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MICROBIAL COMPOUNDS IN COSMETIC FORMULATIONS: A COMPREHENSIVE REVIEW

ROY S[1*], SARKAR S[2] AND CHOUDHURY L[3]

1: Assistant Professor, Post-Graduate & Research Department of Biotechnology, St. Xavier's College (Autonomous), 30, Mother Teresa Sarani, Kolkata-700 016, West Bengal, India

2: 3rd Year Integrated M. Sc. (5 Year Integrated) student, Post-Graduate & Research Department of Biotechnology, St. Xavier's College (Autonomous), 30, Mother Teresa Sarani, Kolkata-700 016, West Bengal, India

3: State-Aided College Teacher, Department of Microbiology, Sarsuna College (under Calcutta University), 4/HB/A, Ho-Chi-Minh Sarani, Sarsuna Upanagari, Kolkata – 700061, West Bengal, India

ORCID ID

Souvik Roy - https://orcid.org/0000-0001-5102-1889

Subham Sarkar - https://orcid.org/0009-0001-9196-5486

Lopamudra Choudhury – https://orcid.org/0000-0002-0519-8904

***Corresponding Author: Dr. Souvik Roy: E Mail: souvikroybiotech@sxccal.edu**

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1. ABSTRACT

The cosmetic industries are one of the biggest revenue-earning centers in the world. With concerns regarding health and environmental pollution increasing among consumers, the cosmetic industries are trying to explore new technologies to manufacture healthy and eco-sustainable affordable cosmetic products with enriched quality. With heightening demand of organic cosmetics, industries are searching for novel biological alternatives of chemical compounds in cosmetics and perfumes. Thus, many industries worldwide are now focusing on producing cosmetics by using microorganisms like bacteria, fungi and algae. The discovered spectrum of biological compounds derived from these microorganisms are used abundantly in cosmetic preparations, and exploring expanding biotechnological research and knowledge, many other potential bioactive compounds are yet to be identified. This review aims in highlighting the prospects and inclusions of different types of biological compounds obtained from microorganisms like antioxidants, proteins, lipids, carbohydrates, pigments, organic acids and bio-surfactants in various skin-compatible cosmetic formulations.

Keywords - algae, bacteria, cosmetic formulations, cosmetic industries, fungi

2. INTRODUCTION

Cosmetics are products constituting different combinations of chemical compounds and substances produced synthetically or obtained from natural sources, used for beautification, embellishment and enhancement of appearances and making one presentable **[1]**. With globalization the demand of people to become more attractive has elevated. Cosmetic industries worldwide have therefore, had come up with advanced technologies to manufacture cosmetics and perfumes, taking into consideration the demands of the customers. As concerns about health and pollution are elevating, the cosmetic industries are exploring various methods of preparing cosmetics from natural sources like microorganisms **[2]**.

Over the last few years, the use of microbes in cosmetics formulation has gained huge significance because of economic progress of the countries, better living standards and changes in tastes and choices in every aspect of life **[3]**. With people widely using biologically-derived cosmetics and perfumes, industries and brand organizations have developed suitable infrastructure and implement new methods to produce and market organic cosmetic products.

The journey of microorganisms like bacteria, fungi and algae from laboratories to industries for making innumerable cosmetics is one of the most enormously funded businesses, generating billions of dollars as revenue every year **[4]**. For this, the industries and enterprises however also have to focus on convenience and budget of the production methodology, affordability of the product, and quality and applicability of the product as per the guidelines and regulations of the administration (US Food, Drug and Cosmetic Act, 2004). The use of bioactive compounds isolated from microorganisms as ingredients is under the authority of the company itself in most cases, as the austerity of directives of the Government is less for cosmetics, as compared to food processing and pharmaceutical companies **[5]**.

Exhaustive research in domains of Microbiology, Immunology, Nanotechnology, Material Engineering and Bioprocess Technology has to be done to ensure that the best cosmetic product reaches the market **[6]**. With advancements in Biotechnology and Material Sciences especially, bioactive compounds extracted from microorganisms can be skillfully used to compose numerous cosmetic products. Sometimes identification, development and selection of the best microbial strain which produces large quantities of desired products over a reasonable time period and upon practicable investment is done by Recombinant DNA Technology (RDT) **[6]**. The technology allows scientists to study and interpret the genomic organization of the microbes and make re-combinations, modifications and customizations of the genetic material to definite extents for better product output **[6]**. *In vitro* studies also include cloning of a DNA fragment within the bacterial cells using appropriate vectors to produce copious amounts of products by allowing the expression of the respective genes **[7]**. However, for production of proteins that cannot be obtained from bacterial systems, the gene of interest is introduced to eukaryotes like fungi or algae, based on the need for post-translational modifications (PTMs) of the proteins **[7]**. RDT can also be used to produce those compounds from microorganisms which have to be efficaciously changed to more viable forms by biotransformation techniques, and this reduces the cost of production and processing appreciably **[7]**. RDT can also be employed to engineer the strains to improve their performance, and enable them to produce humongous amounts of the preferred product with upgraded stability and functionality **[7]**. This benefits the multidimensional aspects of industries, and meets the standards and expectations of the market **[7]**. Different other techniques are also used to extract and use biological compounds of microbial origin in cosmetics and perfumes because of their advantages to both customers and industries **[7]**.

