

Algae-Sourced Bioactives with Promising Applications in Skincare Cosmeceuticals



Gunjan Kulkarni¹, Annie Abraham², Madhur Kulkarni*²

¹Institute of Chemical Technology, Nathalal Parekh Road, Matunga East 400019

²SCES's Indira College of Pharmacy, New Mumbai Pune Highway, Tathawade, Pune 411033

madhur.kulkarni@indiraicp.edu.in

INTRODUCTION

Skin is the largest organ of the human body, accounting for 16% of body weight and having a surface area of 2 sq. m. Apart from being a protective barrier of the body, skin is also an epitome of beauty. A glowing, wrinkle-free and blemish-free skin is considered as a sign of young age, beauty and good health. Among peoples of countries especially from tropical belt, light or fair skin receives the highest acceptance and appreciation.

While securing the internal organs and tissues, skin itself faces various assaults. Climate, ultraviolet radiation, chemicals, allergens, and pathogens are the causative factors in precipitating various unhealthy skin conditions such as dryness, sunburns, tanning, hyperpigmentation, melasma, wrinkles, dermatitis, eczema to name a few. Genetic factors also play a vital role in manifesting undesirable skin issues. Compromised external appearance due to these conditions can have psychological implications among the suffering people. A strong desire to look beautiful and young has led to the growth of the skincare and age-defying products into the largest segment of cosmetic and cosmeceutical market. A wide array of formulations including solutions, creams, lotions, gels, serums, masks, powders, and pastes are available to prevent &/or treat the aforementioned skin problems and to enhance beauty, overall appeal and persona. [1]

The pie chart presented as figure 1 clearly depicts the dominance of skincare products in the world of cosmetics.[2]

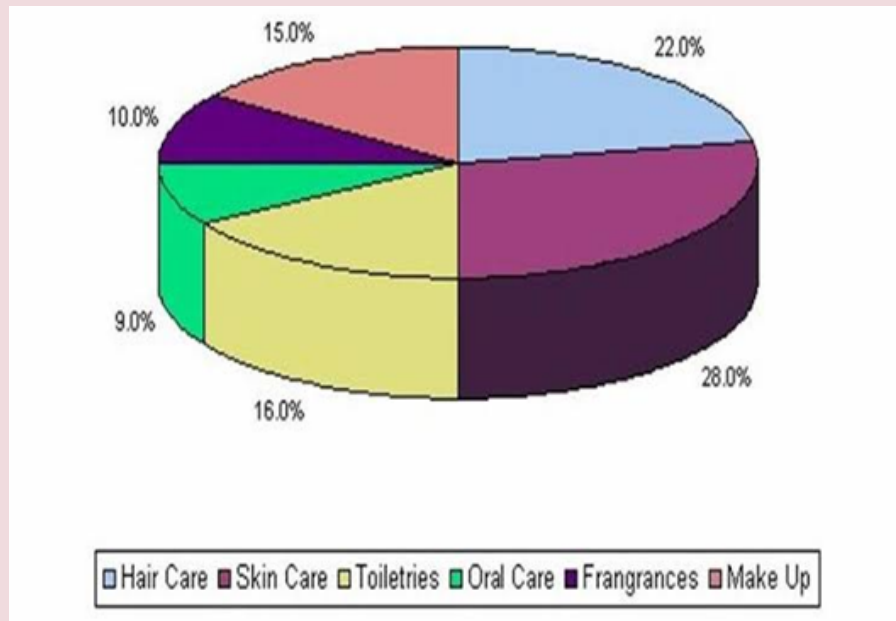


Figure 1: Distribution of cosmetics market

Skincare products market size valuation was estimated at about 129.23 billion USD in the year 2020 which is forecasted to increase with a compound annual growth rate (CAGR) of 4.8% from 2021- 2028 (figure 2). Rising demand for face creams, sunscreens, and body lotions has significantly benefited market growth. [3]

