

Review

Applications of Bioactive Compounds from Marine Microalgae in Health, Cosmetics, and Functional Foods

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Abstract: Marine microalgae have emerged as promising biofactories for the sustainable production of high-value bioactive compounds with significant applications in human health, cosmetics, and functional foods. This review offers a comprehensive overview of the primary classes of bioactives synthesised by marine microalgae, including polyunsaturated fatty acids, carotenoids, phycobiliproteins, peptides, sterols, polysaccharides, phenolic compounds, vitamins, mycosporine-like amino acids, and alkaloids. These compounds demonstrate diverse biological activities, such as antioxidant, anti-inflammatory, antimicrobial, anticancer, immunomodulatory, and photoprotective effects, increasingly validated through in vitro, and clinical studies. Their mechanisms of action and roles in disease prevention and wellness promotion are examined in detail, with an emphasis on pharmaceutical (e.g., cardiovascular, neuroprotective), cosmetic (e.g., anti-ageing, UV protection), and nutraceutical (e.g., metabolic and immune-enhancing) applications. The review also addresses critical challenges in strain selection, cultivation technologies, downstream processing, product standardisation, and regulatory approval. Simultaneously, emerging opportunities driven by synthetic biology, omics integration, and circular biorefinery approaches are transforming marine microalgae into precise platforms for next-generation bioproducts. By summarising current knowledge and future directions, this work underscores the essential role of marine microalgae in advancing the blue bioeconomy and tackling global sustainability challenges.

Keywords: blue bioeconomy; functional ingredients; marine biotechnology; microalgal metabolites; microalgal nutraceuticals; sustainable bioactives

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1. Introduction

The oceans, covering more than 70% of the Earth's surface, are a vast and underutilised reservoir of biodiversity, holding enormous potential for discovering novel bioactive compounds [1]. Among the most promising marine resources are marine microalgae, microscopic photosynthetic organisms fundamental to freshwater and marine ecosystems [2]. Major taxonomic groups include Chlorophyta (green algae), Rhodophyta (red algae), Haptophyta, Cryptophyta, Bacillariophyta (diatoms), Dinophyta (dinoflagellates), and cyanobacteria (blue-green algae) [3,4].

Marine microalgae are not only a vital component of marine food webs but also act as prolific producers of secondary metabolites. These metabolites include

polyunsaturated fatty acids (PUFAs) such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), pigments like fucoxanthin and astaxanthin, polysaccharides, sterols, peptides, and phenolic compounds, each demonstrating diverse biological properties such as antioxidant, anti-inflammatory, antimicrobial, and anticancer activities [3,5].

Recent years have witnessed a surge in biotechnological interest in marine microalgae, largely due to their rapid growth rates, adaptability to diverse environmental conditions, and ability to be cultivated in controlled systems such as photobioreactors. These features make them a sustainable alternative to terrestrial plants and synthetic sources for producing high-value compounds with health-promoting attributes [6]. Additionally, microalgal cultivation does not compete with agricultural land or freshwater resources, aligning with global goals of environmental sustainability and climate change mitigation [7].

The potential applications of microalgal compounds extend across several high-growth sectors. In human health and pharmaceuticals, n-3 PUFAs derived from microalgae have demonstrated positive effects in reducing cardiovascular disease risk, neurodegeneration, and inflammation [8,9]. Pigments such as astaxanthin are potent antioxidants shown to enhance immune function and protect against oxidative stress-related conditions, including ageing and cancer [10]. Similarly, microalgal polysaccharides and sterols have displayed immunomodulatory and cholesterol-lowering effects, offering potential as functional ingredients in nutraceutical products [11].

In the cosmetics sector, the demand for naturally derived ingredients with anti-ageing, moisturising, and photoprotective properties is growing rapidly. Microalgae-derived compounds like fucoxanthin and mycosporine-like amino acids (MAAs) have demonstrated photoprotective effects by absorbing ultraviolet radiation and reducing oxidative damage in skin cells [12]. Their antioxidant, anti-inflammatory, and collagen-stimulating properties further support their use in anti-ageing skincare formulations.

In functional foods, microalgal ingredients are incorporated to enhance nutritional profiles and offer added health benefits. Algal biomass or extracts can be integrated into beverages, supplements, dairy alternatives, and energy bars. Species such as *Chlorella* and *Spirulina* (formerly *Arthrospira platensis*, and currently reclassified as *Limnospira platensis*) are widely approved and utilised in food-grade applications due to their established safety and health-promoting profiles [13].

Despite the growing body of evidence supporting microalgae's bioactive potential, the transition from laboratory to market faces several challenges. These include strain optimisation, scalable cultivation systems, cost-effective downstream processing, and regulatory hurdles related to food and cosmetic safety. Advances in metabolic engineering, synthetic biology, and bioreactor design are gradually addressing these limitations, enabling higher yields and greater consistency in compound production [14]. Moreover, omics technologies are being leveraged to uncover biosynthetic pathways and enhance the discovery of novel compounds.

The integration of marine biotechnology into blue bioeconomy strategies holds the promise of sustainable industrial-scale production of microalgal bioactives [15]. Europe, in particular, is investing heavily in this transition through programmes that foster interdisciplinary collaborations and support technology transfer between research institutions and industry [16]. However, further efforts are required to enhance the commercial readiness of these technologies, ensure regulatory compliance, and conduct large-scale clinical trials validating the health claims of these compounds [17].

This review aims to provide an up-to-date overview of the diversity, biological roles, and biotechnological potential of bioactive compounds derived from marine microalgae.

It focuses on: (1) classifying major compound groups: PUFAs, pigments, peptides, sterols, polysaccharides, phenolics, MAAs, vitamins, alkaloids, and phycobiliproteins; (2) evaluating their mechanisms of action and relevance in human health, cosmetics, and functional foods; and (3) discussing key challenges and emerging opportunities in strain optimisation, cultivation, extraction, and commercialisation. Drawing on recent advances in molecular biology, bioengineering, and applied phycology, the review highlights the role of microalgae in supporting a sustainable blue bioeconomy.

To ensure a comprehensive analysis, the literature was retrieved from major scientific databases PubMed, Scopus, and Web of Science. The search strategy employed a combination of keywords and Boolean operators, using terms such as “marine microalgae”, “bioactive compounds”, “PUFA”, “carotenoids”, “polysaccharides”, “nutraceuticals”, “cosmeceuticals”, and “marine biotechnology.” Filters were applied to prioritise peer-reviewed articles published from 2015 onward, with a focus on experimental studies, reviews, and meta-analyses relevant to health, cosmetics, and functional food applications. Articles were screened for relevance based on titles, abstracts, and full texts where necessary. Preference was given to studies reporting specific bioactivities, chemical characterisation, mechanisms of action, and commercialisation potential of marine microalgal compounds. Data were synthesised qualitatively to highlight trends, applications, and technological advances across disciplines.

2. Marine Microalgae Diversity and Biotechnological Relevance

Marine microalgae are among the most promising and multifaceted groups of organisms in modern biotechnology. These microscopic, photosynthetic organisms form the base of the marine food web and are responsible for nearly half of global oxygen production and carbon fixation. Their exceptional biodiversity, metabolic versatility, and environmental resilience render them critical to ocean ecosystems and industrial innovation across health, food, energy, and environmental sectors. As biotechnology increasingly moves toward sustainable and renewable resources, microalgae have emerged as ideal candidates for scalable, eco-friendly bioproduction platforms [18].

Microalgae encompass diverse organisms spanning multiple taxonomic groups (Chlorophyta, Rhodophyta, Haptophyta, Cryptophyta, Bacillariophyta, Dinophyta, and cyanobacteria) that have arisen through billions of years of evolution and adaptation to various aquatic environments, from sunlit surface waters to nutrient-rich deep-sea zones. Each taxonomic group exhibits distinct physiological traits and biochemical profiles that influence their suitability for different biotechnological applications. For example, diatoms possess unique silica shells and are known for their rich lipid content, while green algae such as *Chlorella* are renowned for their protein and chlorophyll content [19].

Beyond taxonomic differences, microalgae are ecologically versatile, thriving in environments ranging from tropical coastal zones to hypersaline lakes and polar regions. This adaptability underpins their use in diverse industrial settings, including open-pond cultivation in tropical climates and controlled photobioreactors in temperate zones [20].