Such cosmetics and perfumes containing microbial compounds significantly reduce health hazards, are more stable than many chemicals, are biodegradable, and prevent environmental pollution **[8]**. Hence, such microbe-derived substances lead to the emergence of new companies and diversification of businesses concerned with cosmetics **[9]**.

3. MICROBIAL COMPOUNDS IN COSMETICS

Besides the rampant application of microorganisms in drug development, food and beverage industries, the exploitation of numerous biologically active compounds isolated from microorganisms in cosmetic and perfume industries is gaining significance.

Not only bacteria, fungi and algae of common prevalence, but marine microorganisms also produce copious quantities of natural products and bioactive compounds which are used in preparation of cosmetics **[10]**. Pigments, proteins, enzymes, polysaccharides, lipids, saturated and unsaturated fatty acids, triglycerides, organic acids and other important and sophisticated compounds obtained from marine microorganisms are widely used in formulating photo-protection creams, lotions, ointments, hydrating agents, moisturizers and emollients because of their anti-UV, antioxidant, moisturizing and cleansing properties **[10]**. Some these compounds also inhibit tyrosinase activity), expedite regeneration and revitalization of skin, foster healing of wounds, guard the fibroblasts of human skin and replenish the skin lipids **[10-14]**. Recent studies have shown that bioactive compounds extracted from marine microorganisms also possess antitumor and anti-inflammatory attributes **[15, 16]**.

Besides microorganisms which grow in normal environments, extremophilic microorganisms which survive in extremes of temperature, pressure, acid concentrations, and salinity, are also subjects of numerous metabolomics experiments and meticulous morphological investigations **[9, 10]**. They can also be used as possible candidates for isolating different bioactive compounds, which will have a host of important functions suitable for cosmetic formulations **[9, 10]**.

All these microbial compounds themselves can either be socio-economically important products, or constituents of the products, or can be modified to more suitable and viable forms by several 'biotransformation' techniques **[17]**. In cosmetic and perfume industries, many such biological compounds obtained from microorganisms are used to manufacture compounds like active agents, esters and aromatic compounds, which are then widely used in different proportions for cosmetic formulations **[8, 9]**. Transformation of the biological compounds procured from microorganisms, to form constituents suitable for cosmetics and perfumes can be accomplished either by chemical reactions like isomerization, esterification, aromatization, substitution, nitration or sulphonation, or by employing microorganisms to carry out the 'biotransformation' through various inherent biochemical processes **[17]**. Although using microbial products in cosmetics and perfumery requires certain stringent and uncompromising processes like maintenance of sterility and constant monitoring of the fermentation, the advantages of the output are far greater than the vigorousness of the efforts of the industry. One of the major advantages is their biocompatibility **[8, 10]**. The other credits include better quality and dependability of the product, being skin friendly, and reduced environmental contamination **[9]**.

3.1. Bacterial compounds in cosmetics

Among all the microbes studied so far, bacteria produce multitudinous biological substances which have remarkable socio-economic value, and are substantially used to make cosmetic products **[9]**. Bacterial compounds like carbohydrates, enzymes, peptides, amino acids, organic acids and secondary metabolites are extensively applied for making cosmetics **[8]**. Bacteria-derived biosurfactants and exopolysaccharides are also used to formulate cosmetic compositions **[8]**.

3.1.1. Biosurfactants

Biosurfactants are active compounds synthesized by different microorganisms. Out of those, bacteria and fungi produce a major group of biosurfactants harnessed for cosmetic formulations **[18]**. Besides being comparatively less deleterious and more eco-sustainable, biosurfactants have a host of other attributes and multifarious properties which make them suitable components for preparing numerous cosmetic products **[9]**. They are generally used in emulsification of cosmetics, and also in moisturizers and humectants **[19]**. Biosurfactants are also present in anti-wrinkle cosmetics, cleansing (detergents and washing powders) and hygiene products **[19]**.

a) **Lipopeptides and Glycolipids**

Out of the different classes of biosurfactants examined so far, most of them constitute fatty acid chains **[20]**. These fatty acid chains can combine with other biomolecules to give rise to lipopeptides and glycolipids, or can undergo a sort of structural or organizational rearrangement to give rise to neutral lipids **[20]**.

