Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Food Science

Review

The impact of microalgae-derived bioactive compounds on gut microbiota modulation

Yixuan Liu, Min Wang, Juan M Castagnini, Francisco J Barba and Andrea Asensio-Grau

Microalgae are emerging as a valuable source of bioactive compounds with significant potential to modulate gut microbiota and improve human health. This review explores the roles of microalgal-derived polysaccharides, peptides, polyunsaturated fatty acids, polyphenols, pigments, and micronutrients in shaping intestinal microbial composition and function. These compounds promote beneficial bacteria, inhibit pathogens, enhance immune responses, and regulate key metabolic pathways through the production of short-chain fatty acids and other microbial metabolites. Moreover, microalgae exhibit antioxidant, anti-inflammatory, and antitumor properties that may support the prevention of chronic diseases. However, challenges such as bioavailability, safety, individual microbiota variability, and industrial scalability must be addressed. Despite these limitations, microalgae hold promise as sustainable, multifunctional ingredients for developing functional foods and therapeutic interventions. Future research could focus on clinical validation, optimized extraction methods, and personalized nutrition approaches to fully harness the health benefits of microalgae-derived bioactive compounds in modulating the gut microbiota.

Address
Research Group in Innovative Technologies for Sustainable Food (ALISOST), Preventive Medicine and Public Health, Food Science, Toxicology and Forensic Medicine Department, Faculty of Pharmacy and Food Science, Universitat de València, Avda. Vicent Andrés Estellés, s/n, 46100 Burjassot, Spain

Corresponding author: Barba, Francisco J (francisco.barba@uv.es)

Current Opinion in Food Science 2025, **66**:101365

This review comes from a themed issue on **Functional Foods & Nutrition**

Edited by **Gerardo Alvarez Rivera**

Available online 24 October 2025

https://doi.org/10.1016/j.cofs.2025.101365

Introduction

With limited water resources, decreasing arable land, and an ever-growing global population, identifying safe and sustainable food sources to meet increasing demand is one of the 21st century's most urgent challenges [1]. As photosynthetic organisms, microalgae, often seen as 'crops of the future,' can thrive in diverse environments, from aquatic to terrestrial, including wastelands and nonarable land, and they are resilient to climate change [2]. Using light-harvesting, the carbon dioxide (CO_2) can be converted into various compounds, including proteins, lipids, vitamins, antioxidants, and pigments, with health-promoting effects that can be utilized in the development of functional foods [3,4]. Despite these advantages, there are safety considerations, including the potential bioaccumulation of microcystin, toxic proteins, and allergens. Therefore, comprehensive risk assessments are necessary for new microalgae proteins to ensure their safety, in line with EC Regulation 258/97 and EU Recommendation 97/618 EC [5].

Types of microalgae include *Chlorophyta* (green algae), *Bacillariophyta* (diatoms), *Ochrophyta* (Ochrophytes), *Euglenophyta* (Euglenoids), *Cryptophyta* (Cryptomonads), *Haptophyta* (Haptophytes), *Dinophyta* (Dinoflagellates), *Rhodophyta* (red algae), and *Cyanobacteria* (blue-green algae) [6]. Moreover, among the large number of available microalgal species, *Spirulina*, *Chlorella*, and *Phaeodactylum tricornutum* (*P. tricornutum*) have been intensively studied [7]. Besides, the *Spirulina*, due to its characteristics and growth conditions, is estimated to be the most commercialized species in the bioresource market, with an estimated to be valued 2025 global market value of USD 522.6 million and forecast to reach USD 884.6 million by 2032 [8]. Microalgae, abundant in unsaturated fatty acids, proteins, carbohydrates, pigments, and other bioactive compounds, present significant potential as a sustainable food source. Microalgae have the potential to produce various bioactive compounds, including polysaccharides, bioactive peptides, lipids (n-3 long-chain polyunsaturated fatty acids (PUFAs)), vitamins, and pigments (β-carotene, astaxanthin, phycocyanin (PC), and fucoxanthin), with health-promoting effects that can be utilized in the development of functional foods [3,4]. Normally, microalgae bioactive compounds will correspond with some potential health benefits, including enhancing oral, cardiovascular, brain, gastrointestinal, and immune functions, and may help prevent non-communicable diseases like diabetes,

hypercholesterolemia, and obesity [4]. The sustainable development and utilization of microalgae resources might be critical for addressing humanity's energy and nutritional needs.

The gut microbiota is essential to overall health by aiding nutrient metabolism, immune function, and disease prevention, but its disruption can cause inflammation and harmful metabolic effects. [9]. For instance, primary factors like genetics and insulin resistance, along with secondary factors such as viruses, drugs, and poor lifestyle, can all contribute to nonalcoholic fatty liver disease by affecting the gut–liver axis [9]. In this sense, precision nutrition involves customizing the intake of micronutrients for human needs, and microalgae can be applied as a promising dietary strategy for managing gut dysbiosis and its related complications [10]. Dysbiosis of the gut microbiota has been implicated in the development of type 2 diabetes, obesity, nonalcoholic liver disease, and other cardiometabolic disorders [11]. Additionally, alterations in gut microbiota are associated with the pathogenesis of various conditions, including cancer, arthritis, autism, depression, anxiety, sleep disorders, HIV, hypertension, and gout [11]. The complex, multilayered cell wall of microalgae, composed of polysaccharides, proteins, lipids, and inorganic salts, poses a significant barrier that must be efficiently, safely, and environmentally breached to extract its high-value components [12]. Most of the bioactive compounds in microalgae are involved in digestive behaviors in the oral-gastrointestinal-tract, and interact with gut microbiota in the colon [12]. In addition, this property of microalgae enables it to resist the digestive process of the intestine and effectively interact with the gut microbiota.

The objective of this review is to comprehensively address the microalgae-derived bioactive compounds and modulation in gut microbiota. Moreover, all the literature referenced refers to microalgae or microalgae-derived bioactive compounds. Particular focus will be given to the *in vitro* or *in vivo* findings to better motivate and understand this review.