One of the most compelling features of microalgae is their ability to biosynthesise a wide variety of primary and secondary metabolites. These include PUFAs like EPA and DHA, carotenoids such as astaxanthin and fucoxanthin, antioxidants, vitamins, polysaccharides, and bioactive peptides. Many of these compounds have demonstrated pharmaceutical and nutraceutical properties, including anti-inflammatory, antioxidant, antimicrobial, and anticancer effects [21].

Microalgae can be cultivated using open ponds, closed photobioreactors, or hybrid systems. Open systems are cost-effective and suitable for robust species like *Spirulina*, whereas photobioreactors provide better control over environmental variables and are

favoured for producing high-value compounds. Environmental factors such as light intensity, CO₂ enrichment, nitrogen levels, and pH are carefully modulated to optimise growth and metabolite yield [22].

Furthermore, microalgae exhibit remarkable metabolic plasticity under stress conditions. Nutrient deprivation, light stress, and salinity fluctuations often trigger elevated synthesis of valuable secondary metabolites. This metabolic responsiveness can be harnessed for controlled production of target compounds in industrial settings [23].

Recent innovations include the integration of wastewater as a nutrient source, which not only cuts costs but also serves environmental goals by reducing effluent pollution. Cultivating microalgae on industrial CO₂ emissions is also gaining momentum as a carbon capture strategy [24].

Emerging technologies such as synthetic biology and omics integration are playing a pivotal role in optimising microalgal bioactive production. Synthetic biology tools, including CRISPR/Cas9, TALENs, and modular pathway engineering, are increasingly being used to enhance yields of targeted metabolites. For instance, genetic modifications in *Nannochloropsis* and *Pavlova* strains have successfully increased EPA and DHA output. Transcriptomic and metabolomic profiling have revealed critical gene clusters associated with lipid biosynthesis and stress-induced metabolite accumulation [25,26].

Furthermore, multi-omics integration (genomics, transcriptomics, proteomics, metabolomics) enables systems-level insights into microalgal biology. These data are used to build predictive models of metabolic flux and identify novel biosynthetic routes. Case studies have shown that omics-guided engineering can lead to 2–3-fold increases in target compound yields under optimised culture conditions. These advances are essential for strain selection, metabolic pathway optimisation, and precision cultivation [27,28].

Artificial intelligence (AI) and machine learning are also emerging as tools for real-time process optimisation in photobioreactors. AI-assisted monitoring systems are being used to modulate light cycles, nutrient delivery, and CO₂ supplementation dynamically, thereby improving both biomass productivity and metabolite concentration [29].

The omics revolution has significantly enhanced our understanding of microalgal biology. These high-throughput tools are used to dissect biosynthetic pathways, elucidate stress response mechanisms, and identify genes responsible for metabolite production. Genomic and transcriptomic data, for instance, can reveal upregulated pathways during nutrient deprivation, pointing to potential targets for metabolic engineering [30].

Moreover, multi-omics integration allows for holistic systems biology approaches, enabling predictive modelling of cellular behaviour under varying conditions. Such insights are crucial for the design of next-generation bioreactors and cultivation regimes [31].

Genetic engineering in microalgae, while still developing, has made significant strides with tools such as CRISPR/Cas9, Agrobacterium-mediated transformation, and synthetic biology circuits. These tools allow for strain enhancement through gene knock-ins or knockouts aimed at improving yield, resistance, or biosynthetic specificity. For example, the transformation of *Pavlova lutheri* with a desaturase gene significantly increased its PUFA content, demonstrating the practical utility of such approaches [32].

In parallel, synthetic biology is being used to construct modular pathways for the de novo synthesis of complex compounds, such as pharmaceuticals and recombinant proteins. This expands the potential of microalgae beyond natural metabolite production into the realm of custom biomanufacturing [33].

Marine microalgae are increasingly recognised as sources of functional foods, nutraceuticals, and dietary supplements. The n-3 fatty acids EPA and DHA, commonly derived from fish, can be sustainably sourced from microalgae without the risks of

bioaccumulated toxins. Other compounds like astaxanthin and lutein are marketed for their antioxidant and eye-health benefits [34].

Microalgae also hold promise in clinical nutrition, with ongoing studies evaluating their potential in managing chronic diseases such as diabetes, hypertension, and neurodegeneration. The approval of *Chlorella* and *Spirulina* as Generally Recognised as Safe (GRAS) ingredients has facilitated their incorporation into a variety of food and beverage products [35].

Beyond health applications, microalgae serve as agents of environmental remediation and contributors to sustainable manufacturing. Their ability to uptake nitrogen, phosphorus, and heavy metals makes them suitable for treating municipal and industrial wastewater. Moreover, lipid-rich strains are used in the production of biofuels, bioplastics, and green solvents [36].

Their use in carbon capture and utilisation is also notable, with pilot projects demonstrating that flue gases from power plants can be directly used to enrich algal cultures, turning waste into biomass [37].

Recent innovations in co-cultivation techniques, where microalgae are grown alongside bacteria or other algae, have shown great promise for enhancing productivity and uncovering novel metabolic interactions. These systems mimic natural symbioses, fostering nutrient recycling, quorum sensing, and co-metabolite production. Studies have revealed that such ecology-driven approaches can boost the synthesis of bioactive compounds beyond what is observed in monocultures. These systems are especially promising for pharmaceutical exploration, where co-culture may trigger “silent” biosynthetic pathways not expressed under standard conditions [38].

Global interest in microalgal biotechnology has led to robust investment from both public and private sectors. In Europe, the Horizon 2020 and BlueBio initiatives have prioritised marine microalgae as part of their blue economy and sustainability strategies. These programmes fund research, support infrastructure development, and aim to de-risk commercialisation pathways [39].

Despite this progress, challenges remain in terms of scaling production, standardising bioactive quantification, and navigating regulatory approval, especially for novel food and therapeutic uses. The integration of responsible research frameworks and international cooperation will be crucial for achieving global impact [40].

As synthetic biology, AI, and systems biology converge with marine biotechnology, microalgae are poised to become precision platforms for the sustainable production of bio-based materials, health products, and renewable energy. The deployment of autonomous bioreactors, real-time omics monitoring, and AI-driven process optimisation will enable year-round, scalable, and cost-effective production [40].

3. Major Bioactive Compounds and Potential Applications

Marine microalgae produce a wide variety of bioactive compounds as part of their primary and secondary metabolism, including PUFAs, carotenoids, peptides, polysaccharides, sterols, phenolic compounds, MAAs, and vitamins. These metabolites support microalgal adaptation to environmental stress and exhibit potent biological activities, such as antioxidant, anti-inflammatory, and antimicrobial effects, that are increasingly valued for applications in medicine, cosmetics, and functional foods. This section explores the major compound classes, organised alphabetically, highlighting their biochemical features, biological functions, and application relevance for human health, nutrition, and care.

3.1. Alkaloids

Alkaloids are a structurally diverse group of nitrogen-containing secondary metabolites, produced by selected marine microalgae, particularly dinoflagellates and cyanobacteria. Though less common than other bioactive classes, alkaloids exhibit potent neurotoxic, anticancer, and antimicrobial effects, and have attracted interest for pharmaceutical, cosmetic, and functional food applications [41].

A major representative is saxitoxin, a tricyclic guanidinium alkaloid synthesised by *Alexandrium*, *Gymnodinium*, and *Pyrodinium* dinoflagellates, as well as cyanobacteria like *Anabaena* and *Cylindrospermopsis*. Saxitoxin and its analogues (e.g., neosaxitoxin, gonyautoxins) block voltage-gated sodium channels (Nav), interrupting nerve signal transmission. Although these toxins are responsible for paralytic shellfish poisoning, controlled doses of neosaxitoxin have demonstrated long-lasting anaesthetic effects, making it a promising non-opioid analgesic with nerve-block duration up to 48 h [42].

Beyond neurotoxins, marine cyanobacteria produce indole alkaloids such as curacin A, lyngbyatoxin A, and dolastatin-10, noted for their anticancer potential. These compounds disrupt tubulin polymerisation, inhibit cell division, and induce apoptosis. For instance, dolastatin-10 exhibits cytotoxicity at IC₅₀ values of 0.5–1.2 nM in leukaemia and carcinoma cells and serves as a template for Food and Drug Administration (FDA) - approved antibody-drug conjugates [43].

Ecologically, alkaloid biosynthesis may serve as a defence mechanism against predators or to maintain ionic homeostasis under stress. For example, elevated Na⁺ and pH levels have been shown to upregulate saxitoxin production and export, pointing to its role in cellular ion regulation [44].

