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Review

Comprehensive Review on the Biomedical Applications of Marine Algal Polysaccharides

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Abstract

Marine algal polysaccharides (MAPs) are multifunctional biopolymers with significant potential in biomedical applications. Derived from brown, red, and green algae, key examples include alginate, agar, carrageenan, fucoidan, ulvan, and laminarin. Their structural diversity underlies a broad range of biological activities, particularly among sulfated polysaccharides, which exhibit antiviral, anticancer, anticoagulant, immunomodulatory, and antioxidant effects. Owing to their biocompatibility and tunable physicochemical properties, MAPs are also valuable in wound healing, tissue regeneration, and drug delivery. Advances in ultrasound-, microwave-, and enzyme-assisted extraction methods have enhanced yield and functionality. This review combines structural, extraction, and biomedical views on MAPs, with a focus on how molecular characteristics relate to their potential as drugs. Future work should focus on scalable green extraction, molecular-level characterization, and clinical validation to develop MAPs-based biomaterials for next-generation drug delivery, wound healing, and tissue engineering.

Keywords: marine algal polysaccharides; sulfated polysaccharides; biomedical applications; extraction techniques; antiviral activity; anticancer properties; wound healing; regenerative medicine

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1. Introduction

Algal polysaccharides represent complex carbohydrates sourced from diverse algal species. They are essential to the structural and functional characteristics of algae and have attracted considerable attention due to their varied applications across several industries, such as food, pharmaceuticals, biotechnology, and environmental management [1,2]. Marine macroalgae (seaweeds) are classified into three major phyla (divisions) based on their

unique photosynthetic pigments and other cellular characteristics: rhodophyta (red algae), ochrophyta, class phaeophyceae (brown algae) and chlorophyta (green algae) [3].

Polysaccharides represent a category of biomacromolecules located within the structural components of marine algal cell walls. Numerous polysaccharides isolated from marine algae have recently attracted significant interest for applications in cosmetics, functional foods, and pharmaceuticals such as anticoagulant, antioxidant, anticancer, and immunomodulatory effects [4]. Various marine algal species across different divisions are rich sources of diverse polysaccharides. For instance, *Enteromorpha linza* (*Ulva*) and *Capsosiphon fulvescens* from the Chlorophyta group produce polysaccharides with well-documented health benefits [5]. The *Phaeophyceae* class, including *Sargassum muticum*, *Ecklonia cava*, *Undaria pinnatifida*, and *Laminaria japonica*, produces fucoidans and alginates with promising biological activities, such as anti-inflammatory, anticoagulant, and immunomodulatory effects [6]. Additionally, red algae from the rhodophyta group, such as *Carpopeltis affinis*, *Chondrus ocellatus*, and *Scinaia japonica*, are known for carrageenan and agar production and are used in the medical, pharmaceutical, and food industries [7]. Collectively, these marine algae serve as rich repositories of bioactive compounds with potential applications in drug development, nutraceuticals, and other health-related fields [8] (Figure 1).

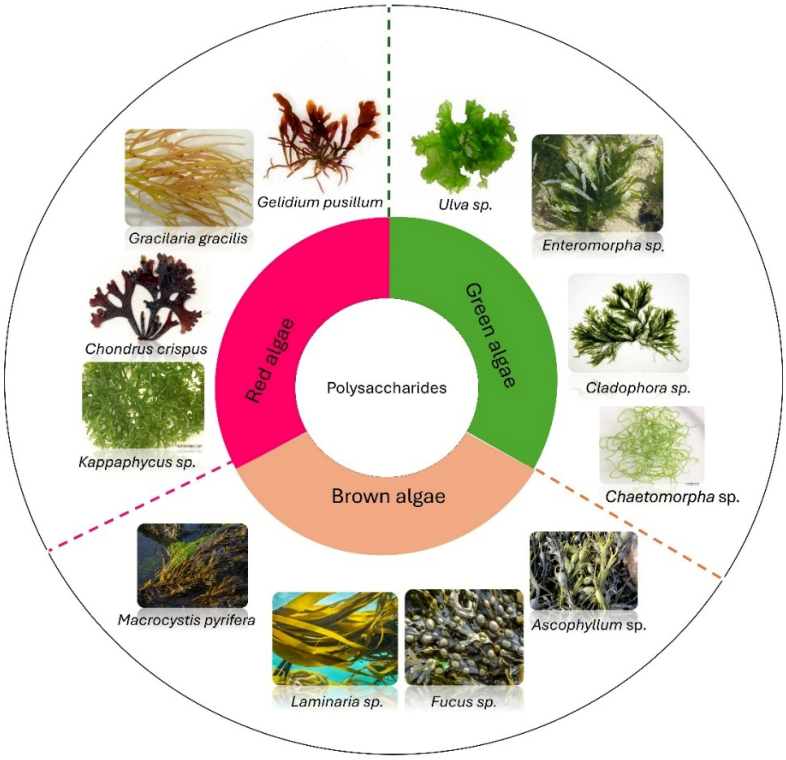


Figure 1. Marine algae species are known for producing a variety of polysaccharides.

Marine macroalgae represent rich sources of polysaccharides, predominantly sulfated polysaccharides, which exhibit remarkable diversity. Sulfate groups play a crucial role in the bioactivity of marine polysaccharides, significantly enhancing their biomedical potential. These groups contribute to various biological activities, including anticoagulant, antiviral, anticancer, and immunomodulatory effects. The presence and degree of sulfation influence the structural conformation, solubility, and interaction of polysaccharides with biological targets. Marine algal polysaccharides, such as fucoidan, carrageenan, and sulfated galactans, derive their therapeutic properties from these sulfate groups, making them promising candidates for drug development, functional foods, and regenerative medicine. Further research is needed to optimize sulfation patterns for enhanced efficacy

in biomedical applications [9]. Marine sulfated polysaccharides exhibit strong binding to cationic proteins and enhanced bioactivity due to their sulfate groups, making them valuable for food, cosmetic, and pharmaceutical applications. Despite significant progress in understanding their structure and biological activity, their complex molecular nature leaves structure–activity relationships only partially understood. Further research is needed to address these gaps [10].