Microalgal-derived bioactive compounds and modulation in gut microbiota

Among the effects on the health of gut microbiota, previous research identified the role in fatigue and antifatigue [13]. An increase in pathogenic bacteria and a decrease in beneficial bacteria coexist when fatigue is present in both rodents and humans, and changes in gut microbiota were reported after intervention with antifatigue foods [13]. Microalgae are recognized as a promising protein source and are rich in bioactive compounds, polysaccharides, bioactive peptides, lipids, polyphenols, pigments, and minerals, with potential human health benefits [4]. Disturbance of the gut microbiota will lead to the occurrence of diseases, and polysaccharides as prebiotics can improve the disease by regulating the composition of gut microbiota [14]. As for the importance of microalgae bioactive compounds of gut microbiota modulation in health benefits, more details can be seen in Figure 1. Furthermore, the chemical composition of microalgal biomass varies significantly across species and is influenced by growth phase, as well as biotic and abiotic factors such as light, temperature, nutrient availability, and salinity [4].

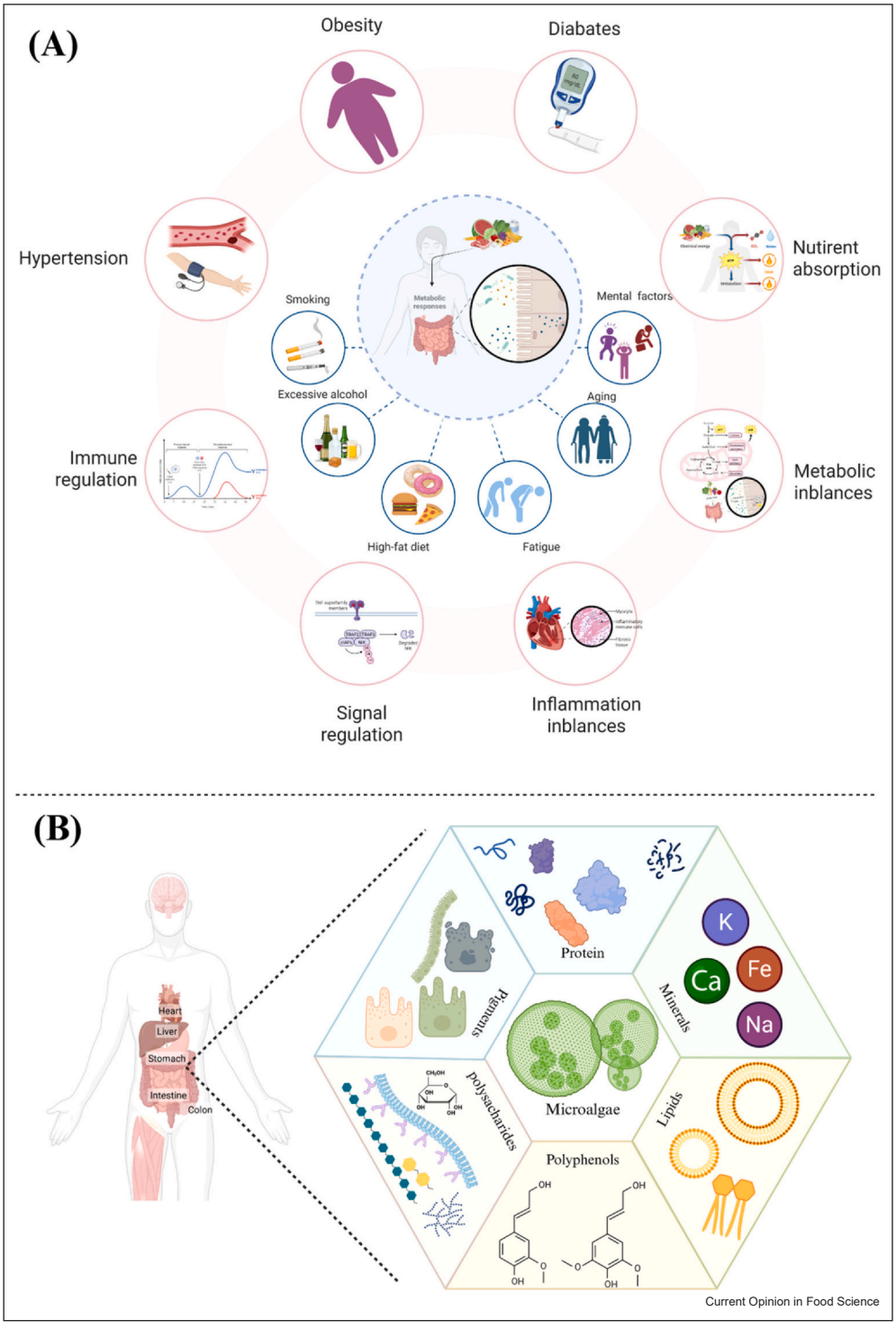
Polysaccharides of microalgae on gut microbiota modulation

Microalgae are rich in carbohydrates, with polysaccharides forming a major component of their cellular structure. These polysaccharides of microalgae fall into three groups [15]: structural cell wall polysaccharides (β-glucans, β-mannans, α-rhamnans, β-galactofuranans, and various heteropolysaccharides), reserve polysaccharides (branched starches and β-glucans), and extracellular polysaccharides (EPS). Microalgal polysaccharides show various biological activities, including immunomodulatory, antitumor, antibacterial, and antioxidant, which can be used as health supplements or can be fermented to produce biofuels [15].