Alkaloids also have relevance in cosmetic applications, with indole derivatives demonstrating antioxidant, antimicrobial, and anti-photoaging effects that support their use in skincare and UV-protective formulations [45].

In the functional food sector, trace alkaloid components in edible cyanobacteria like *Spirulina* may contribute to immune modulation and microbial balance in the gut. However, due to their bioactivity, rigorous safety assessments are essential to ensure consumer protection [46].

In summary, alkaloids from marine microalgae are biochemically potent molecules with diverse therapeutic prospects. Their ability to act on specific cellular targets, such as ion channels or the cytoskeleton, positions them as valuable leads for drug development in neurology, oncology, and anaesthesiology. Advances in biosynthetic gene discovery and heterologous expression systems will be key to expanding their accessibility and industrial scalability [47].

3.2. Mycosporine-like Amino Acids

MAAs are small, water-soluble secondary metabolites produced by marine microalgae, cyanobacteria, and macroalgae as a defence against ultraviolet radiation. These compounds absorb UV-A (320–400 nm) and UV-B (280–320 nm) radiation with high molar extinction coefficients (typically 28,000–50,000 M⁻¹ cm⁻¹), dissipating the energy as heat without generating free radicals, thus providing effective photoprotection [48]. Common MAAs include shinorine, porphyra-334, mycosporine-glycine, and palythine, with concentrations in microalgae ranging from 0.1% to 1.2% of dry weight, depending on species and light exposure [49].

In marine cyanobacteria and green microalgae, MAA production is upregulated under environmental stress, including high solar radiation, nutrient limitation, or salinity changes. For example, engineered *Nannochloropsis salina* strains expressing genes from red algae can produce up to 25 mg g⁻¹ dry weight of porphyra-334 under UV exposure [50]. This has led to increasing industrial interest in scalable production for use in photoprotective skincare formulations.

In addition to UV absorption, MAAs exhibit broad-spectrum antioxidant and anti-inflammatory properties. Mycosporine-2-glycine (M2G), for example, has demonstrated strong radical-scavenging activity and reduced nitric oxide (NO) production by 2–3-fold in lipopolysaccharide-stimulated macrophages, outperforming other MAAs such as shinorine and porphyra-334 [51]. These effects are linked to NF- κ B pathway inhibition and downregulation of pro-inflammatory mediators such as cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS).

MAAs also contribute to anti-ageing and skin-regenerating effects in cosmetic formulations. In vitro studies using HaCaT keratinocyte cells showed that MAA treatment after UV exposure restored levels of elastin and procollagen C proteinase enhancer, both of which are essential for skin elasticity and repair [52]. Additionally, increased expression of involucrin, a marker of epidermal stress, was suppressed by MAA treatment, further confirming their role in photoprotection and dermal homeostasis.

In the nutraceutical and functional food domains, MAAs are being explored for oral photoprotection, antioxidant supplementation, and anti-inflammatory support. Their water solubility, low toxicity, and resistance to photodegradation make them suitable for inclusion in beverages and dietary supplements. Several MAAs are also being investigated for antiviral and anticancer activities, although these applications remain largely preclinical [53].

In summary, MAAs are multifunctional metabolites produced by microalgae and cyanobacteria with diverse applications in medicine (anti-inflammatory, anti-ageing), cosmetics (natural sunscreens, skin protection), and functional foods (antioxidant and immune support). Their stability, specificity, and biosafety profile make them attractive candidates for integration into next-generation bioproducts.

3.3. Peptides (Bioactive Peptides)

Bioactive peptides are small protein fragments typically composed of 2 to 20 amino acids, produced through the enzymatic hydrolysis of larger protein molecules. Marine microalgae, especially species like *Chlorella vulgaris*, *Spirulina*, and various marine diatoms, are emerging as rich sources of these peptides. Owing to their high protein content, *Spirulina* and *Chlorella vulgaris* provide between 50 and 70% as well as 40–60% protein by dry weight, respectively, representing promising platforms for generating bioactive peptides with therapeutic value [54].

These peptides demonstrate a broad spectrum of biological activities, including antioxidant, antihypertensive, antimicrobial, anti-inflammatory, immunomodulatory, and anticancer effects. The presence of specific amino acid sequences, such as those rich in proline, arginine, or histidine, enhances their activity and specificity for biological targets [55,56]. Peptides derived from microalgae are particularly attractive due to their bioavailability, digestibility, and minimal allergenic potential [57,58].

A key health-promoting function of microalgal peptides is their antihypertensive activity via inhibition of angiotensin-converting enzyme (ACE). Enzymatic hydrolysates from marine diatoms like *Bellerophcea malleus*, prepared using proteases such as papain or trypsin, have demonstrated significant ACE-inhibitory activity and in vivo reduction in systolic blood pressure by up to 17 mmHg in hypertensive rat models [59]. This positions these peptides as candidates for natural blood pressure management in functional foods.

Antioxidant activity is another well-documented property of microalgal peptides. They scavenge reactive oxygen species, chelate transition metals, and inhibit lipid peroxidation in biological membranes. Peptide-rich hydrolysates from *Spirulina* and *Chlorella* have shown high DPPH and ABTS radical scavenging capacity, with IC₅₀ values as low as 45 μ g/mL. Such peptides are also capable of protecting DNA from oxidative

damage and modulating antioxidant defence enzymes, making them relevant to anti-ageing skincare and metabolic health formulations [60].

Bioactive peptides from microalgae have also shown anticancer potential. Peptides obtained from *Spirulina* and *Chlorella* can inhibit proliferation and induce apoptosis in various human cancer cell lines, including MCF-7 (breast), HepG2 (liver), and AGS (gastric), at concentrations ranging from 25 to 100 µg/mL. Mechanistically, these peptides may activate mitochondrial apoptotic pathways, suppress NF-κB signalling, or inhibit angiogenesis, depending on their structure and sequence [61].

In cosmetics, microalgal peptides offer multifunctional benefits: they reduce inflammation, promote collagen synthesis, enhance wound healing, and protect against UV damage. Several studies have shown that bioactive peptides from *Spirulina* suppress cytokines like IL-6 and TNF-α in keratinocyte models, while also promoting fibroblast proliferation. This suggests utility in anti-ageing, soothing, and regenerative skincare applications [62].

Functionally, peptides also serve as natural preservatives or bio-stabilisers in food and personal care products due to their antimicrobial properties. Peptides from marine diatoms and cyanobacteria have shown inhibitory effects against both Gram-positive and Gram-negative bacteria, including *Listeria monocytogenes* and *E. coli*. This positions them as sustainable, clean-label preservatives in formulations aiming to reduce synthetic additives [63].

From an industrial standpoint, the production of microalgal peptides involves a multi-step process: biomass harvesting, protein extraction, enzymatic hydrolysis, and peptide purification. Techniques such as membrane filtration, ultrasonication, and high-pressure homogenization are being employed to improve yield and maintain activity. Peptide enrichment through gel filtration, reversed-phase high-performance liquid chromatography, or ion-exchange chromatography further ensures bioactivity specificity [64].

Recent innovations also involve using omics-based tools (proteomics, metabolomics) to identify novel bioactive sequences, and employing synthetic biology to engineer microalgae capable of producing designer peptides. These advancements are facilitating scalability and opening opportunities for developing patented peptide products with standardised efficacy profiles [65].

In conclusion, bioactive peptides from marine microalgae are versatile biomolecules with growing significance in health, wellness, and biopharmaceutical sectors. Their multifunctionality, safety, and adaptability to diverse formulation types make them compelling alternatives to synthetic compounds. Continued investment in omics-driven discovery, clinical validation, and regulatory pathways will be vital for their future commercialisation and public health impact.

3.4. Phenolic Compounds

Phenolic compounds are a structurally diverse class of secondary metabolites characterised by aromatic rings bearing one or more hydroxyl groups. In marine microalgae, phenolics, including simple phenolic acids (e.g., gallic, chlorogenic), flavonoids (e.g., quercetin), and complex phlorotannins, are produced in response to environmental stressors such as UV exposure, salinity, or oxidative stress. These compounds have attracted increasing interest for their antioxidant, anti-inflammatory, anticancer, and antimicrobial properties, which make them highly relevant in pharmaceuticals, functional foods, and cosmetics [66].