b) **Surfactin-derived lipopeptides**

Because of the increasing demand of cosmetics, and to benefit the growing industries in Asian countries like China, Japan and Korea, improvisations have been made in the chemical composition of cosmetics, like use of surfactin-derived lipopeptides **[21]**. Surfactin used in cosmetics is mainly produced by numerous industrially important strains of *Bacillus*, which are often engineered to produce other compounds with huge socio-economic values **[22]**. Low critical micelle concentration (CMC) and extraordinary foaming ability form the characteristics of surfactin, which makes it one amongst the ideal biomaterials in producing topically applied dermatological products, and in formulation of emulsion cosmetics **[23]**.

3.1.2. Bacterial Cellulose

Certain genera of bacteria produce cellulose which has enormous advantages and applications in cosmetics. Gram negative bacteria like *Azotobacter, Acetobacter*, *Agrobacterium* and *Pseudomonas*, along with Gram positive *Sarcina ventriculi* are considered to be the most effective and potent producers of cellulose **[24]**. Generally, in industries *Acetobacter hansenii* and *Acetobacter xylinum* are preferred for commercial scale production of cellulose **[25]**. Cellulose and its derivatives are used in cosmetics to enhance the texture of creams and lotions and make them smooth by acting as slip agents and to form films to ensure application of nail polishes in thin layers **[26]**. Cellulose is also used in anti-caking agents in cosmetics, abrasives, absorbents, adhesives, skin repair creams and in wound dressing **[26, 27]**.

3.1.3. Exopolysaccharides

Exopolysaccharides (EPS) can be classified as heteropolymers and homopolymers, both of which have immense applications in cosmetic formulations. EPS are generally non-toxic and hugely biocompatible, therefore, they find a myriad of applications in cosmetic preparations **[28]**. Certain intrinsic factors of EPS are also taken under consideration while formulating numerous cosmetic substances, like its hydrophilicity that allows high water retention ability, which significantly minimizes dehydration of the skin when skin-care products are applied **[28]**. EPS like alginate, dextran and xanthan are some of the biologically most important compounds as an ingredient in different cosmetic products **[9, 28]**.

a) **Alginate**

Alginate is used enormously in thickening agents and gels. Many alginate-producing bacteria of *Pseudomonas* genera are exploited extensively, like *Pseudomonas aeruginosa* **[29]**. Studies have also highlighted the alginate-producing ability of *Azotobacter vinelandii*, and hence, are also applied in the production of certain cosmetics **[29]**.

b) **Dextran**

Dextran is a homo polysaccharide, synthesized by polymerization of glucose in bacteria, and has a wide range of properties, from making the skin smooth to being an anti-inflammatory compound **[30]**. In industries, bacteria of *Leuconostocaceae* family are well used for production of dextran **[31]**. Recent approaches in Bioprocess Technology in dextran production have also witnessed the use of *Streptococcus mutans*, because of certain advantages **[31]**. Dextran's characteristics as a skin brightening agent have been identified, and hence it is widely used in skin-care products **[32]**. Apart from promoting firmness to the skin and making skin radiant and wrinkle-free, dextrans also have immunological importance as they are known to improve the blood circulation, oxygenation of the dermis and augment nitric oxide synthesis in keratinocytes of the epidermis **[30]**.

c) **Xanthan**

On the other hand, xanthan is a complex heteropolymer **[9]**. Due its unique structure and speciality as a thickening and gelling agent, xanthan can be applied in moisturizers and smoothing agents **[9]**. Xanthan is known to perform a variety of other functions like reduction in transepidermal loss of water in keratinocytes, emulsification and foaming in various skincare products **[33, 34]**.

3.1.4. Hyaluronic acid and other organic acids

Hyaluronic acid (HA) is a glycosaminoglycan made up of repeats of two disaccharides, namely β-3-N-acetylglucosamine and β-4-glucuronic acid, linked together by glycosidic bonds **[35]**. It is widely used in facelift, facial augmentation, aesthetic and reconstructive surgeries, as a dermal filler **[36]**. Sodium salts of HA is often used in lotions, humectants, toners, exfoliating and occlusive creams as it moisturizes the skin, decreases wrinkles and makes the skin firm and flexible **[37]**. Although majority of HA used in cosmetics is obtained from combs of gallinaceous birds like roosters, some industries emphasize on obtaining HA from bacteria like species of *Streptococcus* **[9]**. Experiments have demonstrated that genetically manipulated *Bacillus* species are also capable of synthesizing substantial amounts of HA, and hence their use is popularized in industrial sectors **[38]**.