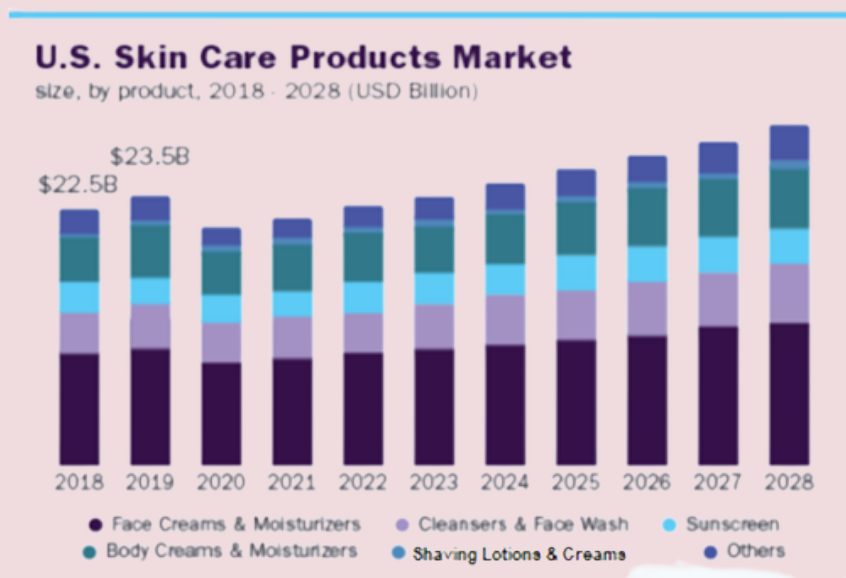


Figure 2: Distribution and sales of U. S. Skin care market

Though synthetically derived actives form integral components of the cosmeceuticals, recent trends show big demand for natural products. Natural products are perceived as safe, healthy and free from any untoward effects by people at large and hence, the cosmetic and cosmeceutical companies thrust on launching the products made with natural bioactives as well as excipients sourced mainly from plants, minerals, microbes, animal, and marine life. These bioactive ingredients obtained from plants were found to have immense beneficial effects on human skin, hair and nails. Although plant-derived products are commonly used, certain limitations like the slow growth of plants and fluctuation in chemical constituents with the changes in the season are observed. On the other hand, algae contain unique biomolecules and can be cultivated swiftly in huge quantities at low cost using contemporary aquaculture techniques.[4] The following section details the applications of various algae-derived bioactives in the field of cosmeceuticals.

ALGAE AND THEIR BIOACTIVE CONSTITUENTS

Figure 3 gives the classification of algae as well as the bioactives derived from them. [5-6] Microalgae are unicellular or multicellular organisms that grow quickly and can tolerate environmental stresses. Microalgae outperform traditional plants in terms of production, seasonal fluctuation, ease of extraction, rapid growth and availability of raw resources. Macroalgae (seaweeds) are prevalent in coastal locations and have fairly basic structures since they lack the organs seen in terrestrial plants. The algal extracts are widely being used in the cosmeceutical industry as they are a prominent source of photosynthetic pigments (chlorophylls, phycobilins and carotenoids), lipids (including fatty acids and squalene), phenols, amino acids, peptides and proteins, carbohydrates (polysaccharides and phycocolloids), pterins and vitamins. Hence these constituents found in algae can be utilized in sunscreens, skin sensitizers, whitening agents, anti-ageing, anti-inflammatory activities and colourants. The most widely studied and widely used algae in cosmetics are marine red and green algae. [7]