Microalgae such as *Nannochloropsis* sp., *Tetraselmis* sp., and *Phaeodactylum tricornutum* have been shown to accumulate phenolic compounds, with contents ranging from 5 to 15 mg gallic acid equivalents (GAE)/g dry biomass, depending on cultivation and extraction

methods [5]. Their antioxidant activity, often measured via DPPH, ABTS, or FRAP assays, correlates strongly with total phenolic content. For instance, *Desmodemus perforatus* acetone extracts demonstrated over 22% radical scavenging activity, while methanolic extracts inhibited MCF-7 breast cancer cells by up to 87% [67].

The anti-inflammatory potential of marine phenolics is mediated through the inhibition of enzymes such as COX-2 and iNOS, and suppression of pro-inflammatory transcription factors like NF- κ B. Studies have demonstrated that phenolic-rich extracts from *P. tricornutum* and *Tetraselmis* significantly downregulate cytokines, including IL-6 and TNF- α in vitro [68]. Furthermore, these extracts exert neuroprotective effects by attenuating microglial activation in models of neuroinflammation, suggesting potential for the prevention of neurodegenerative diseases [69].

Phenolic compounds have also shown anticancer potential, particularly through mechanisms involving oxidative stress regulation, apoptosis induction, and anti-proliferative activity. Phlorotannins, for example, modulate mitochondrial apoptosis pathways and interfere with cancer cell signalling. Extracts from *Acutodesmus obliquus* and *Desmodemus* sp. induced apoptosis in breast cancer cell lines, with methanolic fractions achieving over 80% inhibition at concentrations below 100 μ g/mL [67].

Beyond therapeutic potential, microalgal phenolics are increasingly used in cosmetic applications. Their antioxidant and anti-inflammatory actions help combat skin ageing, reduce UV-induced damage, and support barrier repair. This makes them suitable for incorporation into photoprotective and anti-ageing skincare formulations. In addition, they have been explored as active agents in formulations targeting acne and hyperpigmentation due to their antimicrobial and tyrosinase-inhibitory effects [70].

In the functional food sector, phenolic compounds offer natural antioxidant protection and contribute to cardiovascular and metabolic health. Studies have reported that dietary intake of microalgal phenolics may reduce oxidative stress markers and improve lipid profiles in animal models. Despite promising results, further research is needed to validate bioavailability, optimise extraction, and standardise dosage levels for human health claims [71].

In summary, phenolic compounds from marine microalgae offer a potent combination of antioxidant, anti-inflammatory, and anticancer properties, with high potential for use in nutraceuticals, pharmaceuticals, and cosmetics. Advances in cultivation, extraction, and encapsulation technologies will be pivotal in fully realising their biotechnological applications and commercial potential.

3.5. Phycobiliproteins

Phycobiliproteins are water-soluble, highly pigmented proteins found predominantly in cyanobacteria and red algae, where they serve as light-harvesting antennae. Among marine microalgae, *Spirulina* is the richest and most studied source, producing three key phycobiliproteins: C-phycocyanin (C-PC), allophycocyanin (APC), and phycoerythrin (PE). For example, *Spirulina* can yield up to 20% C-PC by dry weight, and *Porphyridium cruentum* accumulates PE levels of ~25–30%. These bioactive molecules not only contribute to photosynthesis but also exhibit diverse pharmacological and nutraceutical properties, making them attractive for applications in medicine, cosmetics, and functional foods [72].

C-PC can constitute up to 12–20% of the dry weight of *Spirulina* biomass, with yields reaching over 120 mg/g under optimised extraction and purification conditions [73]. This pigment is especially valued for its antioxidant properties, scavenging reactive oxygen species (ROS) like nitric oxide and peroxyl radicals, and thus mitigating oxidative damage. Purified C-PC has demonstrated EC₅₀ values for NO scavenging as low as 4.5 μ g/mL, comparable to vitamin C [73].

In anti-inflammatory and immunomodulatory applications, phycobiliproteins suppress the expression of COX-2, iNOS, and pro-inflammatory cytokines such as TNF- α and IL-6, while enhancing macrophage and NK cell activity. These effects have been validated in models of metabolic syndrome, nephrotoxicity, and neuroinflammation, where C-PC modulates apoptosis regulators (e.g., Bcl-2, Bax) and reduces caspase-3/9 activity [74].

In the cosmetics sector, C-PC and PE offer both bioactivity and pigmentation. Beyond their natural blue colour, popular in clean-label formulations, they provide UV-protection, anti-ageing, and skin-soothing effects. Studies demonstrate that C-PC downregulates oxidative and inflammatory mediators in keratinocytes, while stimulating fibroblast proliferation, enhancing collagen synthesis, and promoting skin regeneration [75]. Additionally, C-PC exhibits strong emulsifying and foaming properties, adding functional value in formulation development [76].

As a nutraceutical ingredient, phycobiliproteins are often marketed for immune enhancement, fatigue reduction, and systemic antioxidant support. Oral supplementation of Spirulina or isolated C-PC has shown benefits in improving lipid profiles, glucose metabolism, and even cognitive function in animal and human studies [77]. Additionally, C-PC-derived peptides show promise as DPP-IV inhibitors, suggesting potential as adjuncts in managing type 2 diabetes [78].

Extraction technologies for phycobiliproteins have also evolved. Ultrasonic-assisted, membrane, and green solvent extraction methods now yield higher purities and bioactivity retention. Supercritical CO₂ pre-treatment has been shown to enhance the purity and functionality of recovered C-PC [79].

In conclusion, phycobiliproteins, especially C-PC from Spirulina, represent highly valuable multifunctional biomolecules. Their broad spectrum of antioxidant, anti-inflammatory, immunomodulatory, cosmetic, and nutritional properties makes them prime candidates for widespread biotechnological use across health, food, and cosmetic industries.

3.6. Pigments (Carotenoids)

Marine microalgae are prolific producers of pigments, especially carotenoids, which include both carotenes and xanthophylls such as astaxanthin, fucoxanthin, lutein, zeaxanthin, and β -carotene. These pigments not only serve essential roles in photosynthesis and light protection but also exhibit potent antioxidant, anti-inflammatory, anticancer, and neuroprotective activities, which support their widespread use in pharmaceuticals, cosmetics, and functional foods [80,81].

Astaxanthin, primarily synthesised by *Haematococcus pluvialis*, reaching up to 3.8% of its dry weight, is considered one of the most potent natural antioxidants, being 10–100 times more effective than vitamin E in quenching free radicals. It has demonstrated significant neuroprotective, cardiovascular, and anti-ageing effects, while also modulating inflammatory cytokines such as IL-6 and TNF- α [82]. Emerging delivery technologies like nanoencapsulation are improving their bioavailability and efficacy in topical and oral formulations [83].

Fucoxanthin, derived from diatoms like *Phaeodactylum tricornutum* and brown algae, has gained attention for its anti-obesity, anticancer, and anti-diabetic properties. It promotes thermogenesis by inducing UCP1 in white adipose tissue and suppresses tumour growth via caspase-mediated apoptosis. In diabetic models, it improves glucose metabolism and reduces insulin resistance [84]. Fucoxanthin also contributes to neuroprotection by inhibiting pro-inflammatory mediators in microglial cells [85].

Lutein and zeaxanthin, abundant in *Chlorella zofingiensis* and *Scenedesmus* spp., are well known for protecting the retina from oxidative stress and harmful blue light. These

xanthophylls accumulate in the macula and are essential for preventing age-related macular degeneration. Microalgae-derived lutein has been shown to reach productivity levels 100–200× higher than marigold crops per square metre, offering a more sustainable industrial source [86].

β-Carotene, especially from *Dunaliella salina*, serves as a provitamin A and is widely used as a colourant and antioxidant in the food and cosmetic industries. Under stress conditions, *D. salina* can accumulate β-carotene up to 12.6% of dry weight, and its carotenoid profile also includes zeaxanthin, lutein, and cryptoxanthin [87].

New microalgal strains like *Bracteacoccus aggregatus* have been found to co-produce astaxanthin and β-carotene simultaneously, making them dual-source platforms for natural pigments. This strain can yield up to 48% astaxanthin and 13% β-carotene of total pigment mass, showcasing high industrial potential [88].

Applications of these pigments extend into cosmetic formulations where they serve not only as natural colourants but also as bioactive ingredients with UV-protective, skin-brightening, and anti-wrinkle effects. They help in reducing melanin synthesis, stimulating collagen production, and improving skin hydration. In functional foods, algal pigments are included in supplements, fortified beverages, and health snacks to enhance antioxidant intake and support vision, cardiovascular, and immune health [89,90].