Bacteria are also viable producers of organic acids like lactic acid, glycolic acid, citric acid, salicylic acid and β-hydroxybutanoic acid, which are very often used in making cosmetics like lotions, anti-acne creams, ointments, toners, exfoliating agents and anti-ageing cosmetics **[39]**.

3.1.5. Oligosaccharides - Cyclodextrins

Out of different carbohydrates produced by bacteria, oligosaccharides have found potential applications in designing the composition of cosmetics **[9]**. Oligosaccharides can undergo cyclization to produce important biomolecules upon association with different moieties **[40]**. Cyclic oligosaccharides combine with glucopyranose to form a ring, which can be achieved either by biologically within the microorganisms or semi-synthetically outside the microbial cell **[40]**. Such group of compounds are known as cyclodextrins **[40]**. In industries, enzymatic conversions of cyclodextrins to more suitable forms are preferred over the synthesis of cyclodextrin derivatives chemically **[41]**. Cyclodextrinase and cyclodextrin glucanotransferase, obtained from different bacterial strains, are two of the most widely used enzymes in synthesis of cyclodextrin **[41]**. Industries typically derive these supramolecular polymers from important and improved strains of bacteria like *Bacillus subtilis* 313, *Microbacterium terrae* KNR 9, *Brevibacillus brevis* CD 162 and strain 9605 of *Brevibacterium* species **[42, 43]**. Studies have exhibited the ability of alkaliphiles like *Bacillus agaradhaerensis* in synthesis of cyclodextrin glucanotransferase, and hence is considerably used cosmetic and perfume industries **[44]**. Cyclodextrins have huge applications in cosmetic industries **[45]**. Many make-up products have cyclodextrins in their composition **[45]**. Cyclodextrins decreases volatility of esters present in perfumes, vaporous deodorants, antiperspirants and room fresheners **[46]**. They are also profusely used in washing powders and detergents, because they impart enduring and steady fragrances **[47]**. Triturated and amorphous cyclodextrins are often used in diapers, hygiene and sanitary products, talcum powders and scented napkins to control the odour emanating from them **[9]**.

3.1.6. Proteins, peptides and enzymes

Not only oligosaccharides, hyaluronic acid, exopolysaccharides and biosurfactants, several other biomolecules like proteins, peptides and enzymes are used far and wide in the cosmetic industry **[9]**.

Keeping in mind the age-old traditional knowledge of importance of proteins in hair and skin care, numerous research and studies are conducted to characterize the proteins, and explore the scope of their contributions in cosmetology **[9]**. As a result, a new spectrum of cosmetic formulations opened up, based on applications of proteins, peptides and enzymes **[10]**. As research progressed in understanding of the mechanisms of action of various proteins and their possible applications in cosmetics, a number of enzymes were identified with properties which can enhance the cosmetic behaviour of products **[8]**.

a) **Peptides**

In addition to keratinases, the peptides spawned due to regulated cleavage of peptide bonds and digestion of proteins by proteases also have extensive utility in the cosmetic industry **[9]**. Both soluble and insoluble peptides are widely used in commercially valuable cosmetics **[48]**. Soluble peptides are used in creams, gels, lotions, emulsions, powders and perfumes, whereas insoluble peptides are present in facial masks **[48]**. Peptides are generally obtained from various species of *Bacillus* **[49, 50]**. A special class of peptides known as penta-peptides consisting of only five amino acids are often used to maintain skin's elasticity, make skin even and free from wrinkles and expression lines **[51]**. Cyanobacteria produce mycosporine-like amino acids (MAA) which protect the skin from harmful UV radiations, and prevent skin disorders like erythema, eczema, dermatitis and even cancer.

b) **Enzymes**

Different enzymes like catalase, glutathione peroxidase, lacto-peroxidase and superoxide dismutase (SOD) have a role in exfoliation **[52]**. They scavenge free radicals and prevent skin problems due to the exposure to ultraviolet (UV) light and air pollution **[52]**. Industries prefer the use of extremophilic bacteria like *Thermus thermophilus* and

Sulfobolus acidocaldarius for the production of different peroxidases and superoxide dismutase **[53]**. However due to their inconvenient growth requirements, genetically-modified lactic acid bacteria (LAB) are now favoured for the production of such enzymes **[54]**. Improved strains of LAB produce enormous quantities of enzymes with enhanced qualities and efficiency **[54]**.

Other than peroxidases and superoxide dismutase, other enzymes like lactate dehydrogenase (LDH) are widely used in formulating numerous substances having dermatological and cosmetic significance **[55]**. Isoforms of LDH catalyse the reduction of pyruvate to lactate by taking up hydride ions from NADH, yielding NAD^+, a reaction important to produce energy in anoxic conditions **[56]**. On sustained exposure to UV radiation, the rate of the reaction gets retarded, and the efficiency of the enzyme is compromised **[56]**. Use of creams comprising of LDH replenishes the enzyme reservoir, which allows the normal functioning of the cells **[52]**.

