have established safety evaluation procedures to approve the use of GMOs [194]. Risk management strategies are proposed to consider potential health and environmental risks [194,195]. The precautionary principle is applied for GMOs that may include hazardous gene products to ensure the implementation of safety measures [196].

To ensure stability of engineered strains, it is essential to consider different strategies. Plasmid stabilization systems like Post-Segregational Killing systems (PSK) help maintain plasmid stability without having to rely on external compounds, and ensure better population homogeneity in cultures [197]. Multimer resolution sites should also be considered as they can enhance plasmid stability by incorporating elements like the "cer site" and thus ensuring equal distribution during cell division [198]. In addition, feeding strategies can contribute to the stability of engineered strains by ensuring their robustness and high performance in industrial applications, like continuous feeding, that may lead to reduced organic acid excretion, better carbon utilization, and lower cell permeabilization [197]. Furthermore, Adaptive Laboratory Evolution is a strategy used for strains with improved phenotypes under certain conditions to magnify their stability and robustness [199]. Next, genome shuffling is a technique where specific phenotypic traits can be improved by inducing mutations and recursive protoplast fusion without the need for gene sequence data [200]. Regarding non-pathogenicity of engineered strains, risk assessments are used to check the potential ecological harm of genetically engineered organisms [201]. Fitness components such as fecundity and viability are measured to predict the organism's ability to spread in nature [201,202]. Pathogenicity testing is also adapted to test properties of strains proposed for biotechnological use, like lethal doses, toxigenicity and dissemination in internal organs [203]. Furthermore, rewriting genetic codes and implementing genetic safeguard technologies such as Xeno nucleic acids (XNAs) can help prevent unwanted interactions with the environment through barriers [204]. Last but not least, high standards for human and animal health are ensured by regulatory oversight, where risk-based assessments are

involved along with approval processes for biotechnology-derived products [205]. Those high standards include the safety evaluation of ingredients, where both local and systemic effects are considered [206], and are enforced by regulatory bodies such as the Scientific Committee on Consumer Safety (SCCS) in the EU and the Food and Drug Administration (FDA) in the US [207,208].

In addition, risk assessment for bioengineered cosmetic formulations involves a process that identifies adverse effects potential [209]. Four key steps are used in the process, hazard identification, dose–response assessment, exposure assessment, and risk characterization [209]. Ethical concerns ensure that traditional methods like animal testing are replaced by alternatives such as in vitro (cell cultures, tissue engineering, etc.) and in silico (computer simulations) which can be combined with in chemico approaches [210,211]. These methods can predict toxicity based on chemical structure and ensure the development of safe products [210,211]. Clinical trials are as well essential to ensure the safety of bioengineered cosmetic formulations, and their regulation depends on the region where they are performed [212]. In the US, premarket approval is not required by the FDA that oversees cosmetics products [212,213]. However, the EU has strict regulations and bans animal testing for cosmetics, thus the need for alternative methods [214,215]. More specifically, the EU has comprehensive safety assessments through systems like Cosmetic Product Safety Report (CPSR) and Cosmetics Products Notification Portal (CPNP), where regulations ensure safety and human health when placing products in the market [216]. In contrast, the US allows animal testing and relies on the Federal Food, Drug and Cosmetic Act (FDCA) but is less stringent on pre-market approval [217].

5.2. Challenges in Global Regulations and Public Acceptance

Current regulations on live microorganisms in cosmetics vary between the FDA and the EU. In the European Union, there is a regulatory framework where the regulation of such cosmetics is rather complex and dependent on the administration method and claims on the product [218]. Categories like cosmetics, medical devices, and pharmaceuticals are what different skin care products fall under for regulatory purposes [218]. Moreover, if a product is classified as a cosmetic, its safety is assessed by an expert, as well as its efficacy [218]. Medical devices and pharmaceuticals are a category that groups the products that prevent or cure diseases, whereas live bacterial cells do not take place in any medical devices [218]. In the EU, safety and efficacy testing ensure that extensive quality is guaranteed by live biotherapeutic products that contain live microorganisms before being allowed in the market [219]. In addition, microbial limit tests provided by manufacturers, as well as preservation challenge test results, are mandatory requirements for microbiological safety set by The European Pharmacopoeia monograph 3053 [219]. As for the US, the FDA proposes regulatory oversight for the cosmetics containing live microorganisms [220]. Quality control ensures the requirement for products to be safe for use, stable, and properly labeled by manufacturers [220]. General considerations like microbial contamination are taken to make sure that cosmetics can be preserved against microbial contamination [221]. Thus, the use of antimicrobial agents ensures consumer safety and product shelf-life [221]. In the US, preservative efficacy criteria must be met by products to avoid contamination by pathogens [222]. Additionally, market surveillance is conducted to regulate compliance with safety standards [223]. Ethical concerns about microbiome modifications primarily involve privacy and data protection [224]. Indeed, patient privacy is concerned as the human gut microbiome contains data about someone's lifestyle, disease history, and mental health [224]. Preventing misuse and ensuring confidentiality is essential while collecting massive microbiome datasets for analysis [225]. It is important to ensure informed consent where the participants are aware of the ways their