In conclusion, pigments like astaxanthin, fucoxanthin, lutein, and β-carotene from marine microalgae represent high-value, multifunctional compounds with broad applications across health, nutrition, and skincare sectors. Their increasing market demand is driving innovation in biotechnological production systems, including genetic engineering, stress-induced cultivation, and photobioreactor optimisation, to enhance yields and cost-effectiveness [91].

3.7. Polysaccharides

Marine microalgae are a valuable source of bioactive polysaccharides, particularly sulphated polysaccharides and β-glucans, which have shown wide-ranging pharmacological effects. These include antiviral, antioxidant, anti-inflammatory, immunomodulatory, and metabolic regulatory activities that support their application in medicine, cosmetics, and functional foods [92].

In cyanobacteria like *Spirulina* and green microalgae such as *Chlorella pyrenoidosa*, β-glucans constitute up to 25–35% of total dry biomass, depending on strain and culture conditions. These β-glucans enhance host immunity by activating macrophages, NK cells, and dendritic cells through receptors such as dectin-1, triggering downstream NF-κB and MAPK pathways [93]. β-glucan supplementation (250–500 mg/day) has shown clinical efficacy in lowering blood lipids, enhancing innate immunity, and improving glycaemic control [94].

Sulphated polysaccharides, especially from diatoms (*Navicula*, *Cochlodinium*, *Sphacelaria*), exhibit strong antiviral activities against HSV, HIV, and influenza viruses. *Porphyridium* produces sulphated polysaccharides at levels exceeding 20% of biomass, which show potent antiviral and immunomodulatory effects. These compounds mimic heparan sulphate and block viral entry into host cells without cytotoxicity, with IC₅₀ values as low as 0.6 µg/mL against HSV-1 [95]. They also act as skin moisturisers and anti-inflammatories, forming protective biofilms and modulating inflammatory enzymes like COX-2, making them ideal ingredients in anti-ageing and soothing skincare formulations [96].

In functional foods, algal polysaccharides have been shown to influence lipid metabolism and gut microbiota. In an in vivo mouse study, daily intake of polysaccharides from *Spirulina* and *Chlorella* significantly reduced weight gain,

inflammation, and liver fat accumulation while improving microbial diversity and short-chain fatty acids production [97].

From an industrial perspective, techniques like ultrasound-assisted extraction, enzyme hydrolysis, and ethanol precipitation are optimised to retain activity and maximise yield. Additionally, chemical modifications such as sulphation and carboxymethylation enhance solubility and bioactivity, particularly for pharmaceutical formulations. Structural parameters, like degree of branching and sulphate content, play a key role in modulating the antiviral and immunomodulatory properties of these compounds [98,99].

In summary, microalgal polysaccharides, particularly β -glucans and sulphated polysaccharides, represent a versatile group of compounds with therapeutic applications spanning infectious diseases, metabolic syndrome, skin care, and gut health. Their functional diversity and safe profiles support growing interest in integrating them into nutraceuticals, dermatocosmetics, and pharmaceutical products.

3.8. Polyunsaturated Fatty Acids

Long-chain n-3 PUFAs, namely EPA (20:5n-3) and DHA (22:6n-3), are among the most therapeutically valuable metabolites derived from marine microalgae. These essential fatty acids support cardiovascular, neurological, immune, and metabolic health, with well-documented effects on reducing inflammation, lowering blood triglycerides, and protecting cognitive function [8,100].

Species such as *Nannochloropsis gaditana*, *Schizochytrium* sp., *Isochrysis galbana*, and *Phaeodactylum tricornutum* are widely cultivated for their lipid-rich biomass. For instance, EPA content in *Nannochloropsis* may reach 30% of total lipids, while *Schizochytrium* sp. can accumulate DHA levels of up to 45% under optimised conditions [101]. *Pavlova lutheri* accumulates up to 30–40% EPA and 7–12% DHA. Likewise, co-cultivation strategies combining DHA-rich species like *Isochrysis galbana* and EPA-rich species like *Nannochloropsis oceanica* have achieved balanced production with a DHA:EPA ratio of 1:1 and increased biomass yields [102].

EPA and DHA functionally integrate into cellular phospholipid bilayers and are enzymatically converted into specialised pro-resolving mediators (SPMs), such as resolvins, protectins, and maresins. These bioactive lipids actively modulate inflammatory signalling, reduce leukocyte infiltration, and facilitate the resolution phase of inflammation, thereby offering therapeutic potential for chronic inflammatory diseases [100,103]. Mechanistically, n-3 PUFAs reduce the availability of arachidonic acid in membrane lipids and suppress the production of pro-inflammatory eicosanoids, including prostaglandins and leukotrienes. In parallel, they inhibit key intracellular pathways such as nuclear factor-kappa B (NF- κ B) and mitogen-activated protein kinases, while promoting anti-inflammatory cytokines like interleukin-10 [104,105].

The cardioprotective role of EPA and DHA has been widely documented in clinical and epidemiological studies. Supplementation with these fatty acids is known to reduce plasma triglycerides, lower blood pressure, and improve endothelial function, while also decreasing the risk of thrombosis through anti-aggregatory effects on platelets. These effects collectively contribute to the reduction in cardiovascular events such as myocardial infarction and stroke [106,107].

In the nervous system, DHA plays a critical structural role, particularly in the grey matter of the brain and in retinal photoreceptor cells. It enhances synaptic plasticity, supports neuronal membrane stability, and protects against neuroinflammation and oxidative stress. Several preclinical and clinical studies suggest that sufficient DHA intake may delay the onset of cognitive decline and mitigate symptoms of neurodegenerative disorders, including Alzheimer's disease and Parkinson's disease [107]. In clinical

settings, EPA/DHA supplementation has demonstrated 25–30% reductions in serum triglycerides and improvements in cognitive function, visual acuity, and neuroprotection in ageing populations [108].

From a cosmetic perspective, PUFAs enhance skin elasticity, barrier repair, and UV protection by modulating eicosanoid profiles and preventing oxidative damage. This supports their use in dermocosmetics targeting inflammation, ageing, and dry skin [109].

Sustainable production is now possible even in tropical regions, thanks to heat-tolerant strains like *Tetraselmis* sp. DS3, which can maintain growth at 40 °C and produce up to 33% n-3 fatty acids of total lipids under nitrogen stress [110]. In colder environments, Antarctic strains like *Chaetoceros brevis* can yield EPA up to 174 µg L⁻¹ day⁻¹, while cold-water *Emiliania huxleyi* produces comparable DHA levels [111].

Beyond health benefits, PUFA-rich microalgae are increasingly incorporated into fortified beverages, capsules, infant formulas, and functional foods to meet rising consumer demand for plant-based, mercury-free alternatives to fish oil [112]. Extraction processes such as ultrasound-assisted enzymatic extraction using ethanol now enable efficient recovery while maintaining lipid bioactivity and environmental safety [101].

In conclusion, EPA and DHA from marine microalgae present a sustainable, scalable, and clinically validated alternative to fish-derived n-3s. Their benefits in cardiometabolic, neurological, dermatological, and nutritional health underscore their growing role in biopharmaceuticals, nutraceuticals, and functional food formulations.

In addition to EPA and DHA, microalgae also produce other biologically relevant PUFAs such as γ-linolenic acid (GLA; 18:3n-6). GLA is an n-6 fatty acid known for its anti-inflammatory and immunomodulatory properties, often acting through its conversion to dihomo-γ-linolenic acid, which competes with arachidonic acid for eicosanoid synthesis. Microalgae such as *Spirulina* and *Chlorella vulgaris* have demonstrated GLA contents ranging from 0.5% to 2.5% of total fatty acids, depending on cultivation conditions [113]. GLA has shown promise in managing inflammatory conditions like eczema, arthritis, and diabetic neuropathy, and its presence in microalgae enhances their value for both nutritional supplementation and dermatological applications [114].

3.9. Sterols (Phytosterols)

Phytosterols are bioactive isoprenoid compounds structurally similar to cholesterol, found in marine microalgae such as *Pavlova lutheri*, *Tetraselmis* sp., *Nannochloropsis* sp., and *Limnospira maxima*. The primary sterols include β-sitosterol, stigmasterol, campesterol, and fucosterol, with concentrations reaching up to 5.1% of dry biomass in *Pavlova lutheri* under optimised cultivation conditions [115]. Microalgae-derived phytosterols are gaining attention due to their broad health-promoting effects and sustainable production potential.