Sulfated alginate (S–Alg) has emerged as a promising heparin-mimetic with applications in drug development and biomaterials. Recent studies (2017–2023) have advanced its synthesis, characterization, and material fabrication, including scaffolds, coatings, and multicomponent biomaterials. Notably, S–Alg shows potential as an antitumor agent, with ongoing research into its safety, biodistribution, and therapeutic efficacy, highlighting its biomedical significance [11]. The chlorosulfonic-acid–pyridine method is a preferred technique for synthesizing sulfated polysaccharides, whose anticoagulant activity depends on sulfate group substitution, degree of substitution, molecular weight, side chain structure, and glycosidic bond conformation. These polysaccharides exert anticoagulant effects through multiple pathways, including inhibiting coagulation factors, activating antithrombin III and heparin cofactor II, preventing platelet aggregation, and promoting fibrinolysis [11,12].

Although some similarities exist between polysaccharides derived from these organisms, they can vary significantly in their structure and composition. The biological origin and biodegradability of these biopolymers, combined with their diverse functionalities, make them promising candidates for applications in pharmaceuticals, therapeutics, and regenerative medicine [13]. MAPs and their composites have garnered considerable interest in biomedical research, owing to their unique properties and potential therapeutic benefits. Polysaccharides, derived from various seaweeds and algae, exhibit a diverse range of chemical compositions and structures, making them versatile materials for biomedical applications. Their biocompatibility, biodegradability, and abundance make them attractive candidates for use in various medical applications [14].

Currently, bioactive natural ingredients are in demand in a range of industries, including food, pharmaceuticals, biomedicine, and cosmetics. Industries highly value bioactive natural ingredients, but synthetic ingredients and genetically modified organisms (GMOs) also play significant roles. While synthetic ingredients provide consistency, cost-effectiveness, and scalability, they frequently spark safety concerns, have greater environmental effects, and are not as popular among consumers. GMOs can enhance production efficiency and yield but face public resistance and regulatory challenges due to concerns about safety and ecological impacts [15]. Developing sustainable and consumer-acceptable solutions remains a key challenge for effective integration of these alternatives. This has led to an increased focus on studying marine species (macroalgae) [16].

The growing interest in natural products for disease treatment and health improvement has intensified research on marine organisms such as cyanobacteria and algae. In the last ten years, research has shown that brown, red, and green seaweeds and their polysaccharides can be good for your health and nutrition [17]. This review provides an integrated analysis of MAPs and their composites, emphasizing structural features, extraction techniques, and biomedical applications. Unlike existing reviews, it offers a comparative perspective linking structural characteristics to therapeutic potential, including anti-inflammatory, antioxidant, antimicrobial, and anticancer properties. Additionally, it outlines current challenges and future opportunities in developing MAP-based materials for pharmaceuticals and regenerative medicine (Table 1).

Table 1. Classification and structural features of major polysaccharides from marine algae.

Polysaccharide	Source Algae	Chemical Composition	Structural Characteristics	Classification	References
Alginate	Brown algae (*Laminaria*, *Ascophyllum*)	β-D-mannuronic acid (M) and α-L-guluronic acid (G)	Linear copolymer of (1→4)-linked M and G residues arranged in blocks (MM, GG, MG)	Structural polysaccharide	[17]
Carrageenan	Red algae (*Kappaphycus*, *Chondrus*)	Sulfated galactose units	Linear galactans with alternating (1→3)-β-D-galactose and (1→4)-α-D-galactose with sulfate groups	Sulfated galactan	[18,19]
Agar	Red algae (*Gelidium*, *Gracilaria*)	Galactose and 3,6-anhydro-L-galactose	Repeating disaccharide units of agarose; low sulfate content	Structural galactan	[19]
Fucoidan	Brown algae (*Fucus*, *Undaria*)	Sulfated L-fucose, with possible galactose, xylose	Highly branched, heterogeneous sulfated polysaccharide with varying structure	Sulfated fucan	[20]
Laminarin	Brown algae (*Laminaria*, *Eisenia*)	Glucose	Storage β-glucan, mostly linear with some branching	Storage polysaccharide	[21,22]
Ulvan	Green algae *Ulva*	Sulfated rhamnose, glucuronic acid, iduronic acid, xylose	Complex branched polysaccharide with high uronic acid and sulfate content	Sulfated rhamnan	[23,24]

2. Biochemical Composition and Structural Characteristics

Polysaccharides are polymers of monosaccharides or simple sugars bound together by glycosidic linkages. MAPs are complex molecules primarily derived from seaweeds that show remarkable biochemical diversity and structural characteristics. Composed of various monosaccharide units, such as glucose, mannose, galactose, and fucose, these polysaccharides exhibit distinct arrangements and functional groups, influencing their solubility, gelation behaviour, and biological activities [25]. The composition may also include sulfate groups, which contribute to the sulfated polysaccharide nature of some algal polysaccharides. The specific composition varies among different algal species, and even within different parts of the same alga [9]. Polysaccharides, particularly cell wall structural polysaccharides, are abundant in marine algae along with mucopolysaccharides and storage polysaccharides. Structurally, they range from linear to highly branched chains, forming intricate three-dimensional networks. These polysaccharides play essential roles in marine organisms as structural components and physiological processes [26]. The seaweed species of interest had a total polysaccharide content ranging from 4% to 76% of dry weight [27]. *Ascophyllum*, *Porphyra*, and *Palmaria* species have the highest levels; however, green seaweed species such as Ulva also have significant contents, reaching up to 65%

of the dry weight [28]. The biochemistry of MAPs is a complex and diverse field that encompasses their composition, structure (Figure 2), biosynthesis, and biological activity. Here, we provide an overview of the biochemistry of MAPs and their composites. The biological activities of these polysaccharides appear closely linked to their structural features, especially the type of glycosidic bonds and the presence of sulphate groups. For instance, both carrageenan and sulphated galactan exhibit anticoagulant properties, suggesting that sulphation plays a key role in blood-thinning effects. The therapeutic potential of fucoidan and laminarin—two bioactive polysaccharides with distinct structures and functions—has been well documented [29]. Fucoidan, composed mainly of fucose and uronic acid, possesses anti-inflammatory and anticancer properties, which are influenced by its α-1,3 and α-1,4 glycosidic linkages [30]. Laminaran, consisting of glucose units with β-1,3 and β-1,6 linkages, exhibits strong anticancer activity. Molecular weight variation plays a crucial role in their bioactivity; fucoidan's higher molecular weight is associated with enhanced anti-inflammatory effects, while laminarin's lower molecular weight contributes to its anticancer potential [31]. These polysaccharides hold great promise for biomedical applications, functional foods, and pharmaceutical development, warranting further investigation into their mechanisms and clinical use [13]. Naturally occurring bioactive compounds, particularly seaweed-derived polysaccharides, are widely recognized for their health benefits and have been traditionally used in folk medicine. These polysaccharides demonstrate diverse biological activities, including antioxidant, anticancer, antiviral, drug-delivery, wound-healing, and anti-inflammatory effects. Recent studies highlight their significant biomedical and pharmaceutical potential [32,33].

