



## Review

# Algal Polysaccharides-Based Nanomaterials: General Aspects and Potential Applications in Food and Biomedical Fields

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**Abstract:** The use of natural polymers has increased due to concern about environmental pollution caused by plastics and emerging pollutants from fossil fuels. In this context, polysaccharides from macroalgae and microalgae arise as natural and abundant resources for various biological, biomedical, and food applications. Different nanomaterials are produced from these polysaccharides to act as effective carriers in the food and pharmaceutical industry: drug and nutrient carriers, active compound encapsulation, and delivery of therapeutic agents to tumor tissues. Polysaccharides-based nanomaterials applied as functional ingredients incorporated into foods can improve texture properties and decrease the caloric density of food products. These nanostructures also present the potential for developing food packaging with antioxidant and antimicrobial properties. In addition, polysaccharides-based nanomaterials are biocompatible, biodegradable, and safe for medical practices to prevent and manage various chronic diseases, such as diabetes, obesity, and cardiovascular disease. In this sense, this review article addresses the use of algal polysaccharides for manufacturing nanomaterials and their potential applications in food and biomedical areas. In addition, the paper discusses the general aspects of algae as a source of polysaccharides, the nanomaterials produced from these polymers, as well as recent studies and the potential use of algal polysaccharides for industries.

**Keywords:** biopolymers; macroalgae; microalgae; nanoparticles; sustainability



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## 1. Introduction

The use of green polymers has increased due to the threat of marine plastic and the discovery of emerging pollutants. Polysaccharides represent macromolecules with monosaccharide units joined by glycosidic bonds. Due to diversified sources, the chemical nature and characteristics are varied significantly. These molecules are abundant in nature and present biodegradability and biocompatibility properties. In addition, they are renewable, non-toxic, and relatively cheap. Other advantages of polysaccharides are their hydrophilicity, mechanical stability, and tunability. Polysaccharides are polymers that can be extracted from renewable sources such as algae, vegetables, microorganisms, and animals [1–6].

Algae and microalgae are sustainable alternative resources for producing biopolymers through the biorefinery model because of their high growth rate, ability to grow in different conditions, carbon dioxide (CO<sub>2</sub>) utilization, and lack of competition with food resources. Quality control measures and advanced cultivation techniques must be adopted to obtain

high-quality polysaccharides. Moreover, the polysaccharide extraction process can influence the composition and molecular weight of the biopolymer. Therefore, it is crucial to choose the best extraction process for obtaining polysaccharides of interest [7,8].

Regarding the applications, algal polysaccharides such as agar, alginates, and carrageenans have been produced industrially for over a century. These polymers have the potential for application in food areas and manufacturing high-value products used in many research and applications in biomedicine. Algae and microalgae have potential as raw materials for biomaterials and nanomaterials. The polysaccharides can also be transformed into nanoparticles, which can have applications in the most diverse areas, such as food, feed, cosmetics, biomedical, and modern medicine, mainly used as a wound dressing, or for gene delivery and drug delivery [7,9–12].

Nanomaterials based on polysaccharides produced using different techniques promote the manufacture of nanoparticle structures [13] with complex designs and high preparation costs. Therefore, the preparation steps, low yield, and high cost are obstacles to promoting nano/microcapsules in the market [6]. Furthermore, extracting valuable components of algal polysaccharides is still challenging from an economic view because all compounds are compacted and filled in the cell, making the process very expensive [14]. Additionally, some polysaccharides have low solubility in common solvents, which limits the chemical modification of polysaccharides [15]. Thus, there is a need for cost-effective advanced synthesis processes, and the use of green and recyclable solvents can be encouraged for the commercial synthesis of nanoparticles, for example, based on seaweed polysaccharides in industries. The derivatization of seaweed polysaccharides with other macromolecules can be focused on developing cost effective and sustainable approaches and products. Research should also focus on the action of seaweed-based polysaccharides *in vivo* for the delivery of nutraceuticals [13].

Nanomaterials have characteristics that promote safety for biomedical applications, such as biocompatibility and biodegradability. Various chronic diseases, such as diabetes, obesity, and cardiovascular disease, were effectively controlled and avoided by the consumption of polysaccharide-based nanomaterials. Nanosystems based on polysaccharides reduce the side effects and toxicity of drugs, reduce the caloric density of foods, and improve the texture of food products [5].

In this context, this review article addresses the use of algal polysaccharides for manufacturing nanomaterials and their potential applications in the food and biomedical areas. In addition, the paper discusses the general aspects of algae as a source of polysaccharides, the nanomaterials produced from these polymers, as well as recent studies and the potential use of algal polysaccharides for industry.

## 2. Algae as Sources of Polysaccharides

In macroalgae, polysaccharides can be found either on the cell surface (structural polysaccharides) or intracellularly (storage polysaccharides). Alginates, carrageenans, cellulose, sulfated polysaccharides, fucoidans, ulvans, and porphyran are the most prominent examples of the former. In the second type, the best known polysaccharides are laminarin and starch [16]. Carrageenans and agar are sulfated polysaccharides found in red algae [17]. On the other hand, fucoidans, alginates, and laminarin are prevalent in brown algae, while ulvans are present in green algae [18]. Cellulose and hemicelluloses can be found in the extracellular covering of green algae Chlorophyta and Charophyta, the red algae Rhodophyta, in the phylum Ochrophyta, and the Phaeophyceae class (brown algae). Some species from Xanthophyceae (yellow green algae), Chrysophyceae class (golden algae), and Dinophyta (thecate dinoflagellates) have cellulose as a structural polysaccharide for their cell wall [19] (Table 1).