These compounds exhibit potent cholesterol-lowering effects by inhibiting dietary cholesterol absorption in the intestine through competition at the Niemann–Pick C1-like 1 (NPC1L1) transporter. Clinical studies support that consumption of 2 g per day of phytosterols can reduce low-density lipoprotein cholesterol by 8–10%, a significant impact in cardiovascular disease prevention [116,117].

Beyond lipid regulation, sterols exert anti-inflammatory, antioxidant, anticancer, neuroprotective, and hepatoprotective effects. *Limnospira maxima*, for instance, produces sterols that have been shown to suppress oxidative stress and inhibit proliferation in cancer cell lines such as MCF-7 and HepG2 [118]. Fucosterol, found in brown algae and microalgae, is particularly notable for its anti-diabetic, anti-Alzheimer's, and anti-obesity properties, acting through modulation of inflammatory cytokines and oxidative stress pathways [119].

In cosmetics, phytosterols support skin hydration, elasticity, and barrier function. They are incorporated into anti-ageing products where they stimulate collagen production, reduce UV-induced damage, and soothe inflammation [70]. Encapsulation technologies are also improving the bioavailability and stability of phytosterols in topical and oral formulations.

In the functional food industry, phytosterol-enriched microalgal products such as spreads, yoghurt drinks, and dietary supplements are already available or in development. These compounds align with vegan and clean-label trends, providing natural and plant-derived alternatives to synthetic or animal-based ingredients [120].

To enhance production yields, cultivation techniques involving nutrient stress, salinity adjustments, and UV-C exposure have been used successfully. For instance, *Pavlova lutheri* cultured under salinity stress exhibited a 2-fold increase in sterol content, reaching commercial viability [115]. Novel screening pipelines and biorefinery models are further enhancing microalgae's competitiveness in the phytosterol market [119].

In summary, marine microalgae represent a sustainable and multifunctional source of phytosterols with documented applications in cardiovascular health, metabolic modulation, cancer prevention, and skin care, underlining their growing relevance in pharmaceutical, cosmetic, and functional food sectors.

3.10. Vitamins

Marine microalgae are increasingly recognised as natural biofactories for essential vitamins, offering a sustainable and bioavailable alternative to synthetic supplements. They produce a wide range of both fat- and water-soluble vitamins, including β -carotene (provitamin A), tocopherols (vitamin E), phylloquinone (vitamin K1), cobalamin (vitamin B12), and various B-complex forms. These micronutrients are critical to metabolic regulation, immune balance, cognitive integrity, and skin health, which positions microalgae at the intersection of nutrition, medicine, and cosmetics [121].

β -Carotene is one of the most commercially valuable microalgal vitamins. *Dunaliella salina* accumulates it up to 10–14% of dry biomass, particularly under stress conditions like high light and salinity. β -Carotene acts as a precursor to vitamin A, supporting vision, immune defence, and epithelial integrity. In cosmetic formulations, it serves as an antioxidant that combats oxidative stress and UV damage, helping maintain skin elasticity and reducing photoaging [122].

Vitamin B12 (cobalamin) is typically absent in plant-based foods, making *Chlorella vulgaris* and *Nannochloropsis oceanica* valuable vegan sources. These species contain bioactive B12 at levels between 1.5 and 3.5 $\mu\text{g/g}$ dry weight, sufficient to meet daily nutritional requirements with modest consumption. B12 is vital for hematologic and neurologic function, and its deficiency is linked to anaemia, neuropathy, and cognitive decline, conditions prevalent among older adults and vegans [71].

Vitamin K1 (phylloquinone), known for its role in blood clotting and bone metabolism, is present in high concentrations in species like *Anabaena cylindrica* and *Scenedesmus obliquus*, with values exceeding 200 $\mu\text{g/g}$ dry weight, vastly surpassing common terrestrial vegetables. Vitamin K1 from microalgae is now being studied for insulin sensitivity modulation and arterial calcification prevention [121].

Vitamin E (α -tocopherol), a lipid-soluble antioxidant, plays a crucial role in protecting PUFA in cell membranes and regulating immune responses. Microalgae such as *Chlorella*, *Tetraselmis*, and *Isochrysis* synthesise tocopherols at levels of 10–80 mg/100 g dry biomass, contributing to their therapeutic potential in oxidative stress disorders and cardiovascular health [123].

In the cosmetic sector, vitamins A, C, and E derived from microalgae are included in formulations targeting wrinkle reduction, skin brightening, and UV defence. Their ability

to neutralise reactive oxygen species and promote collagen synthesis enhances the skin barrier and slows ageing processes [70].

In functional foods, microalgae are used as natural vitamin fortifiers in beverages, bars, and dairy analogues. Fortified food products with *Spirulina* or *Chlorella* are widely available, offering a full spectrum of B-complex vitamins and antioxidant activity. These products appeal to consumers seeking clean-label, plant-based nutrition [124].

From an industrial perspective, microalgal vitamin production offers advantages including low land use, renewability, and control over quality and yield through biotechnological and environmental modulation. Techniques such as two-phase photobioreactor cultivation, UV and salinity stress, and strain engineering have successfully increased vitamin yields, especially β -carotene and tocopherols [125].

In summary, marine microalgae serve as eco-friendly, potent sources of essential vitamins, enabling sustainable innovation in functional foods, dietary supplements, and cosmetics. Ongoing research continues to enhance their bioavailability, yield, and industrial scalability, strengthening their role in preventive nutrition and health.

Table 1 provides a comprehensive overview of the principal classes of bioactive compounds synthesised by marine microalgae, encompassing a diverse array of chemical groups such as carotenoids, phycobiliproteins, polysaccharides, peptides, PUFAs, sterols, phenolics, MAAs, alkaloids, and vitamins. For each compound class, the table highlights representative bioactive molecules, their known microalgal sources, and documented biological activities, including antioxidant, anti-inflammatory, immunomodulatory, antimicrobial, anticancer, and metabolic effects. It also outlines the relevance of these compounds in the context of human health, cosmetics, and functional foods, offering a consolidated view of microalgae's potential as a sustainable and multifunctional platform for bioactive production.

Table 1. Summary of major classes of bioactive compounds produced by marine microalgae, including major molecules, producing species, key biological activities, and application relevance across the health, cosmetics, and functional food sectors.

Compound Class	Major Compounds	Microalga Sources	Biological Activities and Potential Applications	References
Alkaloids	Saxitoxin, Neosaxitoxin, Dolastatin-10, Curacin A, Lyngbyatoxin A	Dinoflagellates (<i>Alexandrium</i> , <i>Gymnodinium</i> , <i>Pyrodinium</i>), cyanobacteria (<i>Lyngbya</i> , <i>Spirulina</i> , <i>Trichodesmium</i>)	Neuroprotection via Nav channel blockade (analgesia); anticancer through tubulin disruption and apoptosis; antioxidant and antimicrobial activity relevant to cosmetics; possible immune modulation in functional foods	[42–46]
Mycosporine-like Amino Acids	Shinorine, Porphyrin-334, Mycosporine-glycine, Mycosporine-2-glycine, Palythine	Cyanobacteria, <i>Nannochloropsis salina</i> , <i>Porphyridium</i> sp.	Photoprotective via UV absorption; strong antioxidant and anti-inflammatory effects; supports skin repair and collagen maintenance; inhibits NF- κ B and COX-2; promising for anti-ageing cosmetics, oral photoprotection, and inflammation-related food supplements	[48–53]
Peptides (Bioactive Peptides)	Antimicrobial peptides, ACE-inhibitory peptides, Dolastatin-10, Apratoxin A, Cyanovirin-N	<i>Chlorella vulgaris</i> , <i>Spirulina</i> , <i>Bellerochea malleus</i> , marine cyanobacteria	Antihypertensive (ACE inhibition), antioxidant, anticancer (cell cycle arrest, apoptosis), anti-inflammatory, antimicrobial; skin regeneration and collagen support in cosmetics; immune modulation and natural preservation in functional foods and personal care products	[54,59–64]
Phenolic Compounds	Gallic acid, Quercetin, Caffeic acid, Chlorogenic acid, Phlorotannins	<i>Nannochloropsis</i> sp., <i>Tetraselmis</i> sp., <i>Phaeodactylum</i>	Strong antioxidant, anti-inflammatory, anticancer, and antimicrobial properties; therapeutic uses include oxidative stress reduction, inflammation control, and cancer cell	[5,66–71]