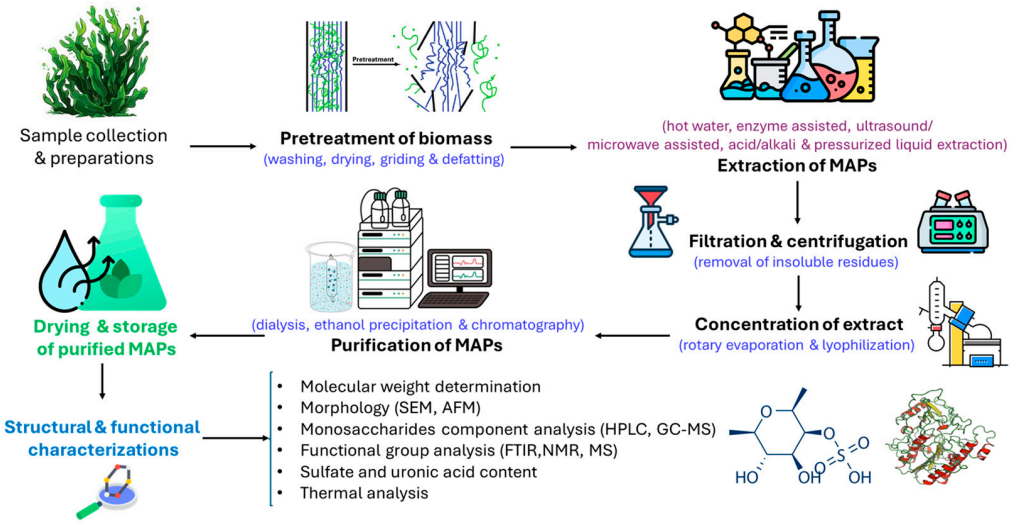


Figure 2. Workflow for the extraction, purification, and structural characterization of marine algal polysaccharides. (SEM-scanning electron microscopy; AFM—Atomic Force Microscopy; HPLC—High-Performance Liquid Chromatography; GC-MS—Gas Chromatography–Mass Spectrometry; FTIR—Fourier Transform Infrared Spectroscopy; NMR—Nuclear Magnetic Resonance spectroscopy and MS—Mass Spectrometry).

2.1. Alginic Acid and Its Derivatives

Brown seaweeds contain polysaccharides called alginates, which were discovered in the 1880s by British scientist E.C.C. Stanford. In 1929, California began producing alginates on an industrial scale [34]. Alginate is in the walls and intracellular regions of algal cells. The properties of alginate can vary based on the species, growing season, and extraction method [35]. Alginates are extracted from seaweeds and exist in both salt and acid forms. The salt form, which can account for a sizable amount of the seaweed's dry weight, is essential for the cell walls of brown seaweeds, while the acid form, alginic

acid, is a linear polyuronic acid [36]. Alginate is primarily composed of linear chains of β-D-mannuronic acid and α-L-guluronic acid, which are synthesized within algal cells by enzymes such as mannuronan C5-epimerase and guluronan C5-epimerase. These enzymes convert precursor molecules, such as GDP-mannuronic acid and GDP-guluronic acid, into their respective monosaccharide units. Subsequently, polymerization occurs via the action of glycosyltransferases, leading to the formation of alginate chains [36]. The arrangement of β-D-mannuronic acid and α-L-guluronic acid units in alginate chains varies, which influences its physical and chemical properties. The presence of these monosaccharide units allows alginate to form gels through ionic interactions with divalent cations such as calcium [36,37]. Brown algae, such as *Laminaria* and *Macrocystis*, are rich sources of alginate [38]. Commercial alginate is primarily extracted from brown seaweeds, such as *Macrocystis pyrifera*, *Laminaria hyperborea*, and *Ascophyllum nodosum* [39,40]. The resultant alginic acid was a white to yellowish-brown powder with a melting point above 300 °C and an average molecular weight of approximately 240,000 Dalton. Its aqueous solution, the viscosity is approximately five times that of starch and is mildly soluble in hot water, but insoluble in cold water and organic solvents [41]. Although it is acid-resistant, when it comes in contact with intense hydrochloric acid, it is decarboxylated. Selective adsorption effects were observed for metal ions, namely Fe (II) ions [42,43].

2.2. Agar

Agar is a hydrocolloid seaweed that is based on polysaccharides and has notable gelling ability [44]. Agarose and agaropectin, components of agar, are synthesized within red algae cells through enzymatic processes [45]. Agarose consists of linear chains of alternating D-galactose and 3,6-anhydro-L-galactose units, whereas agaropectin has a more heterogeneous structure. Agar biosynthesis involves glycosyltransferases and modifying enzymes that catalyze the polymerization and modification of precursor molecules. Agarose forms double helices through hydrogen bonding between D-galactose and 3,6-anhydro-L-galactose units, which contributes to its gel-forming properties [46]. On the other hand, agaropectin has a more branched structure with various glycosidic linkages. Red algae species, such as *Gracilaria* and *Gelidium*, are commonly used for agar extraction [47]. Several species of macroalgae, such as *Gracilaria*, *Gelidium*, and *Pterocladia*, are rich sources of agar. Variations in agar content among different species can be attributed to genetic factors, environmental conditions, and cultivation techniques. For example, *Gracilaria* species are commonly cultivated for agar production because of their high agar content and robust growth in various aquatic environments. In contrast, *Gelidium* species thrive in colder waters and are preferred for agar extraction in certain regions [48].

