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Algae as Alternative Source of Bioactive Compounds for Cosmetics

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Abstract

The applications of algae in cosmetic products have recently received attention in the treatment of skin problems, such as aging and pigment disorders. Many secondary metabolites from macro- and microalgae are known for their skin benefits, which include protection from UV radiations and prevention of rough texture, wrinkles, and skin flaccidity. There are, therefore, potential uses in the areas of anti-aging, skin-whitening, and pigmentation reduction products. Several macro and microalgae are used in cosmetics due to the presence of bioactive compounds like polysaccharides used as moisturizing agents or thickeners in creamy cosmetic formulations. In the present review, several algal functional compounds (phlorotannins, xanthophylls, sulphated polysaccharides, tyrosinase inhibitors) have been presented and discussed toward cosmeceutical application.

Keywords: *Macroalgae; Skin Aging; Skin Health; Skin Whitening; Microalgae; Bioactive Compounds*

Introduction

Algae (macroalgae and microalgae) are unicellular or multicellular photosynthetic organisms that can thrive and reproduce in every type of aquatic habitat: from freshwater to marine, brackish or hypersaline waters, and more generally anywhere there is permanent humidity. Algae include highly heterogeneous evolutionary organisms from different phylogenetic groups with about 30,000 species described to date [1]. These organisms that populate the planet for almost 2.5 billion years, through the photosynthetic activity of conversion of solar energy into chemical energy, accumulate a wide spectrum of secondary metabolites that possess different biological activities and for this reason called "bioactive compounds" or "functional molecules". The other main features of algae are the high growth rate and the ability to live and reproduce in different environmental conditions such as heat, cold, anaerobiosis, salinity, photooxidation, osmotic pressure and exposure to ultra-violet radiation, in difficult or extreme ecological niches that can promote the synthesis and accumulation of many bioactive compounds that constitute the chemical defence of algae [2]. Microalgae are superior to plants in terms of productivity, limited seasonal variation and abundant raw materials [1]. The ability to synthesize a wide range of primary and secondary metabolites, such as triglycerides, fatty acids, vitamins and compounds/pigments with antioxidant activity, makes interesting the use of microalgae in different fields, such as that of human and animal nutrition (in the production of particular foods, food supplements, etc.), the cosmetic one and the production of biodiesel and energy [3]. These organisms have been used by humans since ancient time; in Asia, traces of the use of *Nostoc* sp. and *Aphanizomenon* sp. as food, dating back to more than 2000 years ago, were found, and in Central America, around the shores of Lake Texcoco, the Aztec civilization already consumed Spirulina (*Arthrospira platensis*) in the form of flour to be integrated into the mixture of different cereals. It was reported that Marco Antonio tried to impress and seduce Cleopatra, offering the whole Dead Sea as a huge personal *spa* to the Egyptian queen, since the water of this sea was rich of the microalga *Dunaliella salina,* able to survive to the extremely saline conditions and capable, with its colored pigments - carotenoids - to strengthen and protect the skin.

The desire and research of wellness, of personal beauty, pursued since ancient times, are the motor of the cosmetics industry, which today has an annual turnover of over 150 billion dollars, according to the French Eurostaf [4]. Moreover, in the next future this industry will continue to develop, also meeting the market demands of emerging countries. Another aspect that must be taken into consideration is the growing demand for natural cosmetic products, which respect the principles of environmental sustainability, as well as economic [5]. And in this regard, algae are an excellent source of functional molecules that can be used in cosmetics. A global tendency for products considered healthy, environmentally and economically sustainable, led to cosmetics industries to fund the research and development of new products containing compounds or extracts from natural sources. In particular, there is an increasing demand for natural pigments derived from carotenoids, compared with those that are chemically synthesized, which are thought to be involved in the onset of certain type of cancer. The price of natural pigments isolated from algae can be as much as 700 Euros per kilo, more than double that of synthetic products [5]. Carotenoids, divided into carotenes and xanthophylls, are isoprenoid molecules, responsible for the color of fruits, vegetables, and flowers, as well as some birds, insects and marine animals. They can be synthesized in relevant amount by microalgae, while others can be derived from brown algae [6].

Skin health

Skin wrinkling and aging are generally attributed by the reactive oxygen species (ROS) [7], which stimulates mitogen-activated protein kinases; these proteins phosphorylate transcription factor activator protein-1, which, in turn, results in upregulation of matrix metalloproteinase (MMPs) that contribute for the degradation of skin collagen, ultimately leading to skin aging [8-10]. Sun radiations damage skin, significantly increasing the levels of active MMP-2 and -9, thus intrinsically aging the skin. Moreover, in chronic inflammation, where ROS are actively involved, pro-inflammatory cytokines induce MMPs that degrade the extracellular matrix and contribute to several inflammatory disorders [10].