		<i>tricornutum</i> , <i>Desmodesmus</i> sp.	inhibition; cosmetic applications in anti-ageing and photoprotective skincare; functional food relevance as natural antioxidants for cardiovascular and metabolic health	
Phycobiliproteins	C-Phycocyanin, Allophycocyanin, Phycoerythrin	Spirulina, cyanobacteria	Antioxidant (ROS scavenging), anti-inflammatory (COX-2, iNOS inhibition), immunostimulatory (NK cell activity, cytokine regulation), anti-apoptotic (Bcl-2/Bax modulation), neuroprotection, skin regeneration, UV protection; applications in cosmetics (anti-ageing, photoprotection), functional foods, and metabolic health (e.g., DPP-IV inhibition)	[72,74,76,77,79]
Pigments (Carotenoids)	Astaxanthin, Fucoxanthin, β -Carotene, Lutein, Zeaxanthin	<i>Haematococcus pluvialis</i> , <i>Phaeodactylum tricornutum</i> , <i>Dunaliella salina</i> , <i>Chlorella zofingiensis</i> , <i>Scenedesmus</i> spp., <i>Bracteacoccus aggregatus</i>	Potent antioxidant, anti-inflammatory, anticancer, and neuroprotective properties; applications in medicine for cardiovascular and cognitive support; in cosmetics for UV protection, anti-wrinkle, collagen boosting, and skin-brightening effects; in functional foods for visual, immune, and heart health	[80,82,86,88–91]
Polysaccharides	Sulphated polysaccharides, β -glucans, Calcium Spirulan, Naviculan	<i>Spirulina</i> sp., <i>Chlorella vulgaris</i> , <i>Navicula</i> , <i>Cochlodinium</i>	Immunomodulatory and antiviral activities (e.g., inhibition of HSV, HIV, influenza); antioxidant and anti-inflammatory properties; β -glucans activate innate immunity via dectin-1 pathway; improvement of metabolic markers (lipids, glucose); modulation of gut microbiota; cosmetic effects via skin moisturization, anti-ageing, and anti-inflammatory action; used in functional foods for metabolic health and immune support	[92–97,99]
Polyunsaturated Fatty Acids	Eicosapentaenoic acid (EPA), Docosahexaenoic acid (DHA), γ -Linolenic Acid (GLA)	<i>Pavlova lutheri</i> , <i>Nannochloropsis</i> sp., <i>Isochrysis galbana</i> , <i>Phaeodactylum tricornutum</i> , <i>Schizochytrium</i>	Clinically significant anti-inflammatory and cardioprotective effects; reduction in plasma triglycerides by 25–30%; enhancement of cognitive function, visual acuity, and neuronal health in ageing populations; incorporation into neuronal membranes enhances synaptic plasticity; used in cardiovascular, neurological, and dermatological health; formulated into fortified foods, nutraceuticals, and dermocosmetics	[8,9,14,100,105,114]
Sterols (Phytosterols)	β -Sitosterol, Stigmasterol, Campesterol, Fucosterol	<i>Pavlova lutheri</i> , <i>Tetraselmis</i> sp., <i>Nannochloropsis</i> sp., <i>Limnospira maxima</i>	Cholesterol-lowering by inhibiting intestinal absorption; cardiovascular protection through LDL reduction (~8–10% at 2 g/day); anti-inflammatory and antioxidant activity; anticancer effects via apoptosis and cell cycle arrest; neuroprotective and hepatoprotective roles; cosmetic use for skin hydration, elasticity, collagen stimulation, and UV protection; present in fortified foods, skincare, and supplements	[5,11,21,120]
Vitamins	β -Carotene (Provitamin A), Vitamin B12, Vitamin E, Vitamin K1, B-complex	<i>Dunaliella salina</i> , <i>Chlorella</i> sp., <i>Nannochloropsis</i> sp., <i>Anabaena cylindrica</i> , <i>Scenedesmus obliquus</i> , <i>Tetraselmis</i> sp.	Antioxidant, anti-inflammatory, and immunomodulatory effects; prevention of vitamin deficiencies; support of vision, skin health, neurological and hematologic function; cosmetic applications include anti-ageing, UV protection, and skin brightening; functional food use as clean-label vitamin fortifiers and immune boosters	[71,121–123,125]

4. Challenges and Opportunities in Marine Biotechnology

The global market for microalgae-derived bioactive compounds is experiencing rapid growth, driven by rising demand for sustainable, functional ingredients in the health, cosmetic, and food sectors. Recent reports estimate that the global microalgae market surpassed USD 1.5 billion in 2023 and is projected to reach USD 2.9 billion by 2030, growing at a compound annual growth rate of approximately 9–10% [126]. Key growth segments include astaxanthin, phycocyanin, PUFAs (especially DHA and EPA), and polysaccharides, with applications expanding across dietary supplements, fortified foods, anti-ageing skincare, and pharmaceuticals. *Spirulina* [127] and *Chlorella* [128] dominate current commercial production, while species like *Haematococcus*, *Nannochloropsis*, and *Porphyridium* are gaining traction for their high-value pigments and therapeutic polysaccharides. For instance, *Haematococcus pluvialis* commands a premium market value due to its capacity to produce astaxanthin at concentrations up to 3.8% of dry biomass, while the global demand for *Spirulina*-derived phycocyanin as a natural colourant is increasing, with applications in beverages, confectionery, and personal care. The increasing focus on clean-label products, plant-based nutrition, and the blue bioeconomy is expected to further accelerate investment and innovation in this space [126].

Marine biotechnology is rapidly emerging as a key driver in the sustainable utilisation of marine microalgae for the production of high-value bioactive compounds. However, the commercial translation of these bioproducts into scalable applications for health, cosmetics, and functional foods remains constrained by several technical, economic, and regulatory challenges. Concurrently, this field presents unique opportunities driven by advances in synthetic biology, systems biology, bioprocess optimisation, and policy support for the blue bioeconomy [129–131].

4.1. Strain Optimisation and Genetic Engineering

Strain selection and improvement are central to advancing marine microalgal biotechnology. Naturally occurring strains show variability in growth and metabolite profiles, making standardisation difficult. For instance, lipid content among microalgal strains can range from 20% to over 60% of dry cell weight, while EPA levels in *Nannochloropsis* species vary between 2% and 10% of total fatty acids, depending on the strain and cultivation conditions. These fluctuations affect consistency in downstream processing and final product quality. Standardisation efforts, such as ISO 19673:2019, which outlines protocols for the characterisation of microalgal biomass, are being increasingly adopted to ensure quality control and reproducibility across production systems [132].

Genetic engineering and adaptive evolution are being used to enhance traits like lipid production or stress tolerance. Importantly, engineered *Pavlova lutheri* strains overexpressing $\Delta 5$ -desaturase genes achieved a 30–40% increase in EPA content under optimised conditions, compared to their wild-type counterparts. Similarly, *Nannochloropsis gaditana* strains modified to overexpress elongase genes have shown DHA yield improvements exceeding 20%, demonstrating the impact of targeted metabolic interventions. While transformation efficiencies and GMO-related regulatory barriers remain a challenge, these case studies underscore the promise of trait enhancement through synthetic biology [132].

From an economic standpoint, the high cost of microalgal biomass production remains a limiting factor, especially when compared to terrestrial plants or synthetic alternatives. However, co-product strategies, circular economy approaches (e.g., use of wastewater or flue gas as inputs), and government subsidies are helping to offset production costs. For example, subsidy programmes under the EU Horizon 2020 Blue Bioeconomy initiative and USDA-funded algae biofuel grants have supported pilot- and commercial-scale algae production by lowering capital and operational expenses.

Furthermore, typical production costs range from approximately \$2–5 per kg biomass in open pond systems and \$5–15 per kg biomass in photobioreactors, depending on technology, scale, and location [133–135].

4.2. Cultivation Systems and Environmental Control

Another bottleneck lies in cultivation systems. Open ponds are cost-effective but susceptible to contamination and environmental fluctuations, whereas closed photobioreactors offer greater control but at higher capital and operational costs. Hybrid systems are being explored to combine the advantages of both. Furthermore, optimising light intensity, nutrient composition, CO₂ levels, and mixing regimes is critical to achieving high biomass and metabolite productivity. Innovations such as LED-regulated light cycles, vertical photobioreactors, and autonomous monitoring systems using AI-based feedback loops are showing promise [40].