Previous research has comprehensively summarized the interactions between polysaccharides and gut microbiota, highlighting three key aspects [16]: 1) the modulation of gut microbiota composition; 2) the metabolism of polysaccharides into short-chain fatty acids (SCFAs), and 3) the regulation of gut microbiota metabolites, including trimethylamine, tryptophan (Trp), and lipopolysaccharides. The microbiota shares a dynamic relationship with its host, serving vital roles in nutrient metabolism and immune function, and it interacts closely with polysaccharides, which serve as a vital energy source for intestinal microorganisms [14]. Although the host cannot digest polysaccharides, gut microbes break them down, fostering microbial growth and contributing to overall gut health [14]. Microalgae-derived oligosaccharides and phenolics increase the abundance of beneficial gut bacteria, with *Spirulina platensis* and *Desmodesmus maximus* exhibiting the strongest prebiotic effects [17]. Besides, previous research has investigated the polysaccharide obtained from *Spirulina* (PSP) and its effects on the metabolic and gut microbiota of lung cancer in mice [18], revealing that PSP increased the abundance of *Lactobacillus*, *Allobaculum*, *Alloprevotella*, and *Olsenella* and decreased *Bacteroides* and *Acinetobacter*, suggesting that PSP can be applied to against lung cancer diseases. Moreover, the indigestible carbohydrates, including oligosaccharides, fibers, and lactose, could be converted into SCFAs by bacteria residing in the large intestine [11].

As a vital component of the human body, the intestinal microbiota plays a crucial role in maintaining overall

Figure 1



Importance of gut microbiota modulation in health benefits **(a)**. The regulation of the human gut microbiota is influenced by factors such as smoking, excessive alcohol, HFD, fatigue, aging, and mental factors. Additionally, the balance of gut microbiota modulation plays a crucial role in various aspects of human health, including obesity, hypertension, immune regulation, signal regulation, inflammation, metabolic, nutrient absorption, and diabetes. Modulation of gut microbiota by main nutrients and bioactive compounds in microalgae **(b)**. The main nutrients and bioactive compounds in microalgae, such as proteins, minerals, lipids, polyphenols, polysaccharides, and pigments, hold significant potential for modulating human gut microbiota. (Created in Bio Render.com).

health. Investigating the impact of microalgae-derived bioactive compounds on regulating intestinal probiotics could have significant and far-reaching implications.

Bioactive peptides of microalgae on gut microbiota modulation

Microalgae are a promising source of protein, offering a nutrient-dense and consistent source. Microalgae proteins possess functional properties, including solubility, emulsification, foaming, gelling, and natural pigmentation, all of which are produced without competing for arable land [19]. Microalgae-derived proteins exhibit diverse bioactive properties, as evidenced by their demonstrated anti-inflammatory, anticancer, antidiabetic, antibacterial, immune-boosting, neuroprotective, hepatoprotective, and antioxidative effects [20]. Studies indicate that large molecular weight peptides from microalgae are initially broken down in the stomach by pepsin. These larger molecular weight peptides are further broken down in the small intestine by enzymes such as trypsin, chymotrypsin, elastase, carboxypeptidase, and other pancreatic enzymes, ultimately yielding free amino acids (AAs) [12].

One notable AA is Trp, an essential component obtained from dietary protein, which serves as a precursor for various metabolites produced by tissue cells and gut microbiota [21]. These metabolites, including SCFAs, Trp, and bile acid metabolites, play crucial roles in maintaining intestinal barrier integrity, promoting gut homeostasis, and regulating immune function. They also influence genetic, epigenetic, and metabolic pathways in both immunosuppressive and proinflammatory immune cells [22]. Furthermore, dietary protein bioactive peptides can enhance intestinal function by improving the diversity and composition of the gut microbiota, which may help reduce inflammation, oxidative stress, and promote overall host metabolism.

Fatty acids of microalgae on gut microbiota modulation

PUFAs produced by microalgae are natural, high-purity, high-quality fatty acids derived from a sustainable, vegetarian source and offer superior sensory qualities compared to animal-based lipids [23]. PUFAs are characterized by multiple double bonds, being in microalgae mainly omega-3 (C20:5 eicosapentaenoic acid (EPA) and C22:6 docosahexaenoic acid (DHA)) are found in microorganisms, plants, and aquatic animals, and when consumed, algal PUFAs can enhance animals' fatty acid profiles (omega-6/omega-3 ratio) and immune function [24]. Recent studies have highlighted promising algal strains for producing PUFAs, indicating that microalgae could emerge as an innovative source of PUFAs for both human and animal nutrition [25].

Furthermore, microalgae produce a higher amount of omega-3 in contrast to animal-based oils [26]. Specifically, *Isochrysis galbana* and *Phaeodactylum tricornutum* yield EPA at levels more than twice as high as those found in traditional sources, while *Crythecodinium cohnii* produces nearly six times the amount of DHA compared to cod liver oil [26]. Effects of *Spirulina platensis* 55% ethanol extract (SPL55) enriched with PUFAs have the potential to improve serum and hepatic lipid metabolic disorders in rats with hyperlipidemia and can regulate the mRNA and protein involved in lipid metabolism in high-fat diet (HFD)-induced hyperlipidemic rats [27]. Disruptions in gut microbiota can impair lipid and carbohydrate metabolism by negatively affecting liver function, thereby altering enterohepatic circulation and increasing gut permeability. This disruption can alter metabolic pathways such as gluconeogenesis and beta-oxidation, compromising the liver's ability to regulate blood glucose and lipid levels [28].

Polyphenols of microalgae on gut microbiota modulation

Dietary polyphenols play an irreplaceable role in improving and regulating gut microbiota [9]. Microalgae can be characterized as a source of polyphenols, including catechols, gallic acid, tannins, terpenoids, and flavonoids [29]. The development and application of microalgae polyphenols are an emerging trend in functional foods or human health promotion that can be used to prevent diseases associated with fat accumulation inhibition, cardiovascular alleviation, and antioxidation [12]. Polyphenol-enriched foods are closely related to gut microbiota, perhaps owing to their significant antioxidative properties [13].