data will be used, as well as the risks involved [225,226]. Another ethical concern is health and safety, since unintended consequences may occur while modifying the microbiome. For example, dysbiosis can lead to various diseases (Rheumatoid Arthritis, Systemic Lupus Erythematosus, Sjögren Syndrome) [227,228], highlighting the importance of maintaining microbiome stability to prevent negative health outcomes [229]. Ethical principles such as beneficence and nonmaleficence should be valued to ensure that more good than harm is achieved with microbiome modifications [225]. This involves the confirmation of safety and efficacy through testing and validation of interventions [225]. Justice and equity also take place with the need to ensure equitable access to microbiome-based therapies and preventing disparities in healthcare [229]. As for the consumer perceptions, awareness and acceptance accompany knowledge and optimism of younger generations while older generations tend to be more cautious [230]. A significant number of people show skepticism and uncertainty about the benefits of microbiome modifications, shedding light on the importance of education and transparency [230]. To gain consumer trust, it is essential to install clear regulatory guidelines to ensure product safety and efficiency [231]. Moral concerns also appear as ethical implications of genetic modification may affect consumer acceptance [226,232]. The future regulatory pathways for microbiome-based biotechnology in cosmetics are likely to evolve significantly [221]. In fact, current regulations emphasize the importance of safety in microbiological cosmetics, and manufacturers are supposed to conduct tests and document stability data to ensure consumer protection [221,233]. In addition, the growing interest in referring to risk-based approaches challenges the traditional hazard-based approach [234]. This involves a more comprehensive assessment of exposure and potential health risks [234]. Some emerging trends and challenges include microbiome specific regulations such as microbiome-based therapies, including Fecal Microbiota Transplantation (FMT) and live biotherapeutic products (LBPs) that are still developing since not all microbiome products have consolidated applicable framework [235]. Future directions include a push towards harmonizing cosmetic regulations to facilitate market access and ensure consistent safety standards [236–238]. Advanced testing methods are seen to be crucial for microbiome-based products by allowing modern instrumental analysis technologies to meet new regulatory requirements [239]. Lastly, the priority remains to ensure consumer safety, this being valorized by addressing concerns on that part while providing transparent information about ingredients used in microbiome-based cosmetics [66,240]. For instance, the European regulation requires clear labeling to avoid misinterpretation and consumer confusion, aiming to ensure safety and proper use of cosmetics [241]. In the US, the Food and Drug Administration's authority over cosmetics is not very comprehensive and might result in manufacturers' negligence to register, test or report adverse reactions, which can result in inconsistencies in ingredient disclosure [242]. The following table (Table 5) compares the regulatory guidelines regarding bioengineered cosmetics in different regions.

Table 5. Regulatory guidelines and GMO use in cosmetics.

Region	Regulatory Framework	Key Requirements	Specifics for Bioengineered Cosmetics	References
European Union (EU)	Cosmetics Products Regulation (EC) No 1223/2009.	Safety assessment, ban on animal testing, responsible person for legal accountability.	Strict safety and efficacy, emphasis on consumer adverse effect reporting.	[216,243]
United States (US)	Federal Food, Drug, and Cosmetic Act (FDCA).	Classification of products as food, drugs or cosmetics, and status for ingredients.	Rigorous scrutiny for drugs compared to cosmetics and duplicative regulatory efforts.	[217,244]