2.3. Carrageenan

Carrageenan is a linear sulfated polysaccharide extracted from red seaweeds [49]. It is composed of repeating D-galactose and 3,6-anhydro-D-galactose units, which are sulfated to varying degrees depending on the type of carrageenan [50]. There are three main types of carrageenan based on their sulfation patterns: kappa-, iota-, and lambda-carrageenan [50]. Kappa carrageenan contains one sulfate group per disaccharide unit, iota carrageenan contains two sulfate groups per disaccharide unit, and lambda-carrageenan contains three sulfate groups. The sulfation pattern in carrageenan plays a crucial role in its gel-forming properties and applications in various industries, such as food, pharmaceuticals, and cosmetics [51]. The unique biochemical structure of carrageenan allows it to form strong and elastic gels, making it a valuable ingredient in a wide range of products per disaccharide unit.

Carrageenan is primarily extracted from various red seaweed species belonging to the class rhodophyceae [52]. *Kappaphycus alvarezii* is another red seaweed species cultivated for carrageenan production in the Philippines and Tanzania (orbita). *Chondrus crispus*, also known as Irish moss, is a wild-harvested red seaweed found in the North Atlantic Ocean, and is a traditional source of carrageenan. Various species of *Gigartina*, such as *Gigartina skottsbergii*, are also used as sources of carrageenan. Red seaweeds are rich in carrageenan, which is extracted from their cell walls and used in various industries for its gelling, thickening, and stabilizing properties [53].

Carrageenan derivatives are modified forms of carrageenan that have been chemically altered to enhance certain properties and functionalities for specific applications. Common carrageenan derivatives include hydrolyzed carrageenan, carboxymethyl carrageenan, and succinylated carrageenan [54]. These carrageenan derivatives offer unique functionalities and advantages compared to native carrageenans, allowing for a broader range of applications in different industries [54]. Several chemical changes have been made to native kappa carrageenan, which have produced new derivatives with unique properties. For example, Barahona et al. [55] synthesized novel cationic kappa carrageenan derivatives with enhanced amphoteric characteristics for use as flocculating agents for wastewater treatment. Similarly, Bardajee et al. [56] synthesized kappa-carrageenan-g-poly (acrylic acid) and graft copolymer (kappa-carrageenan-g-vinylsulfonic acid), known for their improved gel-forming, hydrophilic, and sensitive qualities. Additionally, Chen et al. [56] reported the synthesis of kappa-carrageenan-g-poly (methacrylic acid)/poly (N, N-diethylacrylamide) with heightened heat and pH sensitivity. Jiang et al. [57] synthesized O-succinyl and O-maleoyl derivatives of kappa-carrageenan, noted for their enhanced molecular stiffness and elevated negative charge density. The derivatives possess potential applications across multiple industries due to their customized properties.

2.4. Fucoidans

Fucoidans are sulfated polysaccharides that are found naturally in brown algae and are thought to be useful metabolic modifiers for cancer treatment because they prevent many types of cancer cells from proliferating, forming colonies, and migrating [58,59]. The composition of monosaccharides (sulfated fucans, sulfated galactofucans, sulfated fucogalactans, etc.), the types of α- and β-glycosidic bonds between the monosaccharide residues, and the substituents (primarily sulfation, acetylation, and/or branching) can differ greatly in the structure of these polysaccharides [60]. Fucoidans from brown algae have various chemical derivatives, such as over-sulfated, aminated, phosphorylated, and acetylated fucoidans, which have more noticeable functional characteristics than native polysaccharides [61]. The wide spectrum of biological activities of these polysaccharides, such as antiviral, anticancer, antioxidant, radio-sensitizing, radioprotective, antithrombotic, and anticoagulant properties, has attracted a lot of attention [62]. It is well known that fucoidans and other marine polysaccharides containing sulfated fucose have anticoagulant qualities comparable to those of heparin. Owing to their plant-based composition and high fucoidan content, brown algae are comparatively safe, inexpensive, and eco-friendly anticoagulants [6].

Several macroalgae species are known for their high fucoidan content, which is a sulfated polysaccharide with various bioactive properties. Among them, species such as *Fucus vesiculosus* (commonly known as bladder wrack) and *Undaria pinnatifida* (wakame) are notable for their commercial importance. *Fucus vesiculosus*, found in cold seawater, is harvested for its fucoidan-rich extracts, which are used in dietary supplements and skincare products because of their antioxidant and anti-inflammatory properties. *Undaria pinnatifida*, native to East Asia and now cultivated globally, is known for its high fucoidan content,

contributing to its use in functional foods, nutraceuticals, and cosmetics. These macroalgae exemplify the potential of fucoidans from marine sources for various industrial and health applications [63]. Not all fucoidans and/or their derivatives exhibit anticoagulant properties [64]. Additionally, smaller molecular weight (Mw) fractions of fucoidan have higher biological activity and are also used as dietary supplements, whereas the low cell permeability and high viscosity of high Mw fucoidan may restrict its pharmacological efficacy [65]. Various derivatives of fucoidan, such as low molecular weight, over-sulfated, phosphorylated, aminated, acetylated, and benzoylated forms, have been studied for their anticoagulant and antioxidant properties. The fucoidan derivative and benzoylated low-molecular-weight fucoidan derivative exhibit greater antioxidant activity [66].

2.5. Ulvan

Green macroalgae (chlorophyta) belonging to the genus *Ulva* are consumable seaweeds that possess many bioactive components that promote good health [67]. *Ulva* has a high dietary fibre content that helps gastrointestinal health and may lower the risk of developing chronic illnesses. The primary active ingredient in *Ulva* is the soluble fibre ulvan, a gelling sulfated polysaccharide that has biological properties that include antiviral, antioxidant, immunomodulatory, antihyperlipidemic, and anticancer properties [68]. Ulvan is a polysaccharide found in marine algal cell walls that accounts for 9–36% of the dry weight of total biomass. It is mostly composed of xylose, glucuronic acid, iduronic acid, and sulfated rhamnose [69]. The main sugar components of ulvans, which are polyanionic heteropolysaccharides, are rhamnose (45.0 mol%), glucuronic acid (22.5 mol%), iduronic acid (5.0 mol%), and xylose (9.6 mol%). Frequently, α- and β-(1,4)-linked monosaccharides (rhamnose, xylose, glucuronic acid, and iduronic acid) with distinctive repeating disaccharide units comprise the ulvan backbone [70].