Skin whitening has been practiced for several centuries by people from a variety of ethnic backgrounds, nowadays especially in Asia as its largest market [11]. The use of whitening agents can be driven by medicinal necessity in the case of people suffering of dermatological conditions linked to an abnormal accumulation of melanin [12] or simply by culture-specific beauty preferences. Melanogenesis is a complex pathway regulated by several enzymes including tyrosinase, which catalyzes the rate-limiting step of pigmentation; for this reason, compounds able to inhibit tyrosinase activity represent the most common approach to achieve skin hypo-pigmentation. In spite of the large number of *in vitro* tyrosinase inhibitors that have been found, only a few have been shown to have any significant effects in clinical trials [10].

Algae for cosmetic use

The growing necessity to obtain safe products by ecofriendly bioprocess has made algae a sustainable resource for new bio-based products in cosmetics [13,14]. The cosmetic industry is interested in using algae as a source of bio-sustainable ingredients since they are extremely rich in biologically active compounds (Table 1), many of which are already documented as functional active skin care agents. There are several algal species that are known for their beneficial effect, very useful in the anti-aging treatment, as a remedy for skin blemishes, or as a skin whitening agent [5]. Several studies have provided insight into biological activities of macroalgae and microalgae in promoting skin, health, and beauty products. Currently, the global production of microalgae and cyanobacteria is primarily aimed at production of high added value compounds, since algal biomass contains pigments, proteins, essential fatty acids, polysaccharides, vitamins, and minerals which are of great interest in the preparation of natural products, both as food and in cosmetics [15]. Recently, biotechnology has enabled the manufacture of high-quality microalgae cultures that are completely free of contaminations. Moreover, microalgae cultivation, using different types of photobioreactors system, allows to obtain high biomass yield in controlled conditions; on the other hand, the variation of some parameters, including light intensity, pH control, amount of CO_2, nutrients, loss of water or even contamination, may influence on the final composition profile of the biomass [16]. Some algae species, both marine or freshwater, such as those shown in table 1, have already been used in some cosmetic formulations as moisturizing agents and thickeners, also in combination with various other functional molecules; while other species of algae remain largely unused due to an apparent lack of knowledge concerning primary and secondary active compounds can be used as ingredients.

Cyanobacteria	Compounds	Antioxidant	Anti-aging	Solar protection	Anti-inflammatory	Use in cosmetics
Cyanobacteria	Amino acids like mycosporin			+		Sunscreen
Marine cyanobacteria	Scytonemin			+		Sunscreen
Nostoc flegelliforme	ß-1,3-Glucan	+			+	Skin care cream
Microalgae						
Anabaena vaginicola	Licopene	+	+	+		Skin care cream
Arthrospira	Exopolysaccharides	+	+		+	Anti-aging cream
Chlamydocapsa	Carotenoids		+			Hair Mask
Chlorella	Polysaccharides		+	+	+	Anti-stretch marks creams, body lotions, eye creams, face masks, shower gels
Chlorococcum	Flavonoids; Carotenoids; Polyphenols; Fatty acids		+			Anti-aging cream; Formulations to prevent hair loss
Dunaliella salina	Carotenoids and Xantophylls	+	+		+	Promoter of hyaluronic acid synthesis
Haematococcus pluvialis	Astaxantin	+		+		Sunscreen
Isochrysis	Carotenoids and Xantophylls	+		+		Tanning booster
Nannochloropsis	Carotenoids and Xantophylls	+	+	+		Tanning booster
Odontella aurita	Chrysolaminarin	+				Skin conditioning
Phaeodactylum	Carotenoids and Xantophylls	+	+	+		Sunscreen; anti-aging cream
Porphyridium	Carotenoids and Xantophylls; ß-1,3-Glucan; Phycobiliproteins; Phycoerythrobilin	+		+	+	Pigments for eyeliner, eyeshadow, lip-gloss

Rhodella reticulata	Sulfonated polysaccharides; Phycobiliproteins	+			+	Colorants; Cream
Skeletonema	ß-1,3-Glucan	+	+		+	Anti-aging cream
Spirulina	Phycobiliproteins; Phycoerythrobilin	+				Eyeshadow
Tetraselmis	Carotenoids and Xantophylls	+		+		Sunscreen
Tetraselmis suecica	α-Tocoferolo	+	+			Anti-aging cream
Macroalgae						
Corallina pilulifera	Phenolic compounds; Metalloproteinase (MMP)	+		+	+	Skin care cream
Eisenia arborea	Phlorotannins				+	Skin conditioning
Fucus vesiculosus	Fucoidan	+	+			Skin conditioning
Laminaria japonica	Fucoxanthin		+	+		Activated sludge against cellulite; Skin protecting
Monostroma obscurum	Flavonoids	+				Face masks
Undaria pinnatifida	Fucoidan; Fucoxanthin	+	+	+		Skin protecting