Table 5. *Cont.*

Region	Regulatory Framework	Key Requirements	Specifics for Bioengineered Cosmetics	References
Asia	Depends on the country (like Japan, India, China).	Japan has strict regulations similar to the EU and the US while India is regulated under the Drug and Cosmetic Act, 1940.	Japan has high safety standards while China and India have an increasing regulatory alignment with global standards.	[236,238,245]
MENA Region	Depends on the country.	Saudi Arabia follows guidelines similar to international standards.	Regulatory frameworks are evolving.	[238]

6. Sustainability Aspects

Assessing the sustainability of bioengineered cosmetics is essential due to their multifaceted environmental, social, and economic implications. This section examines the comparative environmental impacts of conventional versus bioengineered cosmetics, emphasizing sustainable microbial production through advanced fermentation and cultivation techniques. It further explores product lifecycle considerations, including eco-friendly packaging, alongside social equity, economic viability, and the evolving metrics and certification standards shaping sustainable cosmetic development.

6.1. Environmental Impact of Traditional vs. Bioengineered Cosmetics

From the environmental perspective, several factors play a role and affect this pillar. First, conventional cosmetics include high amounts of harmful chemicals [246]. Heavy metals such as lead, arsenic and mercury and petroleum derivatives like parabens and microplastics are found in cosmetic products [247]. Not only do these components impose skin issues and health risks, but they also contribute to water, air and soil pollution and contamination and limit organic growth [246–249]. Furthermore, product packaging used in the cosmetics industry is mainly plastics with 70% being non-recyclable, thus significantly contributing to environmental pollution as well [250]. Conversely, bioengineered alternatives offer environmentally friendly products by replacing synthetic chemicals with organic and harmless ones [251,252]. These products are recyclable, thus reducing waste and packaging focus and they are also refillable and contain bio-based materials [68,253]. Bioengineered cosmetics play an important role in ensuring renewability and biodegradability by producing eco-friendly cosmetics [254]. Implementing natural ingredients such as biopolymers and biosurfactants ensures low toxic products and bio-degradable formulations [254,255]. The shift towards green solvents also helps in reducing the chemical load of the production process of cosmetics [256,257]. Additionally, the choice of preservatives considerably affects the product formulation [257]. Thus, traditional products use synthetic preservatives such as parabens whereas microbiome-based cosmetics rely on biodegradable ones (zingerone analog, *B. stenostachya* extracts) [250,257,258]. Moreover, both biodegradability indicators, the Primary Biodegradability Index (PBI) and the General Biodegradability Index (GBI), show high biodegradability for bioengineered cosmetics [254]. A case study of a bioengineered bar soap conducted by Borowska et al. showed a 98.8% PBI and a 92.8% GBI [254]. Evaluating environmental sustainability expands to include an evaluation of carbon footprint and energy use. Generally, traditional cosmetics have a high carbon footprint due to its energy intensive process [259–261], whereas bioengineered alternatives have significantly lower carbon footprint [244]. For example, the traditional production of shea butter yields 10.374 Kg of CO_2 per Kg due to the extensive use of firewood [262]. These emissions can be reduced up to 82% through microbiome technologies [262]. Bioengineering also showcases its potential in cosmetics by reducing the carbon footprint of carotenoid extraction using castor oil by 75% [263]. Evaluating the toxicity of

both methods can be made using environmental hazards (EH) scoring tools like the IARA matrix [264]. This tool identifies hazardous cosmetic ingredients by scaling them from 0 to 6, with 6 attributed to a highly hazardous ingredient [264]. Bioengineered cosmetics appear less environmentally harmful than conventional cosmetics, with naturally derived humectants having the lowest EH score [264].