Skin contains various proteins like collagen, elastin and keratin. Alkaline aspartic proteases, which cleave down these proteins, are obtained from alkaliphilic bacteria **[57]**. These are used to treat skin diseases like psoriasis, xerosis, ichthyoses and sometimes dermatitis, rosacea and epidermolysis bullosa as well **[57]**. Keratinases like subtilisin, hydrolyse keratin which augments healing of scars, cicatrices, freckles and blemishes on skin by allowing revitalization of the epithelia **[58]**. Keratinases also make the skin surface smooth and sleek, and repair and alleviate skin damage **[59]**. Therefore, hydrolysates of keratin are used in creams, liniments, lotions, balms and unguents for palms, elbows, knees, soles and heels **[59]**. For enhancement of complexion, refinement of skin appearance and treatment of patches, discoloration and imperfections of the skin, enzymatic peeling treatments using keratinases are often recommended **[60]**. Keratinases are also used in depilatory products and creams which retard hair growth and development **[61]**. One of the extensively exploited bacteria used for industrial production of keratinase is *Bacillus licheniformis* **[60]**. There are several other groups of bacteria which produce different kinds of keratinases **[61, 62]**. Thermophilic bacteria like *Thermoanaerobacter* and *Thermococcus*, Gram negative bacteria like *Vibrio*, *Xanthomonas*, *Chryseobacterium* and few Gram positive bacteria like *Lysobacter, Nesterenkonia* and *Microbacterium* are largely used for production of keratinases **[61, 62]**.

3.2. Fungal compounds in cosmetics

Other than bacteria, the cosmetic industry also prepares and develops cosmetics from the fungal metabolites **[63]**. The burgeoning cosmetic industries make use of fungi to produce myriad of antioxidants, skin care and hair care products, owing to the different attributes possessed by them **[64]**. Fungi are enigmatic, and belong to one of the most diverse kingdoms of organisms. Moreover, a wide range of habitats, characteristics, life cycle, physiology, morphology and their contribution to the ecosystem make fungi apt for sundry experimentation and research **[63]**. The different metabolites and biological compounds produced by fungi are significantly used in the preparation of many creams, lotions, embrocations, humectants, salves and ointments (64).

3.2.1. Antioxidants

Mushrooms are known to produce antioxidants like ergothioneine, which prevent oxidative damage of the skin cells **[65]**. Ergothioneine obtained from *Portabella* and *Cremini* species are either directly used in creams and lotions, or used upon isomerization and racemisation **[66, 67]**.

Besides ergothioneine, gallic acid and trehalose also have extraordinary antioxidant properties and used in different cosmetic products **[68, 69]**. Gallic acid scavenges free radicals and ameliorates oxidative stress in skin cells, besides having antibacterial activity **[68, 69]**. Industrially, *Fusarium solani*, *Trichoderma viridae* and *Aspergillus niger* is used in gallic acid production **[68, 69]**.

Trehalose, apart from being an excellent antioxidant, is also a skin-hydrating agent **[70]**. Although compared to gallic acid, trehalose production needs additional effort and expenditures, the socio-economic importance of trehalose is much more in contrast to the cost of fermentation and processing **[9]**. Mushrooms like *Lentinula edodes*, *Grifola fondosa*, *Pholiota nameko* and *Auricularia auricula-judae* are widely used for obtaining trehalose **[9]**.

3.2.2. Aromatic compounds

Among the recent advancements and improvisations in perfumery, aromatic compounds produced by genetically-engineered yeasts are replacing flower extracts in scents because of certain advantages, like being a time-saving process, enrichment of the perfume texture, enhancement and consistency of the fragrances, guaranteed production throughout the year and longer shelf life **[71]**.

3.2.3. Biosurfactants

Biosurfactants like sophorolipids are also isolated from fungi like *Candida* and are used in detergents, foaming and emulsifying agents **[72]**.

3.2.4. Chitin-glucan complexes & Chitosan

The fungal cell wall is made up of chitin, a homopolymer of N-acetyl glucosamine

(NAG) **[73]**. Chitin participates in *in-vivo* polymerization with a class of glucose containing polysaccharide known as glucans to produce chitin–glucan complexes **[74]**. These chitin-glucan complexes, when used in cosmetics, can help to retain moisture in the skin, and makes the skin soft and clear **[75]**.