**Table 1.** Polysaccharides from algae.

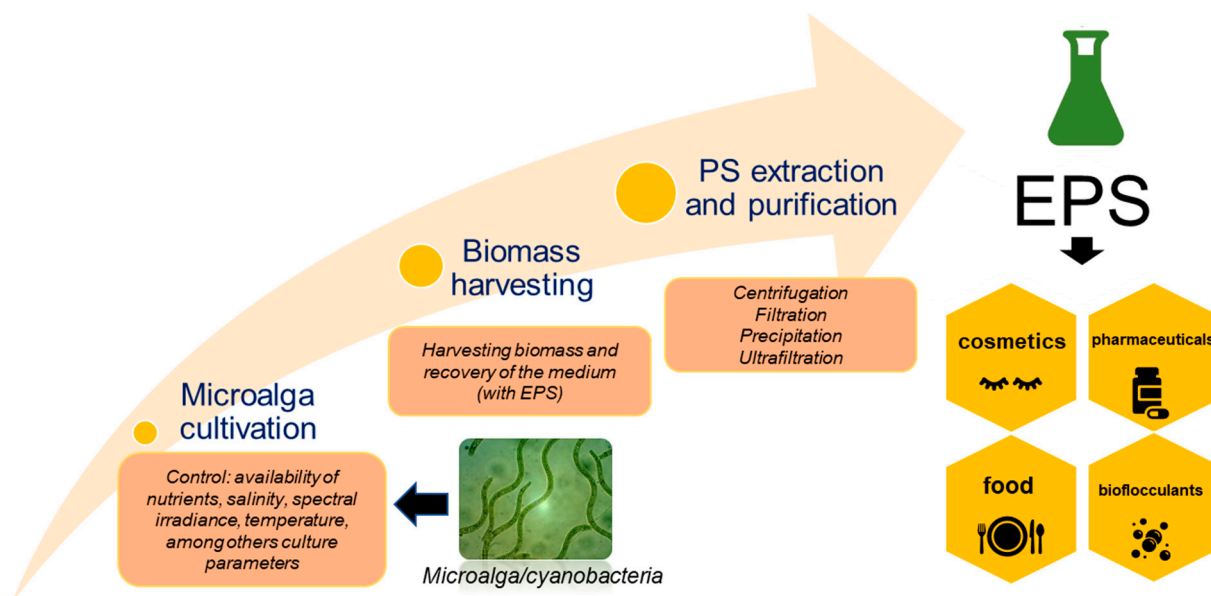
| Macroalga/Microalga           | Macroalgae Extraction Method/<br>Microalgae Cultivation Strategy  | Polysaccharides Type                         | Polysaccharides Yield (% <i>w/w</i> ) | Reference |
|-------------------------------|---|--|---------------------------------------|-----------|
| <i>Alaria esculenta</i>       | Preservation with formic acid (4 weeks; 20 °C)  | Alginates                                    | 32.5 *                                | [20]      |
|                               | Short alkaline extraction (1–5 h), pH 9, 20 °C  |  | 24.0                                  | [21]      |
|                               | Sequential extraction of fucoidan/laminarin, alginate, and cellulose using mild chemical methods  |  | 7.1                                   | [22]      |
| <i>Chondrus crispus</i>       | Hydrothermal processing with subcritical water during non-isothermal heating up to 140 °C   | Carrageenans                                 | 75.5                                  | [23]      |
|                               | Dark cultivation for 21 days  |  | 44.3                                  | [24]      |
|                               | Dispersion with demineralized water stirred with a magnetic rod at 500 rpm for 8 h at 90 °C   |  | 39.2                                  | [25]      |
| <i>Laminaria japonica</i>     | Ultrasound-assisted Extraction (195 W for 30 min at 60 °C).   | <i>Laminaria japonica</i><br>polysaccharides | 9.7                                   | [26]      |
|                               | Alkaline extraction (NaOH solution of pH 10.0 for 4 h at 80 °C)   |  | 44.6                                  | [27]      |
|                               | Ultrasonic-enzyme synergistic method (0.3% cellulase, 0.7% pectinase, and 1.5% papain; 30 min 55 °C)  |  | 19.4                                  | [28]      |
| <i>Padina tetrastromatica</i> | Subcritical water extraction (150 °C, 5 MPa, 15 min)  | Fucoidans                                    | 14.0                                  | [29]      |
|                               | Water extraction (12 h at room temperature)   |  | 9.5                                   | [30]      |
|                               | Treatment with selective solvents (EtOH, CaCl <sub>2</sub> , HCl, Na <sub>2</sub> CO <sub>3</sub> )   |  | 9.4                                   | [31]      |
| <i>Saccharina latissima</i>   | Preservation with formic acid (16 weeks; 20 °C)   | Cellulose                                    | 18.0                                  | [20]      |
|                               | Typical extraction (acidification—HCl, alkaline extraction—Na <sub>2</sub> CO <sub>3</sub> ), solid/liquid separation, precipitation, and drying) |  | 26.0                                  | [32]      |
|                               | Sequential extraction of fucoidan/ laminarin, alginate, and cellulose using mild chemical methods   |  | 6.9                                   | [22]      |

Table 1. Cont.