6.2. Sustainable Production of Engineered Microbes

The sustainable production of engineered microbes involves various fermentation and cultivation methods aimed at reducing energy consumption and environmental impact [265]. One of the key approaches is low-energy bioreactors, where a continuous fermentation process can help maintain stable conditions, enhance productivity and reduce energy consumption, contamination risks and costs over long periods of time without the frequent need for sterilization [265]. Additionally, hybrid systems combine dark and electro-fermentation to increase biohydrogen yields, resulting in a more sustainable and efficient process [266,267]. Green media derived from agricultural by-products or waste materials is another approach where it is possible to utilize inexpensive and renewable feedstocks like plant biomass and plastic waste that can make microbial fermentation more economically viable and sustainable [268,269]. As for waste biomass, its use for biohydrogen production is a promising method, regardless of the commercial-scale production challenges [267]. Dilute acids and additives such as iron-based materials improve efficiency when used in pretreatment techniques [266]. Precisely, dilute acids enhance pretreatment efficiency by improving hemicellulose solubilization and increasing enzyme accessibility [270–273]. Iron-based additives reduce enzyme dosage and improve dephosphorization and desulphurization, leading to higher ethanol yields and better iron removal efficiency [274–277]. Furthermore, engineered microbiomes can be produced through cultivation techniques such as co-cultivation systems, where productivity can be enhanced by 100% to 500% through co-cultivation of microalgae with other microorganisms [278]. This method also reduces contamination risks and makes the process more sustainable [278]. Another technique is solid-state fermentation which has the potential to improve efficiency and sustainability by up to 60% in food production processes [279]. Thus, it requires cultivating microorganisms on solid substrates to reduce water and energy usage [279]. Last but not least, some technical innovations contribute to the sustainable production of engineered microbes, addressing both environmental and economic challenges [280]. For example, iron-based, titanium dioxide and cobalt ferrite nanoparticles are incorporated in fermentation processes due to their potential to enhance microbial activities and increase yields of biofuels [280].

Genetic engineering is another modern tool that creates resilient green cell factories that produce biofuels directly, and simplify harvesting processes, leading to higher environmental benefits and productivity [281]. On the other hand, some renewable feedstocks such as plant biomass and algae include microbial engineering for biofuel production, as engineered microbes like plant biomass and industrial waste [282,283]. Likewise, the production of bio-based chemicals like succinic acid can help replace petrochemical-based ingredients, leading to a more sustainable process [284,285]. Another way to produce sustainable engineered microbes is through waste valorization [286]. By converting waste into valuable products, microbial consortia and engineered microbial cell factories (MCFs) are being developed to provide an alternative to petrochemical-derived products [286,287]. In addition to that, bioremediation converts waste like oil and petroleum waste, and heavy metal contaminated waste into non-toxic substances like carbon dioxide, water and stable metal sulfides and this waste management process is essential for sustainability of the environment [288,289]. Thus, the circular economy is a closed-loop biomanufacturing sup-

ported and established by the integration of microbial processes, involving the continuous use of resources and promoting sustainability [287,290]. The following table (Table 6) offers insight on different types of ingredients used in cosmetics, notably the comparison between natural and synthetic ingredients.

Table 6. Sustainable versus traditional ingredients.

Aspect	Natural/Bioengineered Ingredients	Synthetic Ingredients	References
Source	Derived from plants, animals and microorganisms.	Chemically synthesized in laboratories.	[291–293]
Environmental Impact	Biodegradable and eco-friendly.	Could generate environmental concerns.	[294,295]
Safety	May contain less contaminants but generally it is safe.	Can cause irritation due to parabens but is regulated for safety.	[296,297]
Efficacy	Sustained effects with benefits like antioxidants and anti-inflammatory properties.	Higher potency but may cause adverse effects.	[298,299]
Regulation	The use of preservatives makes it less restricted.	Strictly regulated to ensure consumer safety.	[206]
Examples of Ingredients	Essential oils, plant extracts, natural antioxidants (polyphenols, carotenoids, tannins).	Parabens (methylparaben), synthetic emulsifiers (polyglycerol fatty acid esters), artificial fragrances (linalool).	[297,300]