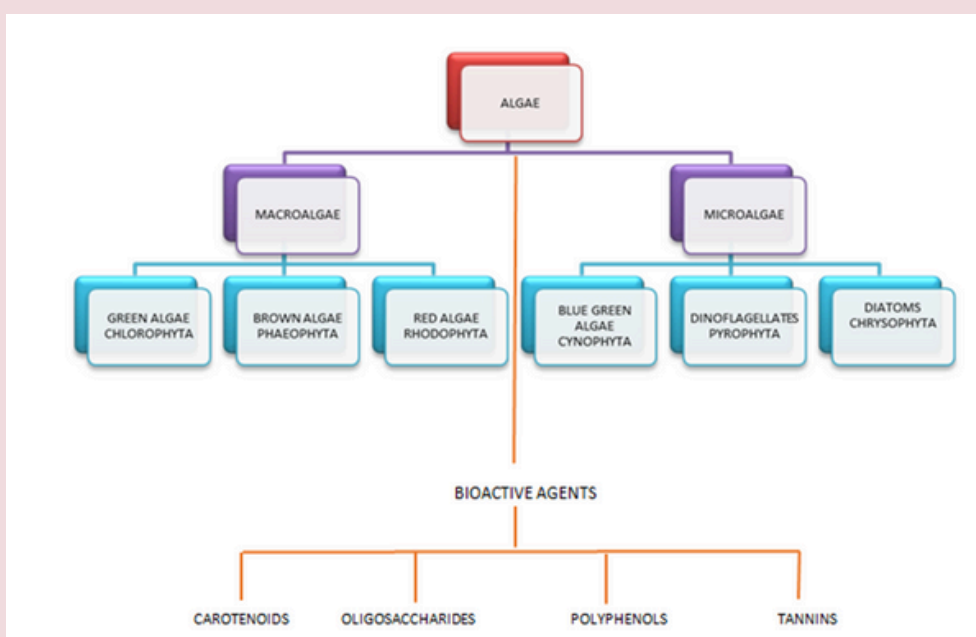


Figure 3: Classification and bioactive compounds of algae

Algae contain various pigments like carotenoids, chlorophyll to absorb light energy and xanthophylls, phycobiliproteins (PBPs) which are accessory photosynthetic pigments. Apart from being used as natural colorants, the pigments exhibit vivid properties like anti-ageing, antioxidant and neuroprotective. The presence of algal porphyrin ring in the pigments attributes to the antioxidant properties. The carotenoid chain absorbs the excited oxygen energy and protects the tissues from damage. PBPs suppress microsomal lipid peroxidation by scavenging alkoxyl, peroxy and hydroxyl radicals. Various carotenoids like lutein exhibit antimutagenic activity, whereas fucoxanthin exhibits antitumour activity by producing apoptosis. The auxiliary activity of these pigments includes anti-inflammatory action caused by controlling the function of the macrophages responsible for releasing pro-inflammatory mediators including nitric oxide, prostaglandin E2 (PGE2), tumor necrosis factor α (TNF- α), interleukin-6 and interleukin-1b, and reactive oxygen species (ROS). Brown algae rich in phlorotannins and fucoxanthin exhibit anti-melanogenic, antioxidant, and anti-inflammatory action. Researchers have investigated the use of algae-derived astaxanthin in fighting wrinkles by rejuvenating and promoting skin elasticity. Arad and Yaron (1996) utilised the pigments obtained from red microalgae to prepare pink and purple coloured lipsticks, eyeshadow and face makeup cosmetics. [8]

APPLICATIONS OF ALGAE-SOURCED BIOACTIVES IN SKIN CARE PRODUCTS

The varied applications of algae-based bioactives in the field of cosmeceuticals are covered below.

1. PHOTO PROTECTION & ANTI-AGEING [9]

Skin cells, being at the outermost surface of the body, have their own defence and damage rectifying mechanisms. DNA repair enzymes, antioxidants, and stress signalling are some known guards of skin. However, protracted exposure to UV rays (UVA and UVB) leads to generation of ROS that lead to DNA damage. Oxidative DNA damage results in a faster ageing process. Skin ageing includes a variety of alterations such as thinning, dryness, laxity, fragility, increased pores, hyperpigmentation, fine lines, and wrinkles. Astaxanthin is a secondary ketocarotenoid obtained from various microalgae such as *Haematococcus Pluvialis*, *Chlorella Vulgaris*, *Chlorella zoofingensis*, and *Chlorococcum*, is shown to provide protection against premature ageing, inflammation, and UV damage. Lutein, a micro algal xanthophyll by absorbing blue-light and scavenging free radicals generated during exposure to sunlight assists in maintaining healthy skin. According to research, phlorotannin present in algae extract inhibits UV-induced MMP-2 and MMP-9 production in human dermal fibroblasts. Microalgae such as *Dunaliella salina* and *Spirulina platensis* and *Porphyridium*, rich in sulfated polysaccharides containing a high concentration of carotenes can reduce the generation of ROS and suppress lipid peroxidation to inhibit oxidative damage. Algal extracts can thus show a promising application in sunscreen type cosmeceutical products.