4.3. AI and Real-Time Process Optimisation

AI and machine learning (ML) are now emerging as transformative tools for real-time optimisation in photobioreactors. ML algorithms like Long Short-Term Memory (LSTM) networks and Support Vector Machines (SVM) are used to model complex growth dynamics by analysing historical and real-time environmental data. For instance, Yeh et al. [29] demonstrated that LSTM models significantly outperformed traditional Monod models in predicting biomass under outdoor conditions. AI systems are also employed to dynamically modulate light cycles, nutrient delivery, and CO₂ injection based on feedback loops, thereby enhancing both biomass productivity and metabolite yield. Recent developments integrate smart bio-panels and vision-based monitoring systems, enabling precise control and prediction of growth stages, as shown in works by Karade et al. [136] and Concepcion et al. [137].

4.4. Downstream Processing and Biorefinery Models

Downstream processing presents another significant challenge in the commercialisation of microalgae-derived compounds. The extraction and purification of target molecules such as peptides, polysaccharides, and carotenoids often rely on energy-intensive, solvent-based procedures that can compromise bioactivity and reduce overall yields. To address these limitations, several emerging technologies are being explored. Supercritical CO₂ extraction offers high selectivity and produces solvent-free products, making it particularly suitable for high-value bioactives like carotenoids and fatty acids. However, this method is constrained by high capital investment and energy demands, which limit its scalability and render it more appropriate for premium, small-batch applications. In contrast, membrane filtration presents a more scalable and energy-efficient alternative, enabling continuous processing and selective separation based on molecular size or charge. Despite its advantages, this technique can be hampered by membrane fouling, lower specificity for certain compounds, and significant maintenance requirements when processing complex microalgal matrices. To improve the economic viability of microalgae bioproducts, biorefinery model approaches, where multiple compounds are sequentially recovered from a single biomass stream, are increasingly being adopted. These models enhance resource efficiency and profitability, and their success will depend on continued process optimisation and comprehensive techno-economic evaluations. Recent studies have demonstrated the valorisation of residual biomass after lipid extraction for biofuel production or bioplastics, aligning with circular economy principles. For example, defatted *Nannochloropsis* biomass has been successfully converted into bioethanol or used as feedstock for thermochemical conversion processes.

Such multiproduct strategies not only increase resource efficiency but also reduce waste and improve overall process sustainability [23].

4.5. Regulatory and Economic Challenges

Regulatory frameworks remain a major obstacle to commercialisation. In many countries, microalgal products are classified as novel foods or new cosmetic ingredients, requiring rigorous safety and efficacy evaluations. The lack of harmonised international standards for labelling, quality control, and environmental safety poses barriers for global trade. One critical regulatory layer is the Nagoya Protocol and associated Access and Benefit-Sharing (ABS) frameworks. These can delay commercialisation by requiring time-consuming legal negotiations to clarify the origin and use of genetic resources, which can vary by country. For example, the commercialisation of *Porphyridium*-derived polysaccharides in the EU was delayed due to unresolved ABS documentation and country-of-origin compliance. Such regulatory inconsistencies contrast with more flexible ABS approaches in countries like the United States and Australia, where frameworks are either non-binding or interpreted more leniently. This regional variability adds uncertainty for product developers and may deter international investment [17].

From an economic standpoint, the high cost of microalgal biomass production remains a limiting factor, especially when compared to terrestrial plants or synthetic alternatives. However, co-product strategies, government subsidies, and circular economy approaches (e.g., use of wastewater or flue gas as inputs) are helping to offset production costs. For example, cultivating microalgae on nutrient-rich industrial effluents can simultaneously produce biomass and mitigate environmental pollution, offering dual benefits [36].

4.6. Omics and Synthetic Biology Integration

Opportunities in marine biotechnology are expanding with the integration of omics technologies. Genomic, transcriptomic, proteomic, and metabolomic analyses enable a systems-level understanding of metabolic pathways and stress responses, facilitating the discovery and engineering of novel bioactives. Predictive modelling based on omics data is now being used to design synthetic metabolic circuits for the de novo synthesis of pharmaceuticals, antioxidants, and immunomodulators. Importantly, several case studies have shown that omics-guided engineering can lead to 2–3-fold increases in compound yields under optimised culture conditions, marking a substantial advance for strain selection and bioproduction precision [33].

4.7. Co-Cultivation Strategies and Ecological Engineering

The use of co-cultivation strategies, growing microalgae with bacteria or other microalgae, offers promising opportunities to enhance productivity and resilience. These consortia promote mutualistic interactions that optimise nutrient recycling, inhibit contaminants, and stimulate novel metabolite synthesis. Research in this area is advancing rapidly, with pilot-scale systems demonstrating increased yields and robustness, pointing to their potential for commercial scalability [38].

4.8. Sustainability and Alignment with Global Goals

Marine biotechnology is also aligning with global sustainability goals. Microalgae use less water and land than terrestrial crops, sequester CO₂ during photosynthesis, and offer bio-based alternatives to petroleum-derived products. Their applications in bioplastics, biofuels, and carbon capture underscore their role in the transition to a circular and green economy. Importantly, microalgae-derived technologies support several United Nations Sustainable Development Goals (SDGs), including SDG 2 (Zero Hunger)

through protein-rich biomass for food and feed, SDG 3 (Good Health and Well-being) via nutraceuticals and therapeutic compounds, SDG 6 (Clean Water and Sanitation) through integration with wastewater treatment, SDG 12 (Responsible Consumption and Production) via biorefinery models and resource recovery, SDG 13 (Climate Action) by capturing CO₂ and offsetting emissions, and SDG 14 (Life Below Water) by offering marine-friendly production systems. These connections highlight the potential of marine microalgae to contribute to sustainable development at the environmental, economic, and social levels [15].

Moreover, the adoption of responsible research frameworks is gaining traction in microalgal biotechnology. For example, Life Cycle Assessment (LCA) is being employed to quantify the environmental impacts of different cultivation and extraction strategies across their entire production chain. In parallel, Techno-Economic Analysis (TEA) is used to evaluate the financial feasibility and scalability of these innovations. As AI becomes increasingly embedded in bioprocess optimisation, there is growing emphasis on ethical AI principles, such as transparency in algorithm design, data privacy, and equitable access to digital tools. These governance models are critical for ensuring that technological advancements align with sustainability, equity, and long-term societal benefit [15].

In conclusion, while marine biotechnology faces big challenges in strain engineering, cultivation optimisation, downstream processing, and regulatory compliance, it also presents transformative opportunities for sustainable bioproduct development. Strategic investment in research, infrastructure, and international collaboration will be essential to unlock the full potential of marine microalgae in addressing pressing global needs across health, food, energy, and environmental sectors [16,129].

5. Conclusions and Future Perspectives

Marine microalgae represent a sustainable, versatile, and underexploited reservoir of bioactive compounds with wide-ranging applications across the health, cosmetic, and functional food sectors. This review has highlighted the structural diversity, biological activities, and therapeutic relevance of major compound classes, including PUFAs, pigments, peptides, sterols, polysaccharides, phenolics, phycobiliproteins, vitamins, mycosporine-like amino acids, and alkaloids, underscoring their multifunctionality and market potential.

Bioprospecting studies and advances in omics technologies have significantly expanded our understanding of microalgal metabolism, revealing novel compounds with antioxidant, anti-inflammatory, anticancer, antimicrobial, photoprotective, and neuroprotective properties. Many of these compounds exhibit equal or superior bioactivity compared to their synthetic or terrestrial counterparts and fulfil increasing consumer demand for clean-label, plant-based, and functional products.

However, realising the full biotechnological potential of marine microalgae still requires overcoming key challenges. These include optimising cultivation systems, improving biomass and metabolite yields, reducing downstream processing costs, and navigating complex regulatory landscapes. Additionally, standardisation of bioactive content, efficacy validation, and scalability remain bottlenecks for widespread industrial adoption.

Future research should prioritise multidisciplinary strategies that combine systems biology, synthetic biology, and bioprocess engineering to enhance compound production and enable precision cultivation. Co-cultivation, stress modulation, metabolic engineering, and biorefinery models are emerging as promising avenues to maximise biomass valorisation while reducing environmental impact.

Strategic investments in infrastructure, international collaboration, and policy support, particularly through frameworks aligned with the blue bioeconomy, will be

critical to facilitate the translation of research into commercial innovation. Furthermore, public engagement and safety assessments are essential to build consumer trust in microalgae-derived products.

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