6.3. Packaging and Product Lifecycle

Some of the sustainability trends in the cosmetic industry include the focus on shifting towards sustainable packaging [301]. Companies are relying on paper-based and eco-friendly packaging that can be recycled and be used as a plastic-free alternative [301]. Usual types of packaging materials include plastic packaging, notably conventional plastics like polyethylene terephthalate (PET) and polypropylene (PP) derived from non-renewable fossil fuels that lead to harmful environmental impacts due to their durability [302–304]. However, using 100% recycled plastics can reduce total carbon footprint by 52% [303]. Paper based packaging is becoming a more popular alternative since it is recyclable and has low environmental impact, ideal for sustainable cosmetic product packaging [301]. Furthermore, glass packaging is highly reusable and a proper recycling can lower environmental impact, but its heaviness could increase transportation emissions [305]. As for aluminum packaging, it is also recyclable, durable, and decreases carbon footprint even if its production is energy-intensive [305]. Some sustainability considerations while designing product packaging include design and material selection to optimize eco-friendliness, and also evaluating the whole process of manufacture through the Life Cycle Assessment (LCA) to ensure low environmental impact [302]. An emerging sustainable practice in the cosmetics industry is the development of waterless products, which are designed to be more economical and long-lasting, thereby reducing water consumption and minimizing environmental pollution [306]. Similarly, the use of renewable raw materials instead of fossil-based materials can reduce manufacturing energy consumption by 25%, making them efficient and sustainable to produce [307]. Nonetheless, younger consumers are more willing to invest in natural products, that is if financial constraints do not limit their choices [308]. The need for more sustainable packaging standards is driven by stricter regulations such as the Packaging and Packaging Waste Regulation (PPWR), as well as the use of recycled content in packaging [305]. Consequently, there is an increased emphasis on sustainable materials to address environmental concerns as the cosmetic market is projected to grow significantly [305,308]. To note that, cosmetic industries are relying more on the circular economy model as it emphasizes reducing waste and reusing materials [309]. This approach promotes sustainable development and consumption practices [309,310]. In addition,

reusable and refillable packaging systems are being adopted as an alternative to single-use packaging [311]. Some key findings and recommendations show that reducing product residue with optimal packaging choices can lower environmental impacts and improve customer satisfaction [312]. Therefore, wide efforts should be made by industries to enhance material compatibility and increase recycled content to optimize packaging design and align with sustainable standards.

6.4. Social and Economic Sustainability

The availability of bioengineered solutions beyond premium markets is a multifaceted issue involving economic, social, and regulatory dimensions. Firms using genetically modified organisms (GMOs) have an economic performance that is influenced by sociopolitical and economic pressures [313]. Activities can positively impact overall firm performance by securing social and economic legitimacy [313]. Indeed, this suggests that market access for bioengineered solutions relies on the balance between economic viability and social acceptance [313]. Moreover, market conditions due to cost and competition hinder the development of bioengineered products [314]. This economic obstacle can limit the availability of these solutions to premium markets due to higher costs absorption [314,315]. The socioeconomic and health benefits of bioengineered microbiome products are also evident, as they contribute to improved human health by reducing exposure to harmful chemicals and environmental pollutants [316]. However, microbiome products must consider ethical implications and regulations to ensure safety and public acceptance [317].

Biotechnology has an economic impact on the production systems especially in cosmetics sectors [318]. This type of technology promotes the production processes by simplifying them and reducing costs related to raw materials and wasted products [318]. Thus, contributing to the Sustainable Development Goal (SDG) 12 (Responsible Consumption and Production) by increasing efficiency in production systems [319]. Also, the economic effects of biotechnology vary across application sectors [318,320]. Indeed, the chemical industry finds that enantiomerically pure active ingredients are very beneficial especially in pharmaceuticals and agrochemicals [318]. Indirect economic effects are also present such as impacts on upstream sectors and supply chains which enhance overall economic performance [320]. Biotechnology offers job creations both directly and indirectly knowing that employment occurs in application industries or upstream sectors while promoting sustainable biotechnology industries [320]. In addition, biotechnology has led to regional and social polarization [321]. Advancements in cosmetic ingredients are also discovered due to cell culture techniques in biotechnology, eliminating the need for traditional growing, harvesting, and extracting methods, leading to safer and more effective skincare products [322]. Biotech-derived ingredients in personal care products are being more adopted due to their benefits [322]. For instance, Epidermal Growth Factor (EGF) has skin generation properties because it is a protein that stimulates cell growth, which contributes to skin healing and prevents aging [124]. Collagen is also a structural protein that enhances elasticity and strength, thus improving skin texture and firmness [124].

In the context of sustainable cosmetic development, inclusive innovation focuses on developing new products that benefit low-income and marginalized populations, playing many crucial roles in promoting social responsibility [323]. First, it empowers local communities by involving them in the process ensuring that the developed products are beneficial and accessible to these communities [323]. Second, it fosters social equity by ensuring the inclusion of women and marginalized groups in the development process, which helps in addressing systemic inequalities and aligning with SDG 5 (Gender Equality) [324] as women can play a critical role in engineering innovation and development [325].