Ulva oligosaccharide, sometimes referred to as a degraded ulvan, has higher solubility and bioavailability [71]. As a result, research on the breakdown and processing of Ulva oligosaccharides has become increasingly important. Ulva oligosaccharides can be divided into three categories based on their preparation: enzymatic, physical, and chemical degradation [71]. Chi et al. employed ulvan lyase to cleave ulvan from *U. clathrata* via a β-elimination reaction [72]. This results in the formation of three degradation products, UO-1, UO-2, and UO-3, each with a distinct molecular weight. UO-1 and UO-2 are disaccharides, D-ΔGlcA-(1 → 4)-α/β-L-Rha3S, and tetrasaccharides, D-ΔGlcA-(1→4)-α-L-Rha3S-(1 → 4)-β-D-Xyl-(1→ 4)-α/β-L-Rha3S, respectively, with lower molecular weights. The study of the UO-3 structure, which has a large molecular weight, revealed that it primarily consists of A3s and U3s type disaccharide repeat units, with a minor presence of U2′,3s type disaccharide repeat units. This indicates that ulvan is a complex polysaccharide predominantly composed of A3s or B3s type disaccharide repeat units, along with a smaller proportion of U3s-or U2′,3 s-type disaccharide repeats units [71]. Give examples of physical and chemical degradation as well as usage/application.

Depending on the intended use, ulvan's structural degradation during the extraction process may decrease or increase its functionality. During the extraction process, the degree of polymerization and the degree of sulfation of ulvan are the two structural characteristics most vulnerable to deterioration [71]. Ulva oligosaccharides are prepared through chemical degradation by breaking the glycosidic bonds in ulvan using strongly acidic or oxidizing agents. Yaich et al. [73] observed that during ulvan extraction, alcohol precipitation under low pH conditions yielded numerous low-molecular-weight components. This finding supports the use of strong acids for further preparation of oligosaccharides, facilitating the effective degradation of the polysaccharide structure. Additionally, ulvan can be degraded using strong oxidants. For instance, hydrogen peroxide (H_2O_2) has been used to

break down ulvan into oligosaccharides with molecular weights of 10.6 kDa and 6.8 kDa, respectively [68]. However, studies on the physical degradation of ulvan are limited. Yu et al. used microwave and high-pressure methods for ulvan degradation [74]. Moreover, Simona et al. showed that ulvan could undergo self-hydrolysis in hot water at high temperatures, and by optimizing the temperature, up to 78.7% of rare sugars like rhamnose, glucuronic acid, and other minor degradation products could be recovered [75].

2.6. Laminarin

Laminarin is a storage glucan composed of 25–50 glucose units linked primarily by β-1,3-glycosidic bonds, with occasional β-1,6-glycosidic branches at the O-6 position. It is found in the fibrillar cell walls and intercellular spaces of brown algae. Structural variations in laminarin depend on the nature of its reducing end—G-type laminarins contain a terminal glucose residue, whereas M-type laminarins possess a mannitol residue, resulting in differences in solubility [76,77]. Laminarin, a water-soluble polysaccharide, exhibits promising medicinal properties but remains underutilized. Due to its biodegradable, biocompatible, and non-toxic nature, it has attracted attention for use in functional foods, nutraceuticals, and biomedical applications [78,79]. This bioactive compound offers a wide range of health benefits, with potential protective effects against cardiovascular diseases, metabolic disorders, cancer, diabetes, obesity, inflammation, osteoarthritis, oral diseases, multiple sclerosis, Alzheimer's disease, Parkinson's disease, and vision-related conditions [80,81]. Kadam et al. [82] investigated the antioxidant and antibacterial properties of crude laminarin extracts, reporting a high free radical scavenging activity that confirms its antioxidant potential. Similarly, Choi et al. [83] demonstrated the anti-inflammatory properties of laminarin and its ability to activate immune responses, underlining its therapeutic potential due to its antioxidant characteristics. Liu et al. [84] further supported these findings, reporting its antioxidant effects against free radicals and oxidative damage caused by reactive oxygen species (ROS).

Laminarin exerts its anti-inflammatory effects by stimulating innate immunity through β-glucan interactions. In tumour microenvironments, it enhances immune responses, suppresses inflammation, and promotes tumour inhibition. Studies indicate that β-glucans enhance antimicrobial activity in macrophages, monocytes, and neutrophils, leading to their maturation and increased release of cytokines and chemokines. Laminarin also activates adaptive immune cells, including CD4+T cells, CD8+ cytotoxic T lymphocytes, and B cells. Furthermore, it induces apoptosis in tumour cells by generating ROS, causing oxidative stress and promoting tumour cell destruction [81,85].

3. Extraction and Purification Methods

A sequence of extraction procedures can be used to successfully separate the crystalline, fibrillar, and matrix polysaccharides found in algal cell walls from the raw materials. Figure 2 illustrates a comprehensive workflow for the extraction, purification, and structural characterization of MAPs. The process begins with macroalgae cultivation, followed by cell harvesting to obtain biomass. Various extraction techniques, including high-pressure steam, Soxhlet, alkali, and acid extraction, are employed to isolate polysaccharides, while advanced methods like hydrothermal, microwave-assisted, ultrasound-assisted, gamma irradiation, and UV degradation further enhance yield and functionality. Enzymatic methods such as enzymatic hydrolysis, agarose application, biosynthesis, and microbial fermentation are also utilized for specific MAPs modifications. Post-extraction, MAPs undergo separation and purification using methods like ultracentrifugation, electrophoresis, membrane separation, aqueous two-phase systems, and ammonium sulfate precipitation. MAPs are structurally characterized to elucidate their potential applications or to determine

their structure–function ratio. The difference in the solubilities of these chemicals serves as the foundation for their isolation. Depending on whether the polysaccharides comprise sulfate or carboxylic groups, the extraction procedure proceeds differently in the following steps [86]. The process begins with cold-water extraction, followed by extraction using hot water and alkali solutions at various temperatures and pH levels. This method is highly effective for isolating key polysaccharides from different types of algae, such as sulfated galactans, agars, and carrageenans from red algae; sulfated fucoidans and xylans from brown algae; and heteroglycuronans and ulvans from green algae. Owing to its versatility, it can be considered a universal technique. This approach can be applied to polysaccharides in a range of media under alkaline, acidic, or neutral conditions [9].