| Macroalga/Microalga                    | Macroalgae Extraction Method/<br>Microalgae Cultivation Strategy   | Polysaccharides Type                         | Polysaccharides Yield (% w/w) | Reference |
|--|--|--|-------------------------------|-----------|
| <i>Ulva</i> sp.                        | Foliose citric acid-based extraction   | Ulvans                                       | 41.0                          | [33]      |
|  | Soxhlet extraction with methanol and 5% of ammonium oxalate  |  | 13.8                          | [34]      |
|  | Microwave-assisted hydrothermal (liquid phase/EtOH, 1:1.5, choline chloride 1%, 120 °C)  |  | 32.5                          | [35]      |
| <i>Arthrospira platensis</i> SAG 21.99 | Indoor cultures; static magnetic fields application for 24 h d <sup>-1</sup>   | Exopolysaccharides                           | 34.8                          | [36]      |
| <i>Chlorella fusca</i> LEB 111         | Outdoor cultures; static magnetic fields application for 1 h d <sup>-1</sup>   | Starch                                       | 10.9                          | [36]      |
| <i>Chlorella vulgaris</i>              | BG 11 medium, light intensity 65 $\mu\text{mol photons m}^{-2} \text{s}^{-1}$ and temperature 28 °C  | Heteropolysaccharides                        | 32.7                          | [37]      |
|  | Three-stage process with stressed conditions applied in the second stage (light intensity of 360 $\mu\text{mol photons m}^{-2} \text{s}^{-1}$ and nitrogen starvation (F/2 medium deprived of NaNO <sub>3</sub> )) | Starch                                       | 21.0                          | [38]      |
| <i>Neocystis mucosa</i> SX             | Cation exchange resin method was used to extract polysaccharides   | Exopolysaccharides                           | 6.2                           | [39]      |
| <i>Nostoc flagelliforme</i>            | H <sub>2</sub> O <sub>2</sub> acclimation method   | Exopolysaccharides                           | 4.7                           | [40]      |
| <i>Spirulina platensis</i>             | Two stage culture: (1) 96 $\mu\text{mol photons m}^{-2} \text{s}^{-1}$ at 28 °C; (2) light intensity 192 $\mu\text{mol photons m}^{-2} \text{s}^{-1}$ and 38 °C of temperature for 3 days                          | Polysaccharide of <i>Spirulina platensis</i> | 27.3                          | [41]      |
|  | Commercial microalgal powder was extracted with ultrapure water and ultrasonic treatment (45 kHz, 300 w) at 60 °C for 1 h.   |  | 16.7                          | [42]      |
|  | Commercial powder and alkaline extraction  |  | 10.8                          | [43]      |
| <i>Spirulina</i> sp.                   | Outdoor cultures   | Exopolysaccharides                           | 49.3                          | [36]      |

\* approximate value.

When discussing algal polysaccharides, the typical approach involves harvesting the algae from its natural habitat and applying extraction and purification methods. Extraction techniques are tailored and optimized for each algal species to obtain the highest possible yield of the polysaccharides with their desired properties [44] (Figure 1). Depending on the specific polysaccharide, these properties may include gelatinization, structural attributes, or even antioxidant properties, as demonstrated by the macroalga *Laminaria japonica* [45].



**Figure 1.** Steps for the obtention of exopolysaccharides (EPS) from microalgae and cyanobacteria cultures and their potential applications [46].

Nevertheless, through aquaculture, it is possible to explore different cultivation techniques for algae to enhance polysaccharide yields and promote environmental sustainability. When investigating cultivation methods for *Chondrus crispus*, Tanoeiro et al. [45] found that the free-floating balloon cultivation method with periodic water changes three times a week resulted in the highest carrageenan yield. However, in terms of production, seaweed cultivation still lags behind harvesting, which typically yields approximately 50% carrageenans content. Nonetheless, aquaculture of this species can provide a sufficient carrageenans supply to sustain the industry without harming natural populations, representing a more sustainable alternative as *C. crispus* becomes increasingly scarce in its natural environment.

Similar to macroalgae, microalgae also possess the capacity to produce polysaccharides. These can either be part of the cell wall (starch) or excreted outside the cells as a self-protective response to environmental stresses, referred to as exopolysaccharides (EPS). Consequently, cultivation strategies can be employed to stimulate the production of these substances (Table 1). For instance, the green microalga *Neochloris oleoabundans* increases its polysaccharide production when cultured mixotrophically with sugars and sodium nitrate [47], while *Chlorella fusca* LEB 111 is stimulated for magnetic fields application in the cultures [36].

Both macroalgae and microalgae benefit from the application of biorefinery techniques. In the case of macroalgae, it is possible to obtain multiple types of polysaccharides from the same species through sequential extractions. Birgersson et al. [22] employed an integrated process to recover alginates, fucoidans, laminarin, and cellulose from *Saccharina latissima* and *Alaria esculenta*. The total yields of polysaccharides were 23.4% and 26.3% of the dry biomass for the respective algae. All extractions were performed using mild chemical methods to preserve the molecular weights of the polysaccharides, particularly alginates.

Regarding polysaccharide production from microalgae, the biorefinery approach differs from that of macroalgae. In microalgal processes, the goal is to extract other high-value

components in addition to exopolysaccharides. These substances are excreted by the microalgae into the culture medium. The remaining products are separated from the biomass. Fatty acids, phycocyanin, other pigments, biofuels, food, biofertilizers, and energy are alternative products extracted alongside EPS [8]. Furthermore, in microalgae cultivation, there is potential to utilize saline and brackish water [48,49] and wastewater [50] as culture media. Gaseous effluents can also be employed as nutrient sources for cultivating microorganisms [51]. In addition to increasing biomass productivity and reducing production costs, it is also possible to enhance microalgae cultivation through strategies such as supplementing cultures with phytohormones [52]. These alternatives render microalgae biorefinery highly productive, sustainable, and economically viable for industrial applications. Moreover, they allow for a higher market share for microalgal polysaccharides.

### 3. Algal Polysaccharides in Food and Biomedical Context

Algal and microalgal polysaccharides have been studied and explored in various food and biomedical contexts due to their functional properties and potential health benefits [9,10]. In the food context, algal and microalgal polysaccharides have been used as natural food additives due to their gelling, stabilizing, and emulsifying properties, as well as for packaging purposes (edible coating or film for active and intelligent packaging) [53]. Microalgae-based polysaccharides, classified as structural polysaccharides (cellulose present in the cell wall), storage polysaccharides (starch and glycogen stored in the chloroplast), and extracellular polysaccharides (secreted outside the cell for intercellular communication), exhibit anti-inflammatory and immunomodulatory properties used for the production of nutraceuticals [54].

Algae and microalgae possess polysaccharides in their biomass with biocompatible properties, low toxicity, and the ability to form gels upon contact with metal ions or pH changes, making them suitable for various applications [9]. Additionally, some marine polysaccharides, such as chitosan, sodium alginate, and agar, have demonstrated antibacterial and antioxidant functions, as well as biocompatibility, which can be applied to food preservation or to enhance the physicochemical properties of food [55].