2. SKIN WHITENING [10–12]

White, spot-less skin is perceived to be most beautiful, hence the multitude of whitening formulations available on the shelves. The colour of skin is greatly influenced by gene expressions and responses to external stimuli, particularly UV rays. UV radiations propel cells to produce melanin. Hyper skin pigmentation can be checked by curbing the activity of

tyrosinase enzyme, which is a capstone in melanin synthesis. Several tyrosinase inhibiting algal compounds have been delineated. Phloroglucinol, present in brown seaweed, can chelate the copper constituent of this enzyme, thus hampering its activity. Similarly, Phlorotannins (7-phloroeckol) sourced from *Ecklonia cava* block the tyrosinase enzymes. Another polyphenol, dieckol, is three times as efficient as kojic acid (ubiquitously used in skin whitening creams) in dampening tyrosinase activity. Carotenoids, Zeaxanthin, astaxanthin, lutein, and β -carotene from various algal sources also provide similar facilities. Astaxanthin is considered to be superior to the others as it can reduce pigmentation by up to 40%. Suppression of prostaglandin E2 synthesis and melanogenic stimulant receptors are postulated as the primary mechanisms of anti-pigmentary effect of fucoxanthin from *Laminaria japonica*. Fucooidan is a fucose-rich sulphated polysaccharide produced by marine brown algae like *Fucus vesiculosus*. Fucooidans have been shown to work on hyper pigmentation by down-regulating microphthalmia-associated transcription factor (MITF), the factor controlling the melanogenic enzymes.

3. ANTI- ACNE

Acne is seen as an inflammatory disease which involves bacterial infestation in sebum and hair follicles. It has the potential to manifest for years, usually in adolescents and young adults, leave permanent scars and disturb the physiological development. *Propionibacterium acnes*, *Staphylococcus aureus*, *Streptococcus epidermidis*, and *Pseudomonas aeruginosa* are the most frequent culprits. Antibacterial and antibiotic treatments are being used as a cure. Considering their side effects and bacterial resistance issues, research has steered towards nature for a solution. Some macroalgae (seaweed) extracts, in addition to their antibacterial properties, show anti-inflammatory activities and are thus able to regulate growth factors and collagen levels. This could provide an excellent solution for acne, fighting the root cause (bacteria) and repairing the damage done to the skin. [13]

Sargafuran, methanolic extract of marine brown alga, *Sargassum macrocarpum*, has been found to be effective for treating acne. Minimum inhibitory concentration (MIC) of sargafuran against *P. acnes* was 15 $\mu\text{g ml}^{-1}$. Sargafuran is found to be stable in the pH range of 4-7, at temperatures of 60°C and a 24 hour UV irradiation and hence is a good addition to cosmeceuticals. [14] In another study, a phlorotannin extract of *Sargassum tenerrium* was investigated against *Propionibacterium acnes*. It was used in an emulsion form, akin to cosmeceutical products, Mohammadi and group found low MIC against *P. acnes* and several other bacteria, notorious for skin infections like *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. [15]

4. ANTI-INFLAMMATORY

The body uses inflammation as the first line of defence against any deleterious stimuli. Skin is the first barrier for any sort of mechanical injury, physical, chemical and biological agents. As it covers the entire body, skin inflammation is highly common. Skin diseases like vulgaris, psoriasis and allergic dermatitis can be attributed to inflammation. [9]