Alginate is primarily extracted from brown seaweeds, including *Macrocystis pyrifera*, *Ascophyllum nodosum*, and various types of laminaria [10]. Two recovery methods are commonly employed for extracting sodium alginate from algal sources. In one method, known as acid precipitation, a sodium alginate solution is treated with acid, resulting in the formation of insoluble alginic acid [36]. The solid was separated from the aqueous solution. Subsequently, alcohol and sodium carbonate were added to convert alginic acid back into sodium alginate. The resulting sodium alginate paste was suitable for drying and milling, enabling its use in various applications. Conversely, another method, referred to as calcium precipitation, involves the addition of a calcium salt to a sodium alginate solution [36,87]. This induces the formation of calcium alginate, which is characterized by a fibrous texture and insolubility in water. The separated calcium alginate was then suspended in water and acid was introduced to convert it into alginic acid. Following separation, alginic acid undergoes a conversion process aided by alcohol and sodium carbonate, reverting to sodium alginate. The resulting sodium alginate paste can be extruded into pellets, dried, and milled for further use. The process of purifying sodium alginate involves dissolving the extracted alginate in an alkaline solution to form a high-viscosity slurry. Seaweeds' biomass residue was separated by filtration and centrifugation. Sodium alginate was then precipitated using sodium alginate, calcium alginate, or alginic acid. The precipitated alginate was isolated, redissolved in an alkali solution, and reprecipitated to achieve the desired purity. These recovery methods offer distinct pathways for the extraction and processing of sodium alginate from marine algal sources, meeting various industrial requirements. In summary, extraction and conversion processes yield sodium alginate, a versatile compound used in various industries, such as food and pharmaceuticals [88].

Agar extract is produced by cooking refined seaweeds at high temperatures above 100 °C with the addition of a precise amount of acid, such as 0.02% sulfuric acid or 0.05% acetic acid, to facilitate proper separation. In the traditional Japanese methods, multiple species of agarophytes are cooked in a single pot with a capacity of 3–8 square meters [89]. In industrial production, modern facilities create standardized agars that meet strict physicochemical and pathological standards while adhering to sanitation protocols. Top manufacturing plants comply with the ISO-9000 standards, ensuring controlled processes and traceability of exported raw materials and finished products [89,90]. Recently, various strategies have been introduced to enhance the MAPs extraction efficiency of macroalgae. These techniques include enzyme-, microwave-, and ultrasonic-assisted extractions [91]. Microwave-assisted extraction is commonly employed for the extraction of polysaccharides from marine algae. The parameters of microwave-assisted extraction, which can be optimized by response surface methods, include the microwave power, irradiation period, solid-to-liquid ratio, and temperature [92]. Compared to conventional methods, microwave-assisted extraction exhibits greater extraction efficiency, albeit at the expense of a shorter extraction time, lower energy consumption, and lower cost [93]. According to Yuan and Macquarrie's research, the conventional extraction approach took three hours

to extract fucoidan, whereas the microwave-assisted extraction method only required 15 min [94]. However, it was also anticipated that polysaccharides would break down when the microwave-assisted extraction approach was used. According to Tsubaki et al., the temperature at which polysaccharides are microwave-processed can affect their molecular weights and viscosities [95]. The decrease in polysaccharide viscosity with rising temperature is mainly due to reduced molecular interactions and possible chain degradation, as viscosity depends on molecular weight, concentration, and temperature. Thus, in microwave-assisted extraction, the effects of the microwave parameters on the molecular weight, sulfate content, viscosity, composition of monosaccharides, and percentage of polysaccharide breakdown were also taken into consideration [96]. Another cutting-edge extraction technique gaining popularity is ultrasonic-assisted extraction, which is used to extract polysaccharides from materials made of marine algae. The cavitation phenomenon can be caused by the propagation of ultrasound waves, which is the reason for the impact of ultrasonic-assisted extraction [97].

4. Advanced Technologies for Polysaccharide Extraction from Marine Brown Algae

Advanced technologies are crucial for polysaccharide extraction from marine brown algae because of the complexity and diversity of the algal matrix and polysaccharides themselves. Traditional methods are often inefficient and can degrade polysaccharides or require harsh chemicals, leading to environmental and economic issues. Advanced techniques such as enzymatic treatments, ultrasound-assisted extraction, and green solvents enhance extraction efficiency, preserve polysaccharide integrity, and reduce environmental impact, enabling scalable, consistent, and eco-friendly processes [98]. The seaweeds must be cleaned, ideally with distilled water, to remove salts and other contaminants. They must also be dried, freeze-dried, and ground to produce a powder with a higher surface-to-volume ratio. To avoid contaminating the target polysaccharide, it is helpful to remove interfering algal components before polysaccharide extraction. Traditionally, hot aqueous or acidic solutions are heated at elevated temperatures for extended periods to extract polysaccharides [98,99].

Pre-treated seaweeds were subsequently exposed to traditional vacuum or freeze-drying techniques before MAPs extraction. Furthermore, because the strong cell walls of seaweed are difficult to break, a pre-treatment known as cell disruption is typically necessary to eliminate or weaken the walls, which allows intracellular molecules to be more easily accessed by the solvent in subsequent extraction processes. Several pre-treatment approaches for cell disruption, including mechanical, chemical, thermal, enzymatic, and sophisticated methods such as ultrasound and microwave, can be used for this purpose [99].

- Modern extraction techniques such as pressurized liquid extraction (PLE), ultrasound-assisted extraction, microwave-assisted extraction, and enzyme-assisted extraction are increasingly being used to isolate polysaccharides from algae [98]. However, the extraction method and conditions can significantly influence the characteristics of MAPs, including their viscosity, sulfate content, monosaccharide composition, molecular weight, and overall bioactivity—due to possible degradation during the process. Therefore, optimizing key extraction parameters such as temperature, extraction time, power, and sample-to-solvent ratio is essential to maximize polysaccharide yield while preserving their native structural and functional properties [98].
- *Microwave-assisted extraction* (MAE) is an efficient technique that overcomes the drawbacks of conventional methods by generating heat directly within a material [98]. This facilitates cell wall rupture and releases intracellular compounds into the extraction solvent. MAE has been successfully utilized for isolating bioactive compounds from

seaweeds and polysaccharides from other plants, with notable effects on the chemical structure and bioactivity of the target polysaccharides [100]. Numerous studies have demonstrated the effectiveness of microwave-assisted extraction (MAE) in terms of operational capability and sustainability [101,102]. Microwave irradiation generates heat through dipole rotation when it interacts with the polar compounds in the material, leading to a high yield of extracted compounds [100,101].