Table 1: *Most common use of algae in cosmetics.*

There are not yet many studies focused on the ability of functional molecules extracted from algae to act on the protection or regeneration of the skin; however, several active ingredients derived from algae that can be used to prevent skin imperfections, seborrhea, repair damaged skin, inhibit inflammatory processes and ensure proper skin hydration have been identified [6].

Only few species of microalgae have been studied for possible commercial applications, including: *Spirulina, Chlorella, Haematococcus, Dunaliella, Botryococcus, Phaeodactylum, and Porphyridium* [1,3,17,18]. For instance, colorants for cosmetic formulations such as eye shadow, face make up, and lipstick are currently obtained from red microalgae [19]. Macroalgae, commonly named seaweeds, have been used in the production of phycocolloids, like agar and alginates, mainly used to thicken (increase the viscosity) of aqueous solutions, to make gels of variable degrees of firmness, to produce water-soluble films, and to stabilize some products [20]. Furthermore, some types of brown and red macroalgae are used in cosmetics due to the presence of vitamins, minerals, amino acids, sugars, lipids, and many other biologically active compounds.

Anti-aging, photo-protection and antioxidant capacity of algal compounds

Maintenance of hydration is one of the main aspects that contributes to slow down the skin aging and to maintain its elasticity. There are several cosmetic products that contain substances promoting proper hydration of the epidermis and new studies are always focused on the search for new compounds in the name of sustainability. In fact, many formulations with a moisturizing action mainly contain hydroxy acids derived from vegetable or animal source, but, due to their limited availability, production costs are high [5]. A possible alternative is represented by polysaccharides extracted from brown and red algae that seem able to bind different water molecules simultaneously, thus maintaining a high degree of hydration of the dermis. Some experimental tests have shown that the polysaccharides extracted from *Saccharina japonica* are more effective than the hydroxy acids in the moisturizing function, thus applying as possible cosmetic additives of great importance [21].

Squalene, a triterpene contained in *Thraustochytrium* and *Aurantiochytrium*, is one of the ingredients of various cosmetic formulations with an emollient and moisturizing action [22].

Protection against UV rays and consequently against skin aging is ensured by some polysaccharides such as fucoidans and alginates extracted from different brown algae such as *Fucus vesiculosus* and *Turbinaria conoides* [23]. Free radicals of reactive oxygen species (ROS), which increase as a result of prolonged exposure to UV rays, are responsible for damaging various structural and functional cellular components, in particular proteins, DNA and membrane lipids. The strongly antioxidant action of polysaccharides such as fucoidan, which is used in various cosmetic preparations together with vitamins and plant extracts, plays a very important role in the prevention of skin inflammation, of melanomas and of skin cancer caused by ROS accumulation. Fucoidan is a fucose-containing sulfated polysaccharides (FCSPs) that have a backbone consisting of (1→3)-linked α-l-fucopyranosyl or of alternating (1→3)- and (1→4)-linked α-l-fucopyranosyl residues; it can also include sulfated galactofucans with backbones consisting of (1 → 6)-β-d-galacto- and/or (1 → 2)-β-d-mannopyranosyl units with fucose [24]. Fucoidan has been studied since the 1970s when many of its beneficial effects on human health, especially related to its cellular antiproliferative activity, have been demonstrated [25]. Moreover, it has been recently showed how fucoidans inhibit the gene expression of some metalloproteinases - enzymes involved in the degradation of different components of the extracellular matrix of the dermis like collagen or fibronectin - whose elevated and prolonged activity, such as later prolonged exposure to the sun, results in the formation of wrinkles, skin spots and other skin blemishes [5]. In particular, fucoidans are able to inhibit UVB-induced MMP-1 expression *in vitro* by the suppression of extracellular signal regulated kinase (ERK) [10]. Similarly, another study by the same author reported that 16 kDa fucoidan could suppress MMP- 3 induction on dermal fibroblasts *in vitro* [10].

A similar protective effect has been found in some secondary metabolites (MMAs - Mycosporine-like amino acids) present in red algae such as *Porphyra umbilicalis*, known especially to be used in sushi preparation, but nowadays, due to its richness in vitamins, even as constituent of several food supplements [26].