The dried biomass of algae such as *Spirulina* or *Chlorella* has been applied to traditional food products like bread, soups, and cookies [56,57]. However, the sensory evaluation indicates a low incorporation of algae (0.5%) as a better concentration accepted by potential consumers due to the sensory characteristics of microalgae [56]. Furthermore, adding microalgae biomass in large quantities tends to modify the rheological and technological properties of the original matrix used. Extracted polysaccharides from algae can serve as an alternative to reduce the impact on flavor while providing functional characteristics to the food. Technologies such as enzyme-assisted extraction or ultrasound are options for recovering polysaccharides from microalgae for use in functional foods, nutraceuticals, or supplements [58]. The microalga *Spirulina* is an example of the application of polysaccharides in food, as it contains polysaccharides widely used as food additives or colorants in ice creams, chewing gums, candies, dairy products, soft drinks, or jellies [59].

Among the polysaccharides, sulfated polysaccharides stand out in food commercial applications. These compounds are applied in the food industry due to their stabilizing, gelling, emulsifying, and viscosity-increasing properties. Because they stimulate and stabilize the structure of food, they are widely used in food preparations such as jams, jellies, ice cream, and other dairy products as additives [60]. In the food industry, sulfated polysaccharides are used to restrict the activity of foodborne pathogens such as *Escherichia coli*, *Staphylococcus aureus*, and *Salmonella enterica* [61].

Agar has a wide application in food processing like pastry fillings, jams and jellies, confections, beverages, spreads, garnishes, puddings, desserts, ice cream, meat, and poultry products. This polysaccharide is widely used to prepare jellies where food colors and flavors are added to hot agar extract followed by molding and cooling [62].

For commercial purposes, carrageenan is also a widely used polysaccharide. Carrageenan, such as  $\kappa$ ,  $\lambda$ , and  $\iota$  carrageenan, must be isolated separately as their combined



form decreases the gel strength, which is not ideal for industrial purposes. Due to their excellent functional properties, they act as a thickener, stabilizer, and texture modifier. They improve the appearance and the quality of food from a commercial perspective. They are widely used in dairy, baking, and food processing industries in the production of foods such as puddings, milkshakes, instant soups, sauces, jellies, and pastes [63]. In the biomedical field, microalgal polysaccharides have been studied for applications such as drug delivery systems, tissue engineering, wound dressings, cancer therapy, bone regeneration therapy, and antibacterial and antiviral agents [10]. The biological activity of polysaccharides and exopolysaccharides obtained from microalgae can be observed through the direct use of extracts or purified compounds. It has been demonstrated that these biomolecules have a variety of benefits, including anti-tumor properties [64], antioxidant effects [65], antiviral activity [66], anti-inflammatory properties [54], and antimicrobial activity [67].

Sulfated polysaccharides derived from marine sources stand out for their immunological, antiviral, probiotic, and prebiotic properties. The diverse structure of sulfated polysaccharides has shown excellent responses against the COVID-19 virus (SARS-CoV-2). These polysaccharides enhance the host's antiviral response by interfering with attachment, adsorption, and virus replications [66]. Moreover, they block the initial entry of the virus or inhibit its transcription and translation by modulating the immune response of the host cell. These compounds can also help modulate immunity against SARS-CoV-2 through various pathways. Polysaccharides such as carrageenans can serve as effective adjuvants to enhance the efficacy of peptide-based vaccines through immunoenhancement [68].

Algal polysaccharides also stand out for their antioxidant activity, which can be utilized in both food and biomedical applications [69]. Polysaccharides from *Chlorella pyrenoidosa* were precipitated using different concentrations of ethanol, and their antioxidant activities were evaluated by determining the hydroxyl radical scavenging, DPPH radical scavenging, and superoxide anion scavenging activities. The results demonstrated that the polysaccharides exhibited positive effects in vitro in the elimination of free radicals [65].

#### 4. Algal Polysaccharide-Based Nanomaterials

With the rapid advancement of nanobiotechnology, nanomaterials have reached the food and pharmaceutical sectors and benefited consumers for clinical and medical treatments [70]. Polysaccharide-based nanosystems can reduce drug toxicity and side effects [5,71]. Nanomaterials based on algae and microalgae have received attention due to their physicochemical properties, stability, and low cost, in addition to characteristics such as hydrophilicity, high biodegradability, and biocompatibility [14,72]. Due to their specific controlled structures, algal biocompounds such as polysaccharides can fabricate nanomaterials (Table 2). According to Qiu et al. [73], polysaccharide-based nanocarriers can be divided into nanoliposomes, nanoparticles, nanomicelles, nanoemulsions and nanohydrogels (Figure 2). Among these materials, nanoparticles, nanofibers, and nanogels stand out [74,75].

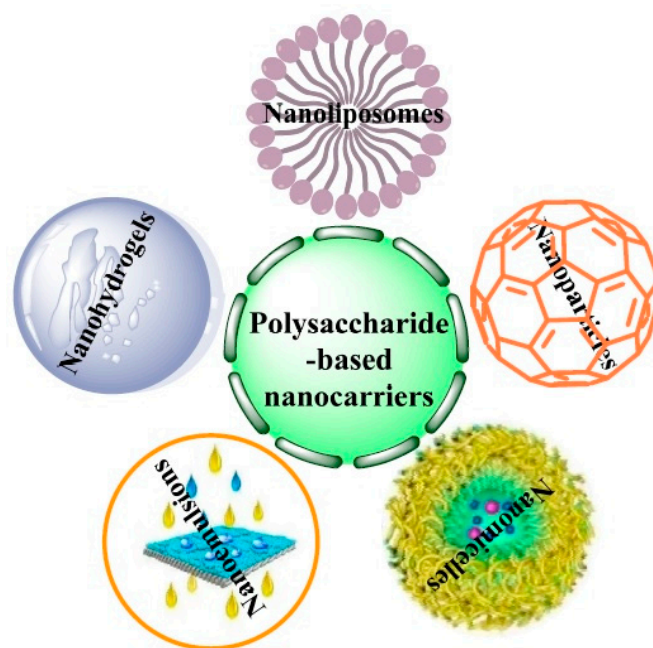
**Table 2.** Production of nanomaterials based on algal polysaccharides.