Various bioactives from algae have been discovered to harbour anti-inflammatory properties. *Dunaliella salina* and *Spirulina platensis* inhibit the synthesis of nitric oxide, a powerful mediator. Similarly, extracts of *Ecklonia cava* and *Ecklonia kurome* have the ability to prevent

Scytonemin, a dimer containing indolic and phenolic subunits, is extracted from *Scytonema*, *Stigonema*, *Nostoc* and many more. It is proven to possess anti-inflammatory activities by blocking expression of inflammatory mediators like TNF- α and nitric oxide, and by down-regulation of NF-kB activity. Astaxanthin, found abundantly in algae, especially *Haematococcus pluvialis*, represses generation of pro-inflammatory cytokines, nitric oxide, prostaglandin E2, TNF- α , and interleukin-1 β . A sterol extract of *Nannochloropsis oculata* has been reported to suppress the expression of inducible nitric oxide synthase and cyclooxygenase-2 (COX-2) proteins, thus yielding an anti-inflammatory effect in RAW 264.7 cells. [16]

Numerous works delineate the potential of fucoidans in prohibiting damage of extracellular matrix caused by MMP. It can suppress the extracellular signal regulated kinase (ERK) and thus inhibit UVB-induced MMP-1 expression. Along with inhibiting ROS and blocking cytokines, marine brown algal phlorotannins including dieckol, and 1-(3',5'-dihydroxyphenoxy)-7-(2',4',6'-trihydroxyphenoxy) 2,4,9-trihydroxydibenzo-1,4,-dioxin can suppress the protein as well as gene expression levels of MMP-1, MMP-3, and MMP-13 in human osteosarcoma cells (MG-63). [17]

5. WOUND HEALING [18]

Wound healing involves a series of contemporary events including hemostasis, inflammation, migration, proliferation and remodelling. In case of substantial or large skin lesions, this process diminishes, leading to a chronic wound healing process. During this process, an immense amount of ROS is produced by neutrophils and macrophages resulting in severe tissue damage hindering the healing process, which otherwise in normal amounts prevents a microbial invasion. The pro-inflammatory cytokine mediators produced during wound healing cause extensive pain. Hence a need exists to include anti-inflammatory bioactive compounds to relieve the pain during the chronic wound healing process. Bacteria when present at the site of the wound aggravates inflammation, hence a formulation containing antibacterial, anti-inflammatory and antioxidant agents is the best suit to treat wounds. Miguel, et al, have discovered carotenoids like lutein, astaxanthin, zeaxanthin, and fucoxanthin obtained from microbial algae as a potent source of bioactive agents exhibiting anti-inflammatory, antioxidant, and wound healing properties. These bioactive carotenoids can thus be exploited for skin regeneration.

CLINICAL STUDIES [12-13], [19]

Actives sourced from algae have been subjected to a number of clinical studies. Table 1 gives an account of the completed trials.