Another class of secondary metabolites extracted mainly from marine algae such as *Corallina pilulifera* and *Sargassum horneri* is represented by phlorotannins, able to promote collagen synthesis and therefore used in some anti-aging cosmetic preparations [10]. Moreover, some *in vitro* study also reported that phlorotannins are able to promote osteosarcoma differentiation by collagen synthesis [27]. In general, brown marine algae are a rich source of molecules potentially useful in cosmetic applications; *Fuco* genus algae contain fucosterols, steroid compounds that, due to their remarkable antioxidant properties, protect keratinocytes from damage caused by exposure to UV rays and promote collagen synthesis [19].

Skin whitening

In Asian culture mainly, but also in Africa and South America, skin whitening is a very common practice and it is considered as an important beauty requirement. For this reason, depigmenting cosmetic products have a thriving market, with estimates of further growth over the next few years [11]. Melanogenesis is a process that involves several biosynthetic pathways and signal transduction mechanisms, but one of the key enzymes in melanin synthesis is a tyrosinase, whose expression and activity are promoted by exposure to sunlight; molecules with the function of inhibiting the action of tyrosinase are therefore the basis of whitening cosmetic products. Marine algae have recently attracted attention due to the presence of secondary compounds that block or decrease the expression levels of tyrosinase, thus favoring the depigmentation process [5]. Some of these compounds, recently studied as components of whitening cosmetic preparations, are the derivatives of phloroglucinol, whose most studied source of extraction is *Ecklonia stolonifera*, a brown alga that populates the Sea of Japan [28]. These compounds, due to their ability to chelate copper, have a good potential to be utilized as skin whitening agents [29].

One of the most interesting pigments for the ability to negatively regulate melanogenesis is fucoxanthin, a xanthophyll present in brown algae, recently subject of several published research. *Laminaria japonica*, a brown seaweed used in Asian cuisine for its high content of mineral salts including iodine (and therefore indicated for the treatment of thyroid dysfunction), seems to accumulate high levels of this pigment capable of suppressing the tyrosinase activity [10]. In some study it was shown also as, following an oral treatment with fucoxanthin, melanogenesis was negatively regulates at the transcriptional level [30]. Further, potential whitening effects of diphlorethohydroxy-carmalol isolated from *Ishige okamurae* have been reported [31,32]. There are numerous advantages of marine algae, such as relatively low production costs, broad spectrum of skin whitening properties, low cytotoxicity, safety, wide acceptability, and novel modes of action, suggesting marine algae as nutritious food which can be used to restore female beauty; however, further studies are needed with clinical trials for their whitening effects [19].

Microalgae and cosmetics

However, microalgae and cyanobacteria such as Spirulina are a very important source of functional molecules; active ingredients extracted from different microalgae are currently used in cosmetic preparations, although a great deal of progress must still be made in the study of their action mechanisms. Several microalgae are used in cosmetics due to the presence of polysaccharides which, as specified above, work as moisturizing agents or thickeners in creamy cosmetic formulations [14].

Chlorella, a microalga very widespread in mild aquatic environments, contains high percentages of β-1,3-glucan, a polysaccharide that, in addition to the properties described above, has recently been found to be an excellent free radical scavenger and an immunostimulatory agent, potentially involved in anti-inflammatory activities [33,34]. Due to the ability to counteract the free radicals produced by exposure to sunlight or by normal cellular metabolism, the possibility of using these compounds in anti-aging cosmetic preparations is being studied. Besides *Chlorella*, *Nostoc flagelliforme* and *Porphyridium* also accumulate relevant percentages of glucans. *Chlorella vulgaris* extracts are currently being studied as additional components of "anti-aging" cosmetic preparations for the ability to induce collagen repair mechanisms [35]. The antioxidant potential of many microalgae and cyanobacteria can be of great interest for the cosmetic industry. The phycocyanins, green/blue protein complexes associated with the photosynthetic systems of blue algae and cyanobacteria, are used in cosmetics as make-up and eye makeup products. Carotenoids, colored pigments (ranging from yellow to red) accumulated in the chloroplast, with the function of protecting the photosynthetic apparatus from the oxidative damage produced by light radiations, are increasingly used for industrial application as dyes, but also as antioxidant additives in different cosmetic preparations [36]. The most commonly used pigments are β-carotene and astaxanthin; the first is extracted from several microalgae, while the second carotenoid, of a bright red color, is accumulated mainly by *Haematococcus pluvialis*. This microalga has a voluminous and strongly thickened cell wall, made up of 75% proteins. In environmental stress conditions, this alga dramatically increases its volume by accumulating in the cytoplasm high levels of astaxanthin, which can reach up to 5% of the total dry weight [37]. Astaxanthin is a xanthophyll with one of the highest antioxidant power in nature - hundred times more powerful than ascorbic acid or vitamin E - and on average 10 times higher than other carotenoids. Its applications in cosmetics, essentially as an ingredient in sunscreens, are related to the protective effect against UV-induced photo-oxidation [33]. Many microalgae are capable of accumulating a high percentage of this xanthophyll; among these, the most studied are *Botryococcus braunii* (up to 0.01% of dry weight), *Chlamydocapsa* sp. (up to 0.04% of dry weight), *Chlorella zofingiensis* and *Nannochloropsis* sp. (up to 0.7% of dry weight), *Neochloris wimmeri* and *Protosiphon botryoides* (up to 1.5% of dry weight), *Scenedesmus sp*. (up to 0.3% of dry weight), *Scotiellopsis oocystiformis* (up to 1% of dry weight) [37, 38]. Other carotenoids accumulated in different microalgae also have very important biological activities, from anti-inflammatory to photo-protective activity; *Dunaliella salina*, among other microalgae, accumulates significant amounts of β-criptoxanthin, a carotenoid implicated in anti-inflammatory mechanisms and involved in induction of hyaluronic acid synthesis [39]. Other pigments (carotenoids and chlorophylls) extracted from microalgae are used in some cosmetic products as deodorants, for their ability to cover odors, in toothpaste or in other body hygiene products [40].