| Alga                     | Polysaccharide | Manufacturing Methodology   | Outcomes   | Reference |
|--------------------------|----------------|---|--|-----------|
| <i>Fucus vesiculosus</i> | Fucoidan       | The polyelectrolyte self-assembly method was used to obtain fucoidan/chitosan nanoparticles to encapsulate quercetin.     | Improved physicochemical properties; controlled release under simulated gastrointestinal conditions; encapsulation efficiency from 97% to 99%. | [76]      |
| Brown algae              | Fucoidan       | Nanoparticles prepared via electrostatic interaction using fucoidan and soybean protein isolated to encapsulate curcumin. | Salt tolerance, heat resistance, and storage stability; encapsulation efficiency of >95%.  | [77]      |

Table 2. Cont.

| Alga                           | Polysaccharide                          | Manufacturing Methodology   | Outcomes  | Reference |
|--------------------------------|---|---|---|-----------|
| <i>Laminaria japonica</i>      | Fucoidan                                | The antisolvent precipitation method was used to produce nanoparticles based on zein and fucoidan to encapsulate resveratrol.   | Photostability; ionic, pH, and storage stabilities; controlled release under in vitro digestion conditions; encapsulation efficiency of 95.4%.                      | [78]      |
| Red algae                      | K-carrageenan                           | The antisolvent precipitation method was used to produce zein-K-carrageenan nanoparticles to encapsulate quercetin.   | Improved water dispersibility, thermal stability, and controlled release under in vitro digestion conditions; encapsulation efficiency of 62%.                      | [79]      |
| <i>Sargassum angustifolium</i> | Fucoidan                                | Ultrasonic treatment was used to prepare nanoemulsions for fucoxanthin encapsulation.   | Controlled release under gastrointestinal conditions; encapsulation efficiency of 79%.  | [80]      |
| Red algae                      | Agar                                    | Precipitation and solvent-casting methods were used to prepare mineralized agar-based nanocomposite films.  | Mechanical and light barrier properties, antimicrobial activity against <i>Staphylococcus aureus</i> .  | [81]      |
| Red algae                      | K-carrageenan                           | Solvent-casting method was used to prepare nanocomposite films from k-carrageenan, konjac glucomannan, and TiO <sub>2</sub> nanoparticles.  | Thermal stability; mechanical and UV barrier properties; antimicrobial and fresh-keeping properties in strawberry preservation.                                     | [82]      |
| <i>Spirulina maxima</i>        | Pectin                                  | Pectin was extracted from microalga and then modified using high temperature and pressure for a specific duration. Subsequently, pectin nanoparticles were created through sonication of the modified pectin. | Potential to modulate gut microbial community, enhance the expression of immune-related genes, and improve gut morphology.  | [83]      |
| <i>Spirulina platensis</i>     | <i>Spirulina</i> polysaccharides        | Selenium nanoparticles with <i>Spirulina</i> polysaccharides have been developed with a solution-phase method. Microalgal polysaccharides were extracted with hot water.                                      | Enhanced cellular uptake and anticancer efficacy, potential candidate for further evaluation as a chemopreventive and chemotherapeutic agent against human cancers. | [84]      |
| Red microalgae                 | Sulfated polysaccharides                | Hydrogels were developed using sulfated polysaccharides, chitosan, and zinc.  | A broad spectrum of antimicrobial activities, potential use as wound dressings.   | [85]      |
| <i>Chlorella vulgaris</i>      | Carbohydrates containing polysaccharide | Secreted carbohydrates by microalgal cells were used for reducing and capping silver nanoparticles.   | Anticancer and antimicrobial applications.  | [86]      |
| <i>Ulva fasciata</i>           | Ulvan                                   | Deionized water was used to produce ulvan/polyvinyl alcohol (ulvan/PVA) nanofibers.   | Desirable thermal stability and mechanical properties for tissue engineering.   | [87]      |