Table 1: Clinical trials of algal based cosmeceuticals

Active/Algae	Dosage, Duration	Parameters tested	Result
Astaxanthin	Oral dosage (6mg) + topical application (1 mL topical application on entire face, twice a day, 78.9 uM solution); 8 weeks	1. Age spot size 2. Wrinkles 3. Elasticity 4. Skin texture	1. Age spot area was significantly treated 2. Parameters like depth and maximum width of deepest wrinkle were reduced 3. Elasticity increased 4. Mean depth texture increased significantly
Astaxanthin	0.7mg/g cream; 2 weeks	Skin wrinkles	Anti-wrinkle effect in all the subjects Lesser puffiness under the eyes
Oligo-saccharide, Laminaria digitata	5% gel formulation; 28 days	Cutaneous sebum level for acne	Reduction of sebum level by 67%
Ascophyllum nodosum and Crithmum maritimum along with 22 herbal extracts, 2 naturally derived antioxidants and 3 synthetic ingredients	18 weeks (12 weeks treatment phase, 6 weeks non treatment)	Hyper pigmentation	Macroalgal extracts were comparable with standard treatment (4% hydroquinone and 0.05% tretinoin)
Ascophyllum nodosum and Crithmum maritimum along with 22 herbal extracts, 2 naturally derived antioxidants and 3 synthetic ingredients	1 year	Hyper-pigmentation	Continuous improvement No lesion rebound No irritation
Codium tomentosum	5% extract cream, 2 times/day; 7 days	Moisture levels in 3 layers of skin	Cream with extract moisturized all the skin levels. It provided 50% more moisturizing effect than placebo.
Codium tomentosum	Single application of cream; Measurement after 0, 10, 15, 30 minutes, 1, 2, 4 and 6 hours	Immediate skin moistening of forearm	Average of 15% higher moisture levels after 6 hours than placebo (5%).
Laminaria japonica	10% extract; 8 hour observation	Moistening of inner forearm skin	After 2 hours, hydration was 31.46% due to cream with extract as compared to the placebo (17.02%) After 8 hours, trans epidermal water loss was only 4.01 g/cm ² which was 20% of the control
Rhizodonium hieroglyphicum	0.3% extract; Short term-1 hour application Long term-1 week application	Skin hydration	Short term effects were similar to that of 0.5% hyaluronic acid (regularly used ingredient of moisturizer) Long term results were comparable with many other standards, glycerin, hyaluronic acid and propylene glycol No irritation or allergic reactions were reported.
Fuoidan, Fucus vesiculosus extract	0.3% extract; 60 days	Melanin index	65% of volunteers noticed reduction of melanin index of age spots, 50% whitening of skin and 45% reduction of wrinkles
Fucus vesiculosus	1% extract daily; 5 weeks	Cheek skin thickness and mechanical properties of human skin	7-8% decrease in thickness Improved elasticity
Combination of Furcellaria lumbicalis and Fucus vesiculosus and retinoid	Topical application of formulation once daily; 12 weeks	Fat thickness	A reduction in fat thickness was observed when compared with placebo
Laminaria digitata and Pelvetia canaliculate and Gelidium cartilagineum	Once daily at night; 4 weeks	Localized fat accumulation	The product reduced the fat thickness of waist by 2.1cm, 1.8 cm for the hips, 2.3 cm for the upper thigh, and 1.8 cm for the thigh

PRODUCTS ON MARKET [20], [21]

Several products containing algae-based active constituents have been successfully launched in the markets across the globe. Table 2 summarizes a few such commercially available products.

Table 2: Algal- based cosmeceuticals available as marketed products

PRODUCT	BIOACTIVE, ALGAE	USE
Alguronic, Algenist	Microalgae oil and alguronic acid from algae	Anti-aging moisturizer
Helionori by Gelyma	Maas from red seaweed <i>Porphyra umbilicalis</i>	Sunscreen
Helioguard365 by Mibelle biochemistry	Maas from red seaweed <i>Porphyra umbilicalis</i>	Sunscreen
Protulines® by Exsymol S.A.M., Monaco	Protein-rich extract of <i>Arthrospira</i>	Anti-aging agent
Dermochlorella DG by Codif, St. Malo, France	Oligopeptide extract of <i>Chlorella vulgaris</i>	Anti-wrinkling agent
OXY, Mentholatum Company	Bladderwrack extracts	Anti-acne care products
Clearskin, Max roduve	Bladderwrack extracts	Anti-acne care products

CONCLUSION

Skincare products occupy the major share of cosmetics and cosmeceutical market. Considering the growing demand for the products comprising naturally- sourced actives and excipients, cosmeceutical companies are continuously in quest of plant, mineral and microbe based bioactives. Active constituents obtained from algae are studied extensively as they are abundant, come with lesser variation and can be sustainably sourced. Carotenoids, polysachharides, tannins sourced from algae have shown excellent activities against common skin problems such as inflammation, hyperpigmentation, wrinkles, wounds, and photo-damage. In vivo and clinical studies of these actives have yielded a number of algae based skin care cosmeceuticals available on the shelves. The abundance of the micro and macro algal flora provides numerous opportunities for exploring more bioactives and their applications which would provide newer and better cosmeceutical options of skincare.

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