Alongside encouraging practices like reducing consumption and supporting alignment with SDG 12 (Responsible Consumption and Production) and SDG 13 (Climate Action) [326], transparent supply chains also play a significant role in advancing sustainable innovation within the cosmetics industry [327]. By ensuring ethical sourcing, supply chain transparency guarantees that all raw materials are obtained sustainably and without causing environmental degradation [327]. Companies can also be held accountable for their supply chain practices, ensuring they adopt good and ethical practices [327]. This transparency supports compliance with both environmental and social regulations, thereby contributing to SDGs such as SDG 8 (Decent Work and Economic Growth) and SDG 16 (Peace, Justice, and Strong Institutions) [328]. Therefore, inclusive innovation and transparent supply chains ensure equitable and beneficial development processes to marginalized communities while improving sustainability and consumer awareness, leading to socially responsible cosmetic products.

6.5. Metrics and Certification Pathways

Bioengineered skin microbiome products are evaluated based on several key performance metrics to ensure their efficacy, safety, and impact on the skin microbiome. These tools include ISO standards, Environmental Working Group (EWG) scores, and Cradle-to-Cradle (C2C) certification [329,330]. First, The International Organization for Standardization (ISO) aids organizations to achieve sustainable development by developing standards [329,330]. The ISO 14001 focuses on environmental management systems and specifies requirements to minimize organizations' environmental impact [329,330]. Moreover, ISO 26000 emphasizes ethical behaviors by providing guidance on social responsibility and respect for stakeholder interests [331]. Also, ISO 9001 and ISO 14001 enhance corporate sustainability by addressing social, environmental and economic aspects [332]. Hence, showing how ISO standards are related to United Nations SDGs.

The Cradle-to-Cradle Certification emphasizes eco-effectiveness and the continuous reuse of materials [332]. Some aspects include material health to ensure the safety of humans and the environment [332]. In addition, recycling used materials in closed loops aids in maintaining their value and minimizing waste [333]. The motivation boost for using renewable energy sources contributes to social responsibility standards and offers practical solutions to go beyond traditional eco-labels [333]. Another metric is Environmental Working Group (EWG) Scores used to assess environmental and health impacts of consumer products based on transparency to provide clear information about ingredients used in the products and their hazards [334]. Indeed, this helps evaluate the safety of the products for human health and environmental footprint [334]. Each sustainability metric offers unique strengths and addresses different aspects of sustainability. In addition, the cosmetics industries focusing on sustainability have led to the emergence of eco-certifications and standards such as COSMOS [334]. The COSMOS-standard is a harmonized certification for organic and natural cosmetics developed by a consortium of European organizations, including Ecocert, Cosmebio, BDIH, ICEA, and the Soil Association [335]. Thus, it ensures that products are made with renewable resources and free from harmful chemicals [335]. By categorizing ingredients into chemically processed water, minerals, and synthetic ingredients, these certifications ensure that products are environmentally friendly, safe, and meet consumer demands in ethical practices.

7. Prospective Advances in Cosmetic Bioengineering

To understand the growth of bioengineering in cosmetic applications over the next decade, we can look at several key trends and advancements. One major trend is the integration of biotechnology and bioengineering to improve formulation processes by

making the production of raw materials more efficient [336]. These raw materials include recombinant proteins and cytokines which are essential in developing anti-aging products that also enhance appearance [336]. As for bioengineering technologies, innovations like tissue engineering and microfluidics expand the scope of cosmetic applications [336]. They also enable the production of more effective and sophisticated cosmetics products [337]. Furthermore, natural and sustainable ingredients are becoming more mainstream due to their safe and sustainable properties [338]. Biosurfactants and marine-derived compounds are an example of those natural ingredients which can be used as safer alternatives for synthetic chemicals in cosmetic formulation [338,339]. Moreover, microalgae and *Cyanobacteria* are organisms that are being investigated for their ability to produce bioactive pigments with antioxidant, immune-enhancing, and anti-inflammatory properties [340]. In addition, nanotechnology and advanced delivery systems help the development of nanoscale cosmetic products, thus being a significant trend [341]. Indeed, nanoparticles that range from 1 to 1000 nm, improve the delivery of active ingredients, allowing a deeper penetration into the skin, and thus enhancing their effectiveness [342]. It is also expected to stimulate innovation in cosmetic dermatology, leading to more biocompatible and biodegradable products [341,343]. Last but not least, market growth is leading to a rising demand for cosmetics, where consumer interest in age-defying and appearance-enhancing products drives this growth [344].