The effects of digested microalgae biomass of *Chlorella vulgaris*, *Desmodesmus maximus*, *Chlorococcum* sp. *cf hypnosporum*, and *Spirulina platensis* or fructooligosaccharides (FOS) on human colonic microbiota during *in vitro* fermentation (48 h) were evaluated by previous researchers [17]. These results revealed that crude microalgae extraction (containing phenolics and oligosaccharides) could increase gut beneficial bacteria abundance by increasing *Lactobacillus-Enterococcus* and *Bifidobacterium* relative abundances and decreasing *Prevotellaceae-Bacteroidaceae*, *Clostridium histolyticum*, and *Eubacterium rectale-Clostridium coccoides*.

Pigments of microalgae on gut microbiota modulation

Microbial pigments, produced by bacteria, fungi, and microalgae, support intestinal and overall health by regulating gut microbiota and strengthening the intestinal barrier [30]. Their antioxidant, antibacterial, and anti-inflammatory properties promote beneficial microbes, inhibit harmful ones, and may help prevent diseases like obesity, diabetes, and cancer [30]. The major classes of photosynthetic pigments that occur among the microalgae are chlorophylls, carotenoids, and phycobiliproteins [31]. Microalgae, particularly *Spirulina*, are a major source of

PC, a natural blue pigment that is increasingly popular for its health benefits and food-safe colorant properties [5].

Gut microbiota plays a crucial role in regulating the response to immune checkpoint therapy; therefore, modulation of the microbiome with bioactive molecules like carotenoids (α-carotene, β-carotene, lycopene, phytoene, lutein, β-cryptoxanthin, zeaxanthin, astaxanthin, and fucoxanthin) might be a very effective strategy to reduce the risk of chronic diseases [32]. Gut microbiota can convert carotenoids into more easily absorbable forms and generate various bioactive metabolites that benefit human health. For instance, carotenoids are promising molecules that influence gut microbiota by activating immune cells, which may help reduce oxidative stress [32]. The relative researcher has concluded that the natural pigments can regulate the intestinal microbiota, according to [30]: 1) reinforcing the intestinal barrier and immune function by encouraging beneficial microbes and suppressing harmful ones; 2) promoting the biotransformation and production of active metabolites such as acetylcholine, AAs, SCFAs, and EPS.

A significant portion of microalgae-derived carotenoids reaches the colon, where they interact with gut microbiota. Some of these carotenoids (β-carotene, astaxanthin, lutein and zeaxanthin, fucoxanthin, lycopene, canthaxanthin, α-carotene, β-cryptoxanthin, phytoene, and siphonaxanthin) can be converted into other compounds during digestion, although the bioavailability of most microalgal carotenoids remains relatively low [33]. Despite their generally low bioavailability, these unabsorbed carotenoids play a vital role in modulating gut microbiota and exhibit significant potential to influence host metabolism [33].

Minerals and vitamins of microalgae on gut microbiota modulation

Vitamins are essential organic micronutrients needed in small amounts for metabolic health, and algae, both seaweed and microalgae, are a natural source [34]. Microalgae can synthesize various vitamins with biotechnological uses, especially β-carotene (a vitamin A precursor), along with water-soluble vitamins B1, B2, B6, B12, and C, and the liposoluble, antioxidant vitamin E [35]. Vitamin content varies by species, and the production, extraction, and purification of these vitamins support antioxidant activity, carbohydrate metabolism, body homeostasis, and the development of functional foods. In terms of some significant bioactive activities of microalgae bioactive

Table 1

Some bioactive activities of microalgae-derived bioactive compounds.

Microalgae-derived bioactive compounds (crude/purified compounds)	Microalgae source	Molecular	Bioactivities	References
Microalgal extracellular polymeric substances	Contain proteins, lipids, exopolysaccharides, and nucleic acids of microalgae	No data	Antiviral capability, inhibition of cancer cell growth, dilatation of bronchial tubes cough relief, lowering blood sugar, antimicrobial capability, loads of drugs, protection against UV rays, moisturizing, and increasing elasticity.	[15]
Oligosaccharide SPO-1	Purified polysaccharides from *Spirulina platensis*	510.8–997.0 Da	Significantly improved the microbial community by increasing the community richness and diversity; increasing the abundance of more beneficial species (including *Bacteroides*, *Escherichia-Shigella*, *Megamonas*), Megasphaera, Blautia, Bifidobacterium, and Lactobacillus).	[36]
Bioactive peptides	Hydrolysis of protein extracted from microalgae	Protein fragments are composed of 2–20 AAs.	Antioxidant, antidiabetic, antihypertensive, antibacterial, anticancer, osteogenic, antiaging, antiviral.	[37]
Antibacterial peptides (KLENCN YAVELGK)	Pepsin hydrolysate of *Limnospira* Sp., and then purification of peptides	466.68 Da	Antimicrobial activity against *E. coli* and *S. aureus*	[38]
Unsaturated fatty acid, DHA, and EPA	Microalgae lipids	No data	Antibacterial, antifungal, antiinflammatory, alleviating cardiovascular, and modulating gut microbiome.	[39]
β-carotene, astaxanthin, lutein and zeaxanthin, fucoxanthin, lycopene, and others	Microalgae-derived carotenoids	No data	Anti-oxidation, anti-obesity, anticancer, anti-inflammation, cardiovascular health, vision protection, skin protection, and others.	[33]
β-carotene (pigments)	Crude extraction or purification from microalgae	No data	anti-oxidation (promote lifespan in lab animals); anti-inflammation (reduce oxidative stress in culture cells)	[40]

compounds and some related research, more details can be observed in Table 1 [15,33,36–40].

Microalgae are a rich reservoir of vitamins (B vitamins and vitamin D) and minerals (including essential minerals such as iron (Fe), calcium (Ca), and magnesium (Mg)) [23]. Minerals constitute a significant fraction of microalgal biomass, accounting for 2–40% of its dry weight [41]. Major minerals include Ca, Mg, phosphorus (P), potassium (K), and sodium (Na), while trace minerals consist of manganese (Mn), Fe, selenium (Se), zinc (Zn), and copper (Cu) [41]. These minerals are vital for numerous biological processes [42]. However, excessive mineral supplementation may negatively affect intestinal integrity and increase susceptibility to enteric infections, potentially by altering gut microbiota composition and function [43].