Among the different chitin-glucan complexes, chitosan is tremendously used in different industries due to its wide range of application in dental medicine, dermatology, cosmetology and trichology **[9]**. Chitosan, in combination with collagen and hyaluronic acid, makes hair thick, voluminous, firm and healthy **[9]**. Chitosans also nourish the hair, induce melanin production and avert damage and loss of hair **[76]**. Hence, chitosans are used in hair-setting sprays and gels, shampoos, pomades, conditioners and hair mousses **[77]**. Chitosans are also used in toothpastes and mouthwashes because of their antibacterial activity against dental plaque **[78]**. Also, minoxidil laden with chitosan nanoparticles help in protracted release of the medication, which ensures effective trans-dermal transportation and stimulates hair growth **[79]**.

3.2.6. Exopolysaccharides

Mushrooms synthesize a number of secondary metabolites which have therapeutic properties and they also help to recuperate and convalesce from diseases **[80]**. Schizophyllan, one such extracellular polysaccharide obtained from *Schizophyllum commune*, comprises of a β-1,3-D-glucose backbone, and is present in water as helix in a rigid triad **[81]**. It is known to be an UV protectant, and minimizes the pre-disposition to skin cancer and lessens the susceptibility of the skin to redness and inflammation **[82]**.

3.2.7. Keratinases

Some fungi, like dermatophytes, produce keratinases on a large-scale, and can degrade keratin **[83]**. Keratinophilic fungi like strains of *Microsporum*, *Trichophyton* and *Epidermophyton* are also gaining importance in cosmetic industries **[83]**.

3.2.8. Lactic acid and poly-lactic acid

Lactic acid has a variety of properties which makes it one of the most comprehensively used components of cosmetics. *Rhizopus* species produces lactic acid from aerobic fermentation of glucose, and the expenditure of fermentation is lesser than fastidious bacteria like *Lactobacillus* **[84]**. Hence, industries prioritize producing lactic acid from fungi, especially when it has to be mixed or combined with some other compounds to make the desired product **[9]**. Lactic acid is a major constituent of creams, balms and moisturizers, as it keeps skin hydrated, smooth and supple **[9]**. Around 12% of lactic acid concentration is present in emollient creams, as it promotes exfoliation, fairness and radiance of the skin, and diminishes the proneness of the skin to acne and pimples **[46]**. Lactic acid can be converted to lactide by esterification **[85]**. Lactide in solution or suspension undergoes tin octoate-catalyzed polymerization with dehydrated lactic acid to produce poly-lactic acid **[85]**. Poly–lactic acid is commonly used in bio-stimulator injections and facial fillers **[86]**. It is also used in skin contour creams, sunscreens, serums and different dermatological products **[86]**.

3.2.9. *Lipids*

a) Mannosylerythritol lipid

Lipids are one of the widely used biosurfactants in different cosmetic products, one among them is mannosylerythritol lipid (MEL) **[87, 88]**. The MEL is most often used in commonly used cosmetics like lipsticks, soaps, sprays, eye-makeup accessories and body care essentials **[87, 88]**. MEL is produced in large-scale by various species of the basiomycetes *Pseudozyma*, like *P. antarctica, P. aphidis, P. rugulosa, and P. parantarctica* **[87, 88]**. These are used in the industrial production of MEL through various strain development processes by RDT techniques **[87, 88]**.

b) Ceramides and glucosylceramides

The epidermis of human skin is stratified in five layers having different organization of cells **[89]**. From outside towards the dermis, these layers are stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum and stratum basale **[89]**. The superficial layer of the epidermis, stratum corneum is rich in ceramides, which are responsible for protecting the intricate inner layers of the skin and preventing the skin from getting chapped and dry **[89]**. Ceramides and their derivatives are therefore, often used in creams and moisturizers to obviate roughness and exsiccation of the skin **[9]**.

However, industrial production of ceramides has certain constraints, one major being absence of ceramide group of compounds in bacteria **[9]**. Moreover, ceramides obtained from other eukaryotic sources like animals can be antigens, can trigger immunological responses, and can cause various diseases in humans **[9]**. Plant ceramides are different in structure and function, as compared human ceramides **[9]**. Hence, appropriate sources have to be identified to derive ceramides from, in large-scale.

Thorough investigations and experimental analyses have shown that fungal ceramides, when applied on skin, have inconsequential side effects, and thus upon clarification, are apposite to be used in cosmetics **[9]**. Fungi are widely used for large scale production of ceramides, their precursors and derivatives **[90]**. *Agaricus bisporus, Armillaria tabescens* and *Candida albicans*, along with genetically modified *Saccharomyces* *cerevisiae*, are used in ceramide production **[91, 92]**. *In vivo* glycosylation of ceramides to glucosylceramides by glucosylceramide synthase occurs in many fungi, which are also used in preparation of numerous cosmetic products **[93]**.