**Figure 2.** Polysaccharide-based nanocarriers [73].

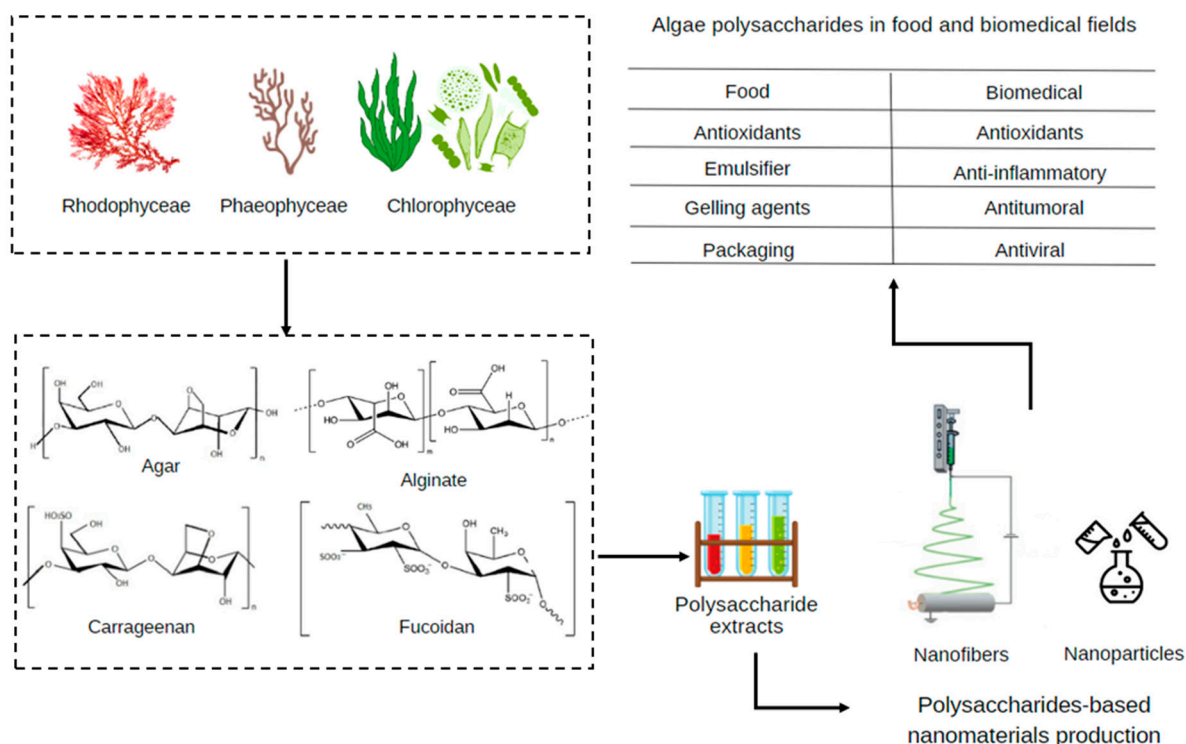
The abundant availability and biocompatibility characteristics demonstrate the ability of polysaccharide-based nanoparticles for use as delivery systems of bioactive compounds. Different techniques (ionic gelation, emulsion, and complexation of polyelectrolytes) can convert polymers, such as polysaccharides, into nanoparticles. Ionic gelation and complexation of polyelectrolytes are commonly employed by adding cationic molecules to these anionic polymers [88]. Thus, polysaccharides of algal origin can produce stable polymeric nanoparticles, with the desired shape, size, and charge, through the opposite charge interaction of the polysaccharide [14].

Nanofibers are elongated thin structures composed of synthetic polymer, natural polymer, or biopolymers. These nanomaterials exhibit different characteristics concerning their mechanical, electrical, and thermal properties, which gives them diverse applicability in the pharmaceutical, cosmetic, textile, and food industries. In addition, nanofibers allow the controlled release of several agents with high transport capacities due to their porosity. Nanofibers can be developed by phase separation, drawing, and electrospinning. Electrospinning has an advantage related to the ease of scaling up, reproducibility, and the application of non-aggressive conditions to the biocompounds used/added for developing fibers as bioactive compounds and polymers [89,90]. Due to their high porosity, small pore size, and high surface area, the application of polysaccharide-based nanofibers includes several fields, such as drug delivery, tissue engineering, bone regeneration, and wound dressing. Polysaccharide-based nanofibers have shown attractive and promising results for the safe administration of drugs [91].

Nanogels are nanometer-sized hydrogels produced by the chemical or physical crosslinking of polymeric chains. The three-dimensional network formed has water retention capacity and does not present solubility in an aqueous system [92,93]. Nanogels are nanomaterials reported for applications in many fields due to their high mechanical stability, strong drug-loading capacity, and smooth response to environmental stimuli for controlled release [91]. Polysaccharides are natural hydrogel-forming polymers. Polysaccharides isolated from algae can produce these nanomaterials [94]. In this way, nanomaterials based on algal polysaccharides are constantly under development to maximize and improve nano-delivery systems based on polysaccharides of algal origin.

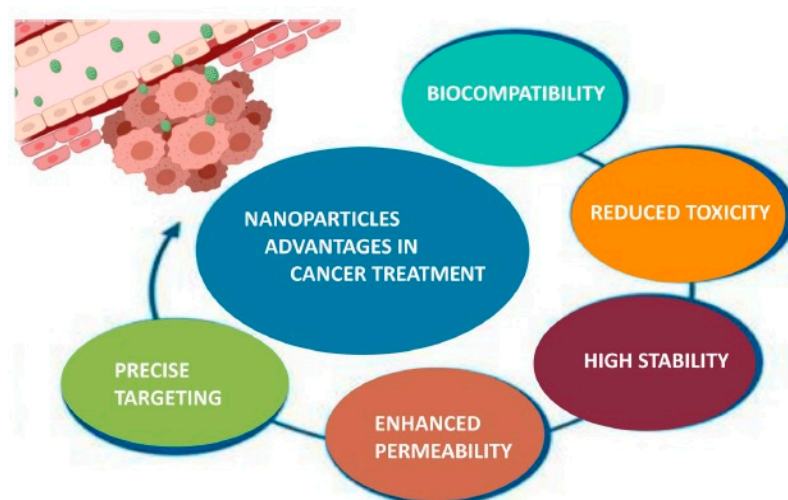
### 5. Nano-Formulations Added Algal Polysaccharides

The growth of the seaweed industry and biorefinery increase the need for high-value applications of biopolymers [94]. The inherent properties of marine polysaccharides, such as biodegradability and biocompatibility [15], make nanocarriers based on marine polysaccharides a high-potential platform in the biomedical, pharmaceutical, and food areas (Table 2, Figure 3). The manipulation of polysaccharides on a nanometric scale has contributed to increasing the potential of these components in a range of applications, boosting interdisciplinarity in the scientific world to maximize the exploitation of all the advantages of nanostructured polysaccharides [95].



**Figure 3.** Algal polysaccharides-based nanomaterials in food and biomedical applications.

Synthesized nanomaterials based on algae biopolymers, such as polysaccharides, can be used for coating and encapsulation and to contribute to sustainability [14]. Polysaccharide-based nanomaterials are reported for biomedical applications, such as wound healing, cancer treatment, tissue engineering, drug delivery, gene delivery, and antimicrobial activities [6]. Nanoparticles have many advantages in the treatment of cancer (Figure 4) and drug delivery. For example, fucoidan nanoparticles loaded with chemotherapeutic agents have potential in cancer treatment. Carrageenan-based nanoparticles are suitable carriers to offer continuous control for drug delivery. On the other hand, nanofibers based on ulvan polysaccharides have potential in different fields, such as dressings, gene delivery, tissue engineering, and drug delivery [14]. Moreover, polysaccharide-based nanomaterials have wide applications as functional ingredients since they have biologically active properties that provide health benefits and can prevent or treat diseases [96]. Another potentiality of polysaccharide-based nanomaterials is to reduce the energy density of several processed food products [97–99]. In addition, polysaccharides can be combined with other commercial biopolymers to form nanomaterials and develop food packaging with biodegradable, antimicrobial, and toxic-free nature [14].