- *Ultrasound-Assisted Extraction* (UAE) has emerged as the most practical industrial technique owing to its simplicity, faster extraction rate, increased yield, reduced cost, and shorter processing time [103]. It can be combined with other technologies, such as enzymatic processing or MAE, utilizing acoustic cavitation to disrupt cell walls, reduce particle size, and enhance contact between the solvent and compounds. UAE induces structural and microstructural modifications in sulfated APS, with efficiency dependent on factors such as ultrasound power, temperature, and solvent ratio, necessitating the optimization of extraction conditions [104,105].
- *Pressurized Liquid Extraction* (PLE) is an innovative technique that utilizes elevated temperatures and pressures to extract compounds from samples in a short time using less solvent. In addition, pressurized fluid extraction, pressurized solvent extraction, accelerated solvent extraction, and PLE can achieve higher solubility and diffusion rates without boiling the solvent. Various static and dynamic methods have been utilized for polysaccharide extraction from brown algae, with commercial options available since 1995 [106,107].
- *Enzyme-Assisted Extraction* (EAE) is a valuable technique for improving the extraction efficiency of bioactive compounds from seaweeds, although it is more commonly used with terrestrial plants [108]. EAE offers a higher extraction yield, faster rates, lower energy consumption, and simpler recovery compared to conventional extraction methods. This involves the use of enzymes capable of degrading cell walls or partially breaking down polysaccharides to facilitate extraction. Commercially available carbohydrate hydrolytic enzymes and proteases are commonly used for polysaccharide extraction from seaweeds [109,110].

Apart from exhibiting fluctuations in MWs, the composition of monosaccharides, and the amount of sulfate, extracted APS are typically tainted with proteins and low molecular weight molecules that are also dissolved in water during the extraction process [98]. As a result, they can be further purified by employing various purification techniques, such as affinity chromatography, ion exchange, membrane separation, ethanol precipitation, and size-exclusion. There are no defined standard purification processes because they all rely on additional functions and purity needs. Although membrane separation can be utilized in scale-up testing, ethanol precipitation is the most employed approach in the functional food industry [4].

In conclusion, the exploration of advanced technologies for polysaccharide extraction from marine brown algae represents a significant advancement in biotechnology and marine science. Researchers have made substantial progress in overcoming the challenges associated with conventional extraction methods through innovative approaches, such as enzymatic hydrolysis, ultrasound-assisted extraction, and subcritical water extraction. These advanced technologies offer several advantages, including increased extraction efficiency, reduced extraction time, and improved preservation of the polysaccharide bioactivity. Additionally, they contribute to sustainable practices by minimizing the use of chemical solvents and reducing environmental impact [4].

5. Biomedical Applications

MAPs have emerged as promising biomaterials with diverse biomedical applications. These natural compounds, which are extracted from seaweeds and algae, possess unique chemical structures and properties that make them suitable for a wide range of medical purposes [13]. From wound healing and drug delivery to tissue engineering and cancer therapy, MAPs have garnered significant attention because of their biocompatibility, biodegradability, and low toxicity [111]. As researchers delve deeper into their potential, these polysaccharides are paving the way for innovative biomedical solutions that harness the power of the ocean for human health and well-being. Algal polysaccharides are essential for several bioactivities, including immune system molecular recognition, cell addition, and cell–cell interactions [112].

Polysaccharides have a wide range of beneficial effects, including antibacterial, antifungal, antiviral, antidiabetic, anticancer, antioxidative, anti-inflammatory, and immunoregulatory [113]. MAPs play crucial roles in various bioactivities, including immune system modulation, cell adhesion, and cell–cell interactions. Several microalgal species produce polysaccharides that have significant applications. *Chlorella vulgaris* is known to produce sulfated polysaccharides, which are utilized for their immunomodulatory and antioxidant properties and have potential antiviral applications. *Spirulina platensis* produces calcium spirulan and other sulfated polysaccharides that exhibit antiviral, antibacterial, and immune-enhancing properties, making them valuable in dietary supplements and functional foods.

Porphyridium cruentum generates exopolysaccharides that possess anti-inflammatory and wound-healing properties and are used in cosmetics and pharmaceuticals [13]. Abu-Rabeah and Marks [114] constructed a highly sensitive amperometric glucose biosensor using alginate-pyrrole as the host matrix. Adrogué and Madias [115] focused their research on investigating the roles of sodium and potassium in the pathogenesis of hypertension. Venkatesan et al. [116] explored potential biomedical applications of seaweed polysaccharides in their paper. Vitko et al. [117] investigated the use of a novel guluronate oligomer to improve intestinal transit and survival in mice with cystic fibrosis. MAPs offer a range of health benefits, including immunomodulatory, antiviral, and antibacterial properties; anticancer potential; wound healing; and tissue regeneration (Figure 3), as discussed below. Their diverse effects render them promising candidates for biomedical applications (Table 2; Figure 3).



Figure 3. Different biomedical applications of polysaccharides extracted from marine algae.

Table 2. Biomedical applications of polysaccharides derived from marine algal strains.

Algal Species	Marine Polysaccharide	Biomedical Applications	References
Sargassum swartzii	Fucoidan	Antiviral activity, antibacterial, anticoagulant, anti-inflammatory, antiviral, antithrombosis, anti-tumor, anticancer	[118]
Laminaria digitata	Laminaran	anti-inflammatory and anti-oxidative, anti-oxidative and anti-inflammatory	[81]
Porphyridium cruentum	Sulfated Polysaccharides (EPS)	Anti-inflammatory, antiviral, wound healing	[119]
Dunaliella salina	β-Glucans, Sulfated Polysaccharides	Antioxidant, anti-inflammatory, immune-stimulating	[120]
Chondrus crispus (Irish Moss)	Carrageenan (κ-, ι-, and λ-carrageenan)	Thickening agent, anti-inflammatory, potential antitumor	[121]
Gelidium amansii	Agar, Agarose	Microbiological media, food industry	[122]
Gracilaria spp.	Agar, Agarose	Food gelling agent, microbiology	[123]
Laminaria spp.	Alginate	Food thickener, wound dressing	[87]
Sargassum spp.	Fucoidan, Alginate	Anti-inflammatory, anticoagulant, potential anticancer	[124]
Ulva spp. (Sea Lettuce)	Ulvan	Antioxidant, anti-inflammatory, antiviral	[125]

5.1. Immunomodulatory Effects

The current trend of using natural products to treat illnesses and improve health has led to a focus on studying marine organisms such as cyanobacteria and macro- and microalgae [126]. Fucoidan, a compound found in certain types of seaweeds, has shown promise for the treatment of atopic dermatitis (AD), a skin condition characterized by inflammation and itchiness. Yang [127] demonstrated that fucoidan effectively alleviated AD-like symptoms in mice treated with 1-chloro 2,4-dinitrobenzene (DNCB), showing comparable effectiveness to dexamethasone, a commonly used corticosteroid. Fucoidan exhibits strong anti-inflammatory effects by downregulating AD-associated cytokine and chemokine expression. In the fucoidan-treated group, the levels of inflammatory factors such as interleukins (ILs) and histamine were significantly reduced, leading to a decrease in mast cell infiltration and immunoglobulin E secretion at the lesion site. This suggests that fucoidan could offer a potential alternative to corticosteroid drugs for treating AD symptoms [127].