3.3. Algal compounds in cosmetics

Algae constitute a phylum of magnificent and gargantuan diversity classified under multiple taxonomic classes based on their organizational characteristics, habitat, phylogenetic relationships amongst them and presence of pigments **[94]**. The biological compounds derived from both natural and genetically-modified algae are enormously used in cosmetic companies to produce numerous products **[95]**. Algae are known to produce a variety of substances like proteins, enzymes, secondary metabolites, carbohydrates, lipids, ceramides, esters, antioxidants and plethora of different kinds of pigments **[9, 96]**.

3.3.1. Algal oil

Algal oil is used in several photo-protective lotions, sunscreens and nano-emulsions, as research has shown its potentiality to restrain the hazardous consequences, and abate the complications of UVA-promoted skin disorders by helping in development of melanocytes, mitigating dehydration of the epidermis, and palliating inflammation and redness of the skin **[9]**.

Algal oil with large quantities of ω-3 fatty acids like eicosapentaenoic acid and docosahexaenoic acid nourishes the follicles of the hair, decreases coarseness and irritation in scalp, prevents deterioration of hair, heals frangible, frizzy, dry hair and hair with split ends, reduces dandruff and curbs hair loss **[9]**. Therefore algal oil is routinely used in shampoos, conditioners, hair oils, hair serums, pomades, hair gels and waxes, and hair-setting sprays **[9]**.

3.3.2. Enzyme Inhibitors

Algal compounds can also act as inhibitors of certain human enzymes like elastase and collagenase, which degrades the elastin and collagen of the skin respectively **[97]**. Phlorotannins extracted from brown algae and sea kelps inhibit elastase performance, and are often used in anti-ageing creams, lotions and salves. Phlorotannins and astaxanthin are also used in skin-brightening creams, as they repress melanin synthesis **[98, 99]**. This is accomplished by its anti-tyrosinase property **[98, 99]**. Tyrosinase is an important enzyme for biosynthesis of melanin **[100]**. Therefore, suppression of tyrosinase activity exceedingly reduces melanin formation. Similar to phlorotannins, *Chlorella* is also used in antiageing creams because of its potential to revamp the texture and appearance of the skin, and countenance by safe-guarding the collagen and elastin fibres from getting disintegrated by collagenase and elastase kind of enzymes **[100]**.

3.3.3. Mycosporine-like amino acids

In addition to pigments, algae also produce a group of UV-protective compounds known as mycosporine-like amino acids (MAA) **[9]**. MAA absorb the wavelengths of UV light more competently than other pigments, and have a high molar extinction coefficient **[96]**. These properties enable them to scatter the UV light, without resulting in formation of free radicals **[101]**. Upon UV exposure, MAA agglomerate and protect the cells from dehydration, plasmolysis and death **[101]**. Also, like MAA produced by cyanobacteria, algal MAA besiege and scavenge free radicals in skin cells produced due to photo-oxidation **[102]**. Therefore, MAA are used to compose sunscreens **[96]**.

3.3.4. Organic acids

Organic acids like hexadecatetraenoic acid, hexadecapentaenioic acid and their isomers, exclusively produced by specific algal families, are also used in anti-ageing creams because they augment deposition of collagen in the skin, and stave off wrinkling and drooping of skin **[103]**. Industries use extracts of algae like *Macrocystis pyrifera* to foster *in vivo* synthesis of syndecan-4, a trans-membrane protein, in the interstitial regions outside the cells of the dermis **[104]**. This syndecan-4 can induce formation of hyaluronic acid in the skin **[104]**.

3.3.5. Pigments

Besides algal oil, algae of different classes also produce lots of pigments as secondary metabolites which have been identified to possess properties to protect the skin from UV radiation **[9]**. Algal pigments are applied in cosmetics because of their excellent antioxidant properties **[9]**. Hence, pigments like anthocyanins carotenoids, phycoerythrin, phycocyanin, allophycocyanins, xanthophylls, syctonemin, alkaloids, flavonoids and isoflavonoids are widely used in photo-protective cosmetics **[105-107]**.

a) **Anthocyanins**

Algal anthocyanins have been substantiated to be acceptable to treat radiation dermatitis during radiation therapy **[108]**.

b) **Carotenoids**

Astaxanthin

In anti-ageing creams, carotenoids like astaxanthin produced by *Haematococcus pluvialis* is also used because of its antioxidant, anti-inflammatory, immune-stimulatory, skin hydrating and prophylactic properties **[9]**. Astaxanthin can rejuvenate the complexion by healing dark spots, melasma, lentigo, ephelides, hyper-pigmentation and post-inflammatory trauma **[109]**. Experiments have reported that melanin concentration in transepidermal cells decreases by 40% upon application of astaxanthin-containing cosmetics (96). Astaxanthin is also present in moisturizers and anti-wrinkling agents, as it hydrates the stratum corneum of the epidermis, reduces wrinkles and corrugations, and prevents desquamation by making the skin more elastic and firm (109). Astaxanthin also behaves as an antioxidant and assuages stress by scavenging free radicals (99).