**Figure 4.** Advantages of nanoparticles in cancer treatment [100].

### 5.1. Application in Food Science

The increasing awareness among consumers about foods that promote health has driven the food industry to develop products with the incorporation of bioactive compounds [101]. In this context, nanotechnology can contribute to obtaining functional foods and nutraceuticals. Nanoencapsulation of bioactive compounds for food enrichment can prevent the degradation of these compounds during processing and storage and increase stability and bioavailability, preserving their bioactivity [102,103]. Furthermore, using polysaccharides as encapsulants in the food industry can prevent the loss of volatile compounds and improve the dispersion of low-solubility compounds in the food matrix [103]. Polysaccharides from algae have characteristics of interest as an encapsulating material, such as bioavailability, biocompatibility, bioactivity, and non-toxicity [104].

Fucoidan has been studied as a component of the polymeric matrix for the nanoencapsulation of bioactive compounds to improve characteristics such as low solubility in water and instability to temperature and pH variations [105]. Studies have shown that the encapsulation of curcumin, quercetin, and resveratrol, using fucoidans as one of the polymeric materials, improved the stability of these compounds, allowing controlled release during simulated digestion in vitro [76–78]. This polysaccharide can be effective in preserving bioactive ingredients incorporated into functional foods.

Roy et al. [106] applied  $\kappa$ -carrageenan as a stabilizer of colloidal zein particles loaded with quercetin. Using this polysaccharide as a coating for the hydrophobic compound zein to encapsulate quercetin resulted in dispersibility in water, thermostability, controlled release, and antioxidant activity. Therefore, this system can be used as a vehicle for hydrophobic bioactive compounds. Gallón et al. [107] investigated the application of exopolysaccharides produced by the microalgae *Chlorella pyrenoidosa* and *Botryococcus braunii* as a stabilizer in the silver nanoparticle's synthesis. The microalgal exopolysaccharides enable the synthesis of particles with controlled and stable size and dispersion. The nanoparticles obtained exhibited antibacterial activity against *Staphylococcus aureus*, *Escherichia coli*, and *S. aureus* that was resistant to the antibiotic methicillin, indicating the potential application of these particles as antimicrobials in food packaging.

Oliyai et al. [80] evaluated the stabilization of nanoemulsions using natural polysaccharides as an emulsifier to encapsulate fucoxanthin. Fucoidans presented higher encapsulation efficiency (79%) compared with gum Arabic. Furthermore, both polymers showed a controlled release of fucoxanthin during simulated digestion in vitro. Richa and Choudhury [108] reported that fucoidans and  $\kappa$ -carrageenan as emulsifiers showed comparable properties to Tween 20 in nanoemulsions formulation for curcumin encapsulation. These authors found that fucoidans and levan increased the antioxidant activity of the system.

Polysaccharides have been investigated for the development of food packaging due to their properties, such as inherent protective function, gel formation capacity, and oxygen and carbon dioxide barriers. However, these compounds have poor barrier properties against water vapor due to their hydrophilic nature and poor mechanical stability [109]. Therefore, nanocomposites obtained from polymer blends with the incorporation of nanoparticles can be an alternative to improve the properties of films produced with algal polysaccharides [110]. Several studies have evaluated the development of films from nanoformulations containing algal polysaccharides and nanoparticles for applications as food packaging material [81,82,106].

The polysaccharide  $\kappa$ -carrageenan was used in the elaboration of a nanocomposite film containing konjac glucomannan and titanium dioxide nanoparticles. The film exhibited thermal stability, barrier properties against UV light, mechanical properties, water vapor permeability, hydrophobicity, and antifungal capacity. When applied as packaging for strawberries, this nanocomposite film resulted in the inhibition of the fungus *Penicillium viridicatum*, as well as a reduction in weight loss and titratable acidity, compared to fruits not packaged or stored in plastic packaging [82]. Similar properties were observed for nanocomposite films based on  $\kappa$ -carrageenan and silver nanoparticles, such as UV barrier, mechanical resistance, thermal stability, and antimicrobial activity against food-borne pathogenic bacteria (*Escherichia coli*, and *Listeria monocytogenes*) [106]. Agar-based nanocomposite films reinforced with Zn mineral also showed improved barrier and mechanical properties and antimicrobial activity against *Staphylococcus aureus* and *Candida albicans* [81]. These studies indicate that nanocomposite films based on polysaccharides of algal origin are promising as food packaging materials to preserve food quality and prevent contamination during storage.

## 5.2. Applications in Biomedical Science

Nanotechnology plays an indispensable role in the field of advanced medicine and biotechnology. Given that polysaccharides derived from algae and microalgae have demonstrated immunomodulatory, anti-inflammatory, antitumor, antibacterial, antiviral, and antioxidant properties [10,66,111], these compounds hold significant potential for utilization in the development of nanotechnological materials for biomedical applications [9,107,112].

Chandrarathna et al. [83] investigated the impact of modified pectin and modified pectin nanoparticles, derived from the microalgae *Spirulina maxima*, on the modulation of the intestinal microbiota of mice and immune responses, including antimicrobial, antiviral, and inflammatory cytokines. The results revealed that mice treated with nanopectin experienced weight gain, attributed to improved digestibility and enhanced nutrient availability resulting from the smaller particle size. Additionally, the smaller particle size (64.11 nm) provided a larger surface area for microbial growth within the gut compared to the longer pectin parent molecules. The mice treated with nanopectin displayed an increased density of goblet cells in the intestinal barrier, which obstructed the access of pathogenic microbes to the intestinal epithelium. Furthermore, these mice exhibited an increased expression of intestinal alkaline phosphatases, known to have an anti-inflammatory effect.