In vitro selenium (Se) bioaccessibility combined with *in vivo* biostability and bioactivity in Se-enriched microalgae (*Chlorella sorokiniana*) has been evaluated [44]. In that study, the results revealed that Se-enriched microalgae were 81% *in vitro* gastrointestinal digestion, whereas the *in vivo* mice supplemented with Se-enriched *Chlorella sorokiniana* showed a high concentration of selenium in the kidney, reflecting a potential mechanism of excretion by urine. Additional studies examining the effects of microalgal biomass on gut microbiota modulation, both *in vitro* and *in vivo*, are summarized in Tables 2 [44–47] and 3 [7,17,48,49].

Challenges and considerations

While microalgal-derived bioactive compounds present promising opportunities for gut microbiota modulation, several challenges and considerations must be addressed before their widespread application. One major challenge is bioavailability [50], such as polyphenols and carotenoids exhibit low absorption rates and limited stability in the gastrointestinal tract, which may reduce their effectiveness. Additionally, the complexity and variability of individual gut microbiota can lead to inconsistent responses among different populations, making it difficult to generalize therapeutic outcomes. Another critical concern is safety. Certain microalgae may accumulate harmful substances such as heavy metals, allergens, or toxins like microcystins, necessitating rigorous screening, purification, and regulatory oversight. Standardization of extraction and processing methods also poses a hurdle; variations in cultivation conditions, strain selection, and extraction techniques can significantly influence the quality and efficacy of bioactive compounds.

Moreover, economic and technological barriers remain, as large-scale production and downstream processing of high-purity compounds are often cost-intensive and technically demanding. Lastly, there is a lack of long-term clinical studies to support health claims and establish dosage guidelines for different populations. To realize the full potential of microalgal bioactives, comprehensive multidisciplinary research integrating

Table 2

Studies on gut microbiota modulation effects *in vivo* assays with microalgae-derived bioactive compounds.

Microalgae	Microalgae biomass	Assay	Major outcomes	References
Spirulina platensis	polysaccharides	*In vivo*	*Spirulina platensis* polysaccharides (SPLP) had significant hypolipidemic and hypoglycemic effects in HFD-fed rats; SPLP significantly modulated the intestinal microbiota dysbiosis.	[45]
Scenedesmus obliquus	protein, carotenoids,	*In vivo* with Wistar rats	High values of protein efficiency ratio after the consumption of microalga; ingestion of microalga *S. obliquus* reduced serum glucose of up to 42%; the intake of the microalga reduced triglycerides of up to 70%; the atherogenic index decreased with increasing consumption of *S. obliquus*.	[46]
Spirulina	lipids	*In vivo*	Dietary Spirulina lipids (SL) reduced the body weight in diet-induced obese mice; SL supplementation also suppressed the hepatic lipid accumulation in obese mice; the anti-obesity and antifatty liver effects of SL were comparable with fish oil; possible mechanisms might be through regulating SREBP-1c, SREBP-2, and PPAR α.	[47]
Chlorella sorokiniana (selenium (Se)-enriched microalgae)	Selenium (minerals)	*In vivo*	The Se bioaccessibility in Se-enriched *Chlorella sorokiniana* evaluated by in *vitro* gastrointestinal digestion of the selenized microalga was 81% (79% as SeMet); mice supplemented with Se-enriched *C. sorokiniana* presented increased Se concentration in the kidney; Se bioavailability and bioactivity were 76–85% in serum from these mice animals	[44]

Table 3

Studies on gut microbiota modulation effects *in vitro* assays with microalgae-derived bioactive compounds.

Microalgae	Microalgae biomass	Assay	Major outcomes	References
Caulerpa lentillifera J. Agardh, *Ulva rigida* C. Agardh, *Spirulina* sp., *Coelastrella* sp. (KKUP1), and *Scenedesmus* sp. (KKUP2)	Protein	*In vitro* digestibility	*Spirulina* sp. had the highest protein content (44.44% of dry matter basis; $P < 0.0001$) and was rich in AAs (Lys, Thr, and Trp). Moreover, protein solubility, digestibility (DPD and $GPD_{Protein}$), and digestible protein of Spirulina sp. were significantly higher than those of other species (52.35%, 49–67% and 20.70%, respectively). Energy digestibility (GPD_{Energy}) and digestible energy were highest in *Ulva rigida* (99.40% and 15.29 MJ kg^{-1}, respectively; $P < 0.0001$).	[48]
Chlorella vulgaris (CHL), Desmodesmus maximus (DES), Chlorococcum sp. *cf hypnosporum (CHLO), and Spirulina platensis (SPI)*	Oligosaccharides and phenolics	*In vitro* (*in vitro* colonic fermentation of digested)	Increase gut beneficial bacteria abundance by increasing *Lactobacillus-Enterococcus* (similar increase in the relative abundance for DES, SPI, and FOS, approximately 30%) and *Bifidobacterium* relative abundances (similar increase in the relative abundance in CHL and SPI, approximately 36–37%).	[17]
Spirulina platensis	PC (pigments)	*In vitro*	Reduces liver fat accumulation in methionine-choline-deficient diet-induced nonalcoholic steatohepatitis mice; regulates liver lipid metabolism by activating the AMP-activated protein kinase pathway.	[49]
Spirulina, Chlorella, and *Phaeodactylum tricornutum* (*P. tricornutum*)	SCFAs	*In vitro (In vitro simulated digestion and in vitro colonic fermentation)*	The bacterial copy numbers were affected by the *in vitro* digestion process and colonic fermentation time in the analyses of quantitative polymerase chain reaction (PCR) technology; microalgal biomolecules' digestion promoted the release of SCFAs during *in vitro* colonic microbiota fermentation, particularly acetic, butanoic, and propanoic, indicating a potential health benefit for the human gut.	[7]

microbiology, nutrition, toxicology, and bioengineering is essential.