Another carotenoid, canthaxanthin, is present in some food supplements aimed to facilitate the tanning of the skin during exposure to sunlight. Many microalgae are rich in this pigment, in particular those of the genus *Nannochloropsis*, which colonize marine ecosystems with very different characteristics and are also known for their ability to accumulate high percentages of polyunsaturated fatty acids (PUFA) [41]. Among the most known carotenoids, there are lycopene and lutein. The first, which is found abundantly in nature in different vegetables but especially in tomatoes, has a very high antioxidant power and is therefore used, as well as other carotenoids described above, as a component in sun protection creams. Several cyanobacteria, particularly *Nostoc* and *Anabaena vaginicola*, accumulate high percentages of lycopene [42].

Lutein, one of the most widespread xanthophylls in nature and commercially extracted from marigold flowers, manifests its powerful antioxidant effect mainly in the macula of the retina [43]. Several microalgae are rich in lutein, especially those of the genus *Scenedesmus, Chlorella* and *Dunaliella*, able to accumulate up to 3 mg / g of dry weight. The biological properties of lutein are various and very well known, ranged from the lowering of cholesterol levels in the plasma, to the protection against some forms of cancer, to the reduction of blood sugar levels [44]. In the cosmetic field, lutein is mainly used as a dye and, in combination with tocopherol or carotene, also as an antioxidant active ingredient [45]. The current production costs of lutein are very high and algae could therefore represent an interesting alternative due to the high amounts of pigments accumulated by the microorganisms under certain environmental stress conditions and for all the advantages mentioned in this article. The possibility, in fact, to cultivate specific microalgae of interest under controlled conditions as in photobioreactors, allows to obtain the biomass necessary for the sustainable production of bioactive compounds on an industrial scale [3]. On the other hand, however, the harvest of biomass and the extraction of the metabolites of interest, which represent the industrial steps downstream of the cultivation of algae, are the most critical points that do not yet allow to significantly reduce production costs. One of the aims of the research is to improve the technology of separation systems of cellular biomass from the culture medium and the extraction efficiency of the desired bioactive compounds, respecting the environment and keeping the cost down.

Concluding Remarks and Future Perspectives

Algae, during growth, produce many secondary metabolites with great industrial potential and accessibility, and thus they have attracted attention for health and cosmetic applications. This review examined the use of macroalgae and microalgae and their derivatives in applications to counteract skin aging, skin disorders as well as for depigmentation. In fact, a wide range of metabolites, studied for cosmetic applications, plays a role of antioxidants and anti-inflammatory agents such as alginates, polysaccharides, carotenoids, and so on. On the other hand, many of these studies did not report which kind of bio-compounds or the exact mechanisms which are responsible for each cosmetic function, since covered by patent. Moreover, it is necessary to consider that overall action of an algal extract is most probably due to the joint action of different substances. For this reason, it should be important to have a complete profile of the extracted bio-compounds from the different algal strains and identify the most active ones, in order to develop new cosmetics products with commercial purposes. Finally, as mentioned above, it is also necessary to improve technology for algal growth and the extraction of the functional metabolites in order to make the entire production process even more sustainable, economically and environmentally.

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