Selenium nanoparticles were synthesized using varying amounts of polysaccharide extract from the marine microalgae *Spirulina platensis*. These nanoparticles were evaluated for their cytotoxicity against multiple cancer cell lines. The synthesized nanoparticles exhibited long-term stability for a minimum of three months and a nearly nine-fold increase in cell uptake. Notably, the material demonstrated selectivity towards cancer cells over normal cells, highlighting its potential for cancer chemoprevention [84].

Liberman et al. [85] formulated hydrogels by incorporating zinc and sulfated polysaccharides derived from three red microalgae (*Porphyridium* sp., *Dixonella grisea*, and *Porphyridium aerugineum*) with chitosan. These nanomaterials can be applied as a physical barrier against bacterial contamination while maintaining a moist environment, offering improved biocompatibility and mechanical properties. The demonstrated characteristics of these hydrogels underscore their potential as effective wound dressings.



Carbohydrates containing polysaccharides from *Chlorella vulgaris* were utilized in the biosynthesis of silver nanoparticles (AgNPs). The resulting particles exhibited a zeta potential of +26 mV, indicating their colloidal stability and making them highly desirable for applications in anticancer and antimicrobial fields. Additionally, the minimum inhibitory concentrations against Gram-positive bacteria (*Staphylococcus aureus*) and Gram-negative bacteria (*Escherichia coli*) found were  $37.5 \mu\text{g mL}^{-1}$  and  $9.4 \mu\text{g mL}^{-1}$ , respectively. When Hep-G2 cancer cells were exposed to AgNPs at a concentration of  $4.7 \mu\text{g mL}^{-1}$ , their viability decreased to 61% after 24 h and 37% after 48 h of treatment [86].

Nanofibers, due to their structural similarity to the extracellular matrix of the human body, have garnered significant attention as a potential material for tissue engineering [113]. Amongst the various candidates, algae belonging to the *Ulva* genus, which contain ulvans as their primary polysaccharides, show promise for nanofiber production in this field. By employing an eco-friendly extraction method using water as the solvent, polysaccharides were successfully extracted from *Ulva fasciata*, and ulvan/polyvinyl alcohol nanofibers were developed. These nanofibers exhibited desirable thermal stability and mechanical properties, rendering them suitable not only for tissue engineering but also for a range of other biomedical applications [87].

## 6. Industrial Potential of Algal Polysaccharides

The potential applications of polysaccharides produced by algae in several industrial sectors and the rising demand for sustainable products can boost the market for these polysaccharides. The global seaweed polysaccharides market has exhibited steady growth in recent years. Projections indicate that sales of these products will increase from USD1 million in 2023 to approximately USD3 million in 2033 [114,115].

In this context, several companies that produce and commercialize polysaccharides from macroalgae have been identified. One such product is FoodGel™ Carrageenan, the polysaccharide  $\kappa$ -carrageenan extracted from the seaweed *Eucheuma cottonii* and produced by the FoodCHEM company [116]. This product is of food-grade quality and is commonly used as an emulsifier and stabilizer in the food industry. Other companies producing this polysaccharide for application in food products are Cargill [117], CP Kelco [118], and Gelymar [119].

Maritech® is the fucoidan polysaccharide extracted and purified from seaweed. It is produced by Marinova Pty Ltd. for application in functional foods and beverages, dermatological formulations, and animal health products [120]. Gely™Alg is a line of sodium alginate products obtained from brown algae by the company Gelymar with wide application in the food and pharmaceutical industries [119]. Qingdao Gather Great Ocean Algae Industry Group produces sodium alginate, carrageenans, and agar-agar extracted from seaweed for use in the food, pharmaceutical, and chemical industries. This company also manufactures empty capsules from these polysaccharides [121].

However, the industrial production of microalgal polysaccharides is still limited. The main market is the production of microalgal EPS for application in the cosmetics industry due to its antioxidant, anti-inflammatory, and antimicrobial properties [122]. Companies predominantly obtain this polysaccharide from the microalgae *Porphyridium cruentum* [8].

Regarding the nanotechnological application of algal polysaccharides, although research has shown promising results in several areas, the commercialization of these products may require further advances in research. Bioavailability, toxicity, and production costs should be further explored, as well as regulatory issues [14,123].

## 7. Conclusions

Algae and microalgae are sustainable resources for producing biocompatible and renewable polysaccharides capable of synthesizing nanomaterials for applications in food and biomedical fields. Nanotechnology combined with polysaccharides of algal origin can prevent the loss of volatile compounds and improve the dispersion of low-solubility compounds in the food matrixes. Moreover, these nanomaterials are promising approaches

for developing packaging systems to preserve food quality. Packaging produced with added nanomaterials based on algal polysaccharides can improve barrier properties against UV light, mechanical properties, and permeability to water vapor.

Polysaccharide-based nanostructures also have attracted much attention in biomedical carriers due to their excellent encapsulation capacity. Polysaccharides derived from algae and microalgae demonstrate immunomodulatory, anti-inflammatory, antitumor, and antiviral properties for developing nanotechnological materials for biomedical applications. Algal polysaccharide nanomaterials can improve digestibility and nutrient availability, and they demonstrate potential for cancer chemoprevention and tissue engineering. In addition, using polysaccharides as a coating contributes to thermostability, a controlled release of bioactive compounds, and antioxidant and antimicrobial activities, which are promising characteristics for biomedical and food areas. Therefore, in addition to minimizing environmental contamination through CO<sub>2</sub> fixation, the contribution of microalgae to the production of polysaccharides extends to the manufacture of nanomaterials for various applications in the food and biomedical industry context.

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