Conclusion and future perspectives

In conclusion, microalgae-derived bioactive compounds offer substantial potential for modulating gut microbiota and improving human health. Through mechanisms involving microbial composition shifts, metabolite production (e.g. SCFAs, Trp derivatives), and immune modulation, these compounds influence a wide range of physiological processes. Polysaccharides, peptides, PUFAs, polyphenols, pigments, and essential micronutrients derived from microalgae exhibit synergistic effects that promote the growth of beneficial bacteria, suppress pathogens, enhance intestinal barrier integrity, and regulate host metabolism and immune response. Such multifactorial actions position microalgae as promising candidates for next-generation functional foods and therapeutic agents in managing gut-related diseases. Despite these promising outcomes, significant challenges remain. Bioavailability, compound stability, inter-individual microbiota variability, and long-term effects require further investigation. Moreover, standardized protocols for extraction, purification, and safety assessment are critical to ensure consistency and efficacy across applications. Future research should focus on well-controlled clinical trials to validate *in vivo* outcomes, particularly in patient populations with chronic diseases or metabolic syndromes. Additionally, advancements in bioprocessing technologies could enhance the scalability and economic feasibility of microalgal products.

Looking ahead, integrating microalgal bioactive compounds into personalized nutrition strategies could revolutionize preventive healthcare. A deeper understanding of host–microbiota interactions, aided by omics technologies, will pave the way for tailoring microalgal-based interventions to individual microbiomes,

maximizing therapeutic outcomes while supporting environmental sustainability through algae-based innovation.

Data Availability

The authors are unable or have chosen not to specify which data has been used.

Declaration of Competing Interest

The authors have no conflict of interest to declare.

Acknowledgements

Yixuan Liu is supported by a PhD fellowship from the China Scholarship Council (CSC), China (No. 202208420013). Andrea Asensio-Grau acknowledges the post-doctoral contract Juan de la Cierva Formación, awarded by the Spanish Ministry of Science and Innovation (JDC2022-048768-I). The publication is part of the projects BLUEWAYSE ("BLUE WAY to a Sustainable Europe" action PCI2024-153460 (Sustainable Blue Economy Partnership, SBEP), funded by MICIU/AEI/10.13039/501100011033 and by the European Union under Grant agreement no.: SBEP2023-961) and AGROALNEXT program (AGROALNEXT/2022/060 – Desarrollo y optimización de procesos innovadores y sostenibles de extracción de aceite y proteínas a partir de microalgas, insectos, residuos y subproductos agroalimentarios: Evaluación de propiedades biológicas (EXTRAOLIOPRO)), supported by MICIU with funding from European Union NextGeneration EU (PRTR-C17. I1) and the Generalitat Valenciana.

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1. •• Yang S, Wang Y, Wang J, Cheng K, Liu J, He Y, Zhang Y, Mou H, Sun H: **Microalgal protein for sustainable and nutritious foods: a joint analysis of environmental impacts, health benefits and consumer's acceptance**. *Trends Food Sci Technol* 2024, **143**:104278.

The feasibility of using microalgal protein for nutritious and sustainable foods is driven by developing technologies and future food systems. The major barriers to the economic viability of protein production, tailored nutrients, and acceptable organoleptic traits are discussed to realize this expectation.

2. Saravana PS, Ummat V, Bourke P, Tiwari BK: **Emerging green cell disruption techniques to obtain valuable compounds from macro and microalgae: a review**. *Crit Rev Biotechnol* 2023, **43**:904-919.

3. Yousefi M, Khorshidian N, Khanniri E, Mortazavian AM: **Microalgae added to beverages, dairy, prebiotic, and probiotic products**. In *Handbook of Food and Feed from Microalgae*. Edited by Jacob-Lopes E, *et al*. Academic Press; 2023:335-347.

4. Silva M, Geada P, Pereira RN, Teixeira JA: **Microalgae biomass – a source of sustainable dietary bioactive compounds towards improved health and well-being**. *Food Chem Adv* 2025, **6**:100926.

5. •• Yu Z, Zhao W, Sun H, Mou H, Liu J, Yu H, Dai L, Kong Q, Yang S: **Phycocyanin from microalgae: a comprehensive review covering microalgal culture, phycocyanin sources and stability**. *Food Res Int* 2024, **186**:114362.

This review highlights the importance of metabolic engineering, multi-omics applications, and innovative delivery systems in unlocking the full potential of this natural blue pigment in the realm of food applications, provides a complete overview of the entire process from production to commercialization of PC, including the extraction and purification.

6. Figueroa-Torres G, Bermejo-Padilla E, Wang G, Hilmisson B, Pittman JK, Theodoropoulos C: **Microalgae Strain Catalogue – A Strain Selection Guide for Microalgae Users**. 4th ed., University of Manchester, Zenodo; 2023.

7. Zhou J, Wang M, Bäuerl C, Cortés-Macías E, Calvo-Lerma J, Carmen Collado M, Barba FJ: **The impact of liquid-pressurized extracts of *Spirulina*, *Chlorella* and *Phaedactylum tricornutum* on in vitro antioxidant, antiinflammatory and bacterial growth effects and gut microbiota modulation**. *Food Chem* 2023, **401**:134083.

8. Market Research Reports: **Spirulina Market Analysis & Forecast: 2025–2032**; 2025.

9. Li H, Liang J, Han M, Gao Z: **Polyphenols synergistic drugs to ameliorate non-alcoholic fatty liver disease via signal pathway and gut microbiota: a review**. *J Adv Res* 2025, **68**:43-62.

10. Zhao W, Zhu J, Yang S, Liu J, Sun Z, Sun H: **Microalgal metabolic engineering facilitates precision nutrition and dietary regulation**. *Sci Total Environ* 2024, **951**:175460.