Zeaxanthin and others

Compared to astaxanthin, the anti-tyrosinase property is more pronounced in compounds like zeaxanthin, phlorotannins and 7-phloroeckol, and hence they are more widely used in treatments of hyperpigmentation, age spots and birthmarks **[110, 111]**. Zeaxanthin is one of the most prominently present carotenoids in cosmetic products used in skin-brightening facials **[111]**. 7-phloroeckol promotes hair growth in outer root sheath cells and dermal papilla cells and makes hair robust **[112]**.

β-carotene

Predominantly obtained from *Dunaliella salina*, β-carotene is a good antioxidant and a precursor of retinol, an important vitamin necessary for rhodopsin synthesis in eyes, and elastic and supple skin **[107]**. Retinol slows down collagen degradation, and maintains the integrity and functionality of mucosa **[107]**.

c) **Phycoerythrin, phycocyanin, allophycocyanins and xanthophylls**

Besides carotenoids, phycoerythrin, phycocyanin, allophycocyanins and xanthophylls, principally isolated from red algae are widely used in cosmetics, as they antagonize peroxidation of lipids caused by free radicals and reactive oxygen species (ROS), and markedly delay the reflection of age **[96, 113]**.

d) **Violaxanthin and lutein**

For preparing sunscreens, pigments like violaxanthin and lutein extracted from green algae are often used in synergy with MAA like porphyra-334 and shinorine isolated from red algae **[9]**.

3.3.6. Polysaccharides

a) **Fucoidan**

Polysaccharides like fucoidan obtained from seaweed are also used as anti-oxidants and skinwhitening agents, because of their potency and effectiveness in protecting the skin, and reducing the spots and macules **[114]**.

b) **Alginates and carrageenan**

Seaweeds and marine algae are known to produce plentiful of alginates and carrageenan **[115]**. Because of their high water-retention capacity, alginates and carrageenans are often used in gels, and as thickening agents in cosmetics **[115]**.

c) **Laminarin and phloroglucinol**

Laminarin and phloroglucinol obtained from brown algae can either be used alone, or in combination with fucoidan in UV-protection creams **[9]**.

3.3.7. Proteins

a) **Collagen and elastin**

Proteins like collagen and elastin derived from algae are widely used in anti-aging and foundation creams, sunscreens, serums, humectants and moisturizers **[9]**.

b) **Sericin**

Microalgae like *Arthrospira platensis* and species of *Chlorella* are used by industries as substitutes of silkworms for the production of sericin, a protein which binds silk filaments together in cocoons **[116]**. Sericin is known to prevent hair damage, make hair smooth and silky, and hence, is one of the major components in many hair care products **[116]**.

3.3.8. Other Algal compounds

Rigorous and punctilious research have showed that *Sargassum macrocarpum*, a marine phaeophyta algae produces sargafuran, which acts as an antimicrobial for *Propionibacterium acnes* **[117]**. Sporopollenin isolated from species of *Chlorella* **[96]** and Scytonemin obtained from microalgae *Lyngbya aestuarii* and species of *Scytonema* are widely used as components of anti-wrinkling creams and sunscreens respectively **[106, 118]**. Also, natural extracts from *Spirulina platensis* are used in lotions, creams and embrocations due to its ability to promote healing effect of keratinocytes **[119]**.

4. CONCLUSION

With a mammoth rise in the human population, cosmetic and perfume industries have proliferated immensely. Hence, the demand for using biologically-derived, skin- and ecofriendly products have also arisen. For making a plethora of products and not compromising with their qualities, the cosmetics and perfume manufacturers are using microbial metabolites and pigments, based on the properties of such compounds. The companies are revolutionizing cosmetic preparations by replacing chemical and synthetic products with biological compounds derived from microorganisms, by using sophisticated technology and assiduous research. Cosmetics basically enter the cells of different types present in different tissues and developmental stages, and react with the immanent components of the cells. Hence, cosmetics containing different compounds of microbial origin like antioxidants, pigments, proteins, biosurfactants and oligosaccharides best substitute the synthetic compounds. However, application of some of these compounds procured from microorganisms can cause detrimental effects and diseases, therefore their properties should be meticulously examined and scrupulously explored by means of immunological and toxicological research before prospective modifications and commercialization.

5. CONFLICT OF INTEREST

There is no potential conflict of interest among the authors.

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