As markets in many countries are expanding rapidly, emerging economies contribute to the overall growth of the cosmetic industry [345]. Another emerging trend is skin microbiome transplantation from a healthy donor to a recipient [346]. Psoriasis and acne vulgaris are skin conditions that can be treated by making the recipient's microbiome more similar to the donor's [346,347]. However, due to the complexity and diversity of the skin microbiome, the feasibility of this method remains a challenge [348]. Facing this challenge, some studies encourage the application of single beneficial bacterial strains that target specific skin conditions [349]. This technique is a way to target bacteriotherapy which also includes engineered strains enabled by synthetic biology [349,350]. Thus, it allows the creation of novel biological components used in advanced cosmetic and therapeutic skincare formulations [350]. Therefore, synthetic biology promotes sustainability by reducing reliance on traditional chemical processes [351]. AI-driven cosmetic innovation enhances consumer experience by providing personalized skincare recommendations leading to more effective and safer products [307]. Interdisciplinary collaboration is essential between AI technologies and synthetic biology to ensure the development of effective, safe, and sustainable products.

Strengths and Limitations

This review provides a comprehensive and multidisciplinary perspective by integrating microbiome science, bioengineering technologies, regulatory frameworks, and sustainability considerations, thereby capturing the multifaceted nature of bioengineered cosmetics. A major strength lies in the structured synthesis of findings, with tables and figures that condense complex scientific advances into accessible formats for both academic researchers and industry professionals. Another important strength is the balanced integration of technological progress with real-world applicability, particularly the discussion of regulatory requirements, ethical concerns, and sustainability metrics, which are often overlooked in purely technical reviews. Nevertheless, several limitations should be acknowledged. First, despite extensive coverage, the rapid pace of innovation in microbiome engineering and synthetic biology means that some very recent developments may not be fully captured at the time of writing. Second, while this review emphasizes the importance of safety and regulation, the implementation of region-specific frameworks

and the availability of long-term clinical data remain limited in the current literature, creating uncertainty in translating bioengineered cosmetics to global markets. Third, the sustainability aspects discussed here highlight promising pathways, including reduced reliance on synthetic chemicals, eco-friendly microbial production, and circular economy principles in packaging. However, comprehensive life-cycle assessments (LCA) and quantitative data remain scarce, preventing a full evaluation of the environmental footprint of these innovations.

By recognizing these strengths and limitations, this review underscores both the robustness of the evidence currently available and the dynamic, evolving character of the field. Thus, it highlights the need for continuous updates, interdisciplinary collaboration, and further empirical validation, particularly in the domains of safety, regulation, and sustainability to ensure that bioengineered cosmetics achieve their full scientific, commercial, and societal potential.

8. Conclusions

This review advances the literature by uniquely integrating microbiome science, bioengineering innovations, regulatory frameworks, and sustainability considerations into a single multidisciplinary synthesis. Unlike previous reviews that primarily focus on technological aspects or clinical outcomes in isolation, this work bridges scientific advances with ethical, safety, and environmental dimensions, thereby providing a comprehensive roadmap for the emerging field of bioengineered cosmetics. The structured tables further enhance its novelty by distilling complex findings into practical, accessible insights for both researchers and industry stakeholders.

Looking forward, several perspectives deserve emphasis. First, deeper integration of AI with microbiome engineering will accelerate the design of tailored formulations and predictive models for skin health. Second, the development of rigorous, region-specific regulatory pathways and standardized safety protocols will be critical for translating laboratory advances into globally accepted consumer products. Third, sustainability must evolve beyond ingredient substitution, moving toward full life-cycle assessments, circular packaging, and renewable microbial platforms that minimize environmental impact. Fourth, longitudinal clinical studies are urgently required to establish efficacy and safety across diverse populations, thereby enabling widespread adoption. Finally, interdisciplinary collaborations between engineers, dermatologists, regulators, and industry stakeholders will define the trajectory of the next generation of personalized and eco-conscious cosmetics.

In sum, the convergence of bioengineering, sustainability, and regulation offers unprecedented opportunities for innovation, but it also calls for vigilance in addressing ethical, ecological, and societal implications. Advancing these perspectives will ensure that bioengineered cosmetics transition from promising prototypes to impactful solutions that shape the future of personalized skincare.

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