11. Madhogaria B, Bhowmik P, Kundu A: **Correlation between human gut microbiome and diseases**. *Infect Med* 2022, **1**:180-191.

12. Zhou J, Wang M, Grimi N, Dar BN, Calvo-Lerma J, Barba FJ: **Research progress in microalgae nutrients: emerging extraction and purification technologies, digestive behavior, and potential effects on human gut**. *Crit Rev Food Sci Nutr* 2023, **64**:11375-11395.

13. Li Y, Li J, Xu F, Liu G, Pang B, Liao N, Li H, Shi J: **Gut microbiota as a potential target for developing anti-fatigue foods**. *Crit Rev Food Sci Nutr* 2023, **63**:3065-3080.

14. Song Q, Wang Y, Huang L, Shen M, Yu Y, Yu Q, Chen Y, Xie J: **Review of the relationships among polysaccharides, gut microbiota, and human health**. *Food Res Int* 2021, **140**:109858.

15. Synytsya A, Sushytskyi L, Saloň I, Babayeva T, Čopíková J: **Intracellular and extracellular carbohydrates in microalgae**. In *Handbook of Food and Feed from Microalgae*. Edited by Jacob-Lopes E, *et al*. Academic Press; 2023:87-102.

16. Zhang D, Liu J, Cheng H, Wang H, Tan Y, Feng W, Peng C: **Interactions between polysaccharides and gut microbiota: a metabolomic and microbial review**. *Food Res Int* 2022, **160**:111653.

17. de Medeiros VPB, de Souza EL, de Albuquerque TMR, da Costa Sassi CF, dos Santos Lima M, Sivieri K, Pimentel TC, Magnani M: **Freshwater microalgae biomasses exert a prebiotic effect on human colonic microbiota**. *Algal Res* 2021, **60**:102547.

18. Lu Y, Peng B, Lin Y, Lin Q, Xia X, Zhong S, Luo L, Huang R: ***Spirulina* polysaccharide induces the metabolic shifts and gut microbiota change of lung cancer in mice**. *Curr Res Food Sci* 2022, **5**:1313-1319.

19. •• Thakur A, Sharma D, Saini R, Suhag R, Thakur D: **Cultivating blue food proteins: innovating next-generation ingredients from macro and microalgae**. *Biocatal Agric Biotechnol* 2024, **60**:103278.

This review delves into the origins, varieties, physical and techno-functional characteristics, and uses of macro and microalgae proteins in food, while also addressing the benefits and drawbacks of algae proteins.

20. Ashaolu TJ, Samborska K, Lee CC, Tomas M, Capanoglu E, Tarhan Ö, Taze B, Jafari SM: **Phycocyanin, a super functional ingredient from algae; properties, purification characterization, and applications**. *Int J Biol Macromol* 2021, **193**:2320-2331.

21. Alves J, Costa P, Sales L, Silva-Luis C, Bezerra T, Alves Souza M, Costa B, Souza E: **Shedding light on the impacts of Spirulina platensis on gut microbiota and related health benefits**. *Crit Rev Food Sci Nutr* 2024, **65**:2062-2075.

22. Wang J, Zhu N, Su X, Gao Y, Yang R: **Gut-microbiota-derived metabolites maintain gut and systemic immune homeostasis**. *Cells* 2023, **12**:793.

23. •• Barros de Medeiros VP, da Costa WKA, da Silva RT, Pimentel TC, Magnani M: **Microalgae as source of functional ingredients in new-generation foods: challenges, technological effects,**

biological activity, and regulatory issues. *Crit Rev Food Sci Nutr* 2022, **62**:4929-4950.
This review aims to provide an overview of the use of microalgae biomass in food products, the technological effects of its incorporation, and their use as a source of health-promoting bioactive compounds. In addition, it presents the regulatory aspects of commercialization and consumption, and the main trends and market challenges.

24. Lu Q, Li H, Xiao Y, Liu H: **A state-of-the-art review on the synthetic mechanisms, production technologies, and practical application of polyunsaturated fatty acids from microalgae**. *Algal Res* 2021, **55**:102281.

25. Gouda MM, Tadda MA: **Microalgae potentials as bioactive phytochemicals for human's health: novel highlights on their production, applications, and emerging analytical technologies**. In *Algal Biotechnology*. Edited by Ahmad A, Banat F, Taher H. Elsevier; 2022:377-408.

26. Katiyar R, Arora A: **Health promoting functional lipids from microalgae pool: a review**. *Algal Res* 2020, **46**:101800.

27. Li T, Tong A, Liu Y, Huang Z, Wan X, Pan Y, Jia R, Liu B, Chen X, Zhao C: **Polyunsaturated fatty acids from microalgae *Spirulina platensis* modulates lipid metabolism disorders and gut microbiota in high-fat diet rats**. *Food Chem Toxicol* 2019, **131**:110558.

28. Huang Z, Deng J, Li Q, Cao Y, Lin Y, Bai W, Liu B, Rao P, Ni L, Lv X: **Protective mechanism of common buckwheat (*Fagopyrum esculentum Moench.*) against nonalcoholic fatty liver disease associated with dyslipidemia in mice fed a high-fat and high-cholesterol diet**. *J Agric Food Chem* 2020, **68**:6530-6543.

29. Jimenez-Lopez C, Pereira AG, Lourenço-Lopes C, Garcia-Oliveira P, Cassani L, Fraga-Corral M, Prieto MA, Simal-Gandara J: **Main bioactive phenolic compounds in marine algae and their mechanisms of action supporting potential health benefits**. *Food Chem* 2021, **341**:128262.

30. Zhang Z, Chen J, Huang X, Aadil RM, Li B, Gao X: **Natural pigments in the food industry: enhancing stability, nutritional benefits, and gut microbiome health**. *Food Chem* 2024, **460**:140514.

31. Barq MG, Hussain W, Khan QF, Azhar N, Afzaal M: **Sustainable microalgae-derived pigments for the food industry**. In *Algae Biotechnology for Biomedical and Nutritional Applications*. Edited by Ahmad A, Ashraf SS. Academic Press; 2025:145-165.

32. •• Bernabeu M, Gharibzahedi SMT, Ganaie AA, Macha MA, Dar BN, Castagnini JM, Garcia-Bonillo C, Meléndez-Martínez AJ, Altintas Z, Barba FJ: **The potential modulation of gut microbiota and oxidative stress by dietary carotenoid pigments**. *Crit Rev Food Sci Nutr* 2023, **64**:12555-12573.
This review highlights the bio-functional effect of carotenoids on Gut Microbiota modulation based on a bibliographic search of the different databases. These studies related to the health-promoting properties of carotenoids and their utilization in the modulation of gut microbiota have been presented. Results showed that there can be quantitative changes in intestinal bacteria as a function of the type of carotenoid.

33. Guo B, Zou J, Zhang W, Liu B: **Microalgae-derived carotenoids: digestive fate and interplay with gut microbiota**. *Trends Food Sci Technol* 2024, **153**:104760.

34. Demarco M, Oliveira de Moraes J, Matos ÂP, Derner RB, de Farias Neves F, Tribuzi G: **Digestibility, bioaccessibility and bioactivity of compounds from algae**. *Trends Food Sci Technol* 2022, **121**:114-128.

35. Coronado-Reyes JA, González-Hernández JC: **Vitamins from microalgae**. In *Handbook of Food and Feed from Microalgae*. Edited by Jacob-Lopes E, *et al*. Academic Press; 2023:111-115.

36. Cai B, Yi X, Han Q, Pan J, Chen H, Sun H, Wan P: **Structural characterization of oligosaccharide from *Spirulina platensis* and its effect on the faecal microbiota *in vitro***. *Food Sci Hum Wellness* 2022, **11**:109-118.

37. Nunes E, Odenthal K, Nunes N, Fernandes T, Fernandes IA, Pinheiro de Carvalho MAA: **Protein extracts from microalgae and cyanobacteria biomass. Techno-functional properties and bioactivity: a review**. *Algal Res* 2024, **82**:103638.

38. Sathya R, Mubarak Ali D, Mehboob Nousheen MG, Vasimalai N, Thajuddin N, Jung-Wan K: **An investigation of pepsin hydrolysate of short antibacterial peptides derived from *Limnospira* Sp.** *Appl Biochem Biotechnol* 2022, **194**:5580-5593.

39. Zhou J, Wang M, Saraiva JA, Martins AP, Pinto CA, Prieto MA, Simal-Gandara J, Cao H, Xiao J, Barba FJ: **Extraction of lipids from microalgae using classical and innovative approaches**. *Food Chem* 2022, **384**:132236.

40. Wang J, Hu X, Chen J, Wang T, Huang X, Chen G: **The extraction of *β*-carotene from microalgae for testing their health benefits**. *Foods* 2022, **11**:502.

41. Maroneze MM, Martinez A: **Minerals and trace elements in microalgal biomass**. In *Handbook of Food and Feed from Microalgae*. Edited by Jacob-Lopes E, *et al*. Academic Press; 2023:103-109.

42. Cai C, Liu Y, Xu Y, Zhang J, Wei B, Xu C, Wang H: **Mineral-element-chelating activity of food-derived peptides: influencing factors and enhancement strategies**. *Crit Rev Food Sci Nutr* 2024, **65**:3241-3255.

43. Knez M, Ranic M, Stangoulis JCR, Glibetic M: **The mineral intake and microbiota**. In *Comprehensive Gut Microbiota*. Edited by Glibetic M. Elsevier; 2022:230-242.

44. Gómez-Jacinto V, Navarro-Roldán F, Garbayo-Nores I, Vílchez-Lobato C, Borrego AA, García-Barrera T: **In vitro selenium bioaccessibility combined with in vivo bioavailability and bioactivity in Se-enriched microalga (*Chlorella sorokiniana*) to be used as functional food**. *J Funct Foods* 2020, **66**:103817.

45. Li T, Huang Z, Jia R, Lv X, Zhao C, Liu B: ***Spirulina platensis* polysaccharides attenuate lipid and carbohydrate metabolism disorder in high-sucrose and high-fat diet-fed rats in association with intestinal microbiota**. *Food Res Int* 2021, **147**:110530.

46. T. da Silva ME, Correa KDP, Martins MA, da Matta SLP, Martino HSD, Coimbra JSDR: **Food safety, hypolipidemic and hypoglycemic activities, and in vivo protein quality of microalga *Scenedesmus obliquus* in Wistar rats**. *J Funct Foods* 2020, **65**:103711.

47. Yang Y, Du L, Hosokawa M, Miyashita K: **Effect of *Spirulina* lipids on high-fat and high-sucrose diet induced obesity and hepatic lipid accumulation in C57BL/6J mice**. *J Funct Foods* 2020, **65**:103741.

48. Pootthachaya P, Puangsap W, Bunchalee P, Plangklang P, Reungsang A, Yuangsoi B, Cherdthong A, Tengjaroenkul B, Wongtangtintharn S: **Investigation of nutritional profile, protein solubility and in *vitro* digestibility of various algae species as an alternative protein source for poultry feed**. *Algal Res* 2023, **72**:103147.

49. Ma P, Huang R, Jiang J, Ding Y, Li T, Ou Y: **Potential use of C-phycocyanin in non-alcoholic fatty liver disease**. *Biochem Biophys Res Commun* 2020, **526**:906-912.

50. Rodríguez-Roque MJ, Flores-Córdova MA, Salas-Salazar NA, Soto-Caballero MC, Valdivia-Nájar CG, Sánchez-Vega R: **Microalgae as source of bioaccessible and bioavailable compounds**. In *Handbook of Food and Feed from Microalgae*. Edited by Jacob-Lopes E, *et al*. Academic Press; 2023:519-527.