In an open-label study by Myers et al., fucoidan was investigated as an immunomodulator. Twelve healthy participants received varying doses of fucoidan orally for four weeks [128]. Fucoidan increased Tc cell count and enhanced monocyte phagocytic capacity. In addition, it decreased the levels of IL-6, a key inflammatory cytokine. These findings suggest that fucoidan is a promising potential anti-inflammatory drug. Carrageenan derived from marine macroalgae can significantly suppress immune responses both in vivo and in vitro. They impair complement activity, humoral responses, and cell-mediated immunity, prolong graft survival, and potentiate tumour growth. Immune suppression by carrageenan is attributed to its selective cytopathic effect on macrophages, making it a useful tool for studying the role of these cells in immune reactivity [129].

Alginate, a natural polysaccharide primarily extracted from marine brown seaweeds (*Phaeophyceae*), has gained significant attention for its diverse biological properties and biomedical potential. Although alginate itself shows no adverse effects on lymphocyte

viability, its particulate and low-viscosity forms can actively modulate immune responses. Studies have shown that particulate alginate elicits a pronounced inflammatory reaction, leading to increased production of cytokines such as IL-1β, IL-8, TNF-α, and IFN-γ [130]. In addition, low-viscosity and particulate alginates are more effective than high-viscosity variants in stimulating dendritic cells, as reflected by enhanced expression of activation markers CD80, CD86, and CD40 [131]. Particulate alginate also induces slightly higher levels of granulocyte colony-stimulating factor (G-CSF) in macrophages. Collectively, these findings suggest that alginate—particularly in its particulate form—can influence immune mechanisms by promoting inflammatory cytokine production and dendritic cell activation, thereby offering potential for therapeutic applications in inflammation-related disorders [40].

Ulvan, extensively researched both in vitro and in vivo, shows a diverse array of medicinal properties, including antioxidant, anti-inflammatory, antibacterial, anticancer, antiviral, and cytotoxic effects [132]. It holds promise as a polymer in pharmaceutical formulations, particularly for creating smart films in bone tissue engineering, emphasizing the importance of preserving its structural integrity. With potent anticancer and immunomodulatory capabilities, ulvan not only inhibits abnormal tumour cell proliferation but also aids in repairing cellular atypia and immune system damage induced by tumours. Its potential medicinal value warrants further exploration for human medical applications; however, investigations into its bioavailability and refining processes are crucial prerequisites for its therapeutic use [133]. Numerous studies have investigated the biological activities and health benefits of ulvan, highlighting its significance in medical research [134]. *Ulvan* polysaccharides contain sulfated groups, which are essential for their therapeutic effects. These groups allow polysaccharides to interact with biological targets and hence have antiviral, anti-inflammatory, antioxidant, and anti-hyperlipidemic properties. Additionally, important functions are performed by ulvan's gelling qualities, which provide support, promote wound healing, and ease medication distribution [135].

Marine-derived polysaccharides such as fucoidan, carrageenan, alginate, and ulvan have potent immunomodulatory characteristics, including anti-inflammatory and immune-enhancing capabilities. They work by modulating cytokines, increasing immune cell function, and treating inflammation-related diseases. These natural chemicals show potential for therapeutic usage, particularly in treating immune-related and inflammatory illnesses, but further study is needed to optimise their use and efficacy [13].

5.2. Antiviral and Antibacterial Activities

The antibacterial properties of MAPs have garnered significant attention in recent years because of their potential application in combating bacterial infections and addressing the global challenge of antibiotic resistance. These polysaccharides, derived from various species of marine algae such as brown, red, and green algae, exhibit a wide range of antibacterial activities against both Gram-positive and Gram-negative bacteria [136]. Global interest in research on the antiviral properties of natural marine materials, particularly marine polysaccharides, has increased recently. Numerous antiviral effects have been demonstrated for marine-derived polysaccharides and their low-molecular-weight oligosaccharide derivatives [29]. The antiviral characteristics of marine polysaccharides, as well as their synergistic effects when combined with other antiviral drugs, demonstrate impressive antiviral responses for future medical research [137]. Antiviral medications derived from marine algal polysaccharides, which are biogenic, biocompatible, and renewable, have been in great demand in the emerging pharmaceutical sector after they have received clinical approval [113].

Buck et al. showed that carrageenans block human papillomavirus (HPV) during its initial infection process [138]. Moreover, γ-carrageenan has a stronger antiviral effect than λ- and κ-carrageenan. According to Talarico et al., γ-carrageenan can prevent dengue virus (DENV) from replicating in both mosquito and mammalian cells, although it acts in both cell types somewhat differently [139,140]. O-Acylated carrageenan polysaccharides with varying molecular weights have been shown by Yamada and colleagues to exhibit enhanced anti-HIV action by depolymerization and sulfation [38,39]. Consequently, the molecular weight and sulfate concentration of carrageenan polysaccharides are linked to their antiviral properties. Xin et al. reported that a marine polysaccharide drug derived from alginate could significantly inhibit acute infection of MT4 cells and chronic infection of H9 cells with HIV-1 [141].

Sulfated fucans from the seaweed species *Lobophora variegata*, *Dictyota mertensii*, *Spatoglossum schroederi*, and *Fucus vesiculosus* can suppress the activity of HIV reverse transcriptase (RT) [142]. A fucan polysaccharide from *Cladosiphon okamuranus* prevents BHK-21 cell infection by dengue virus type 2 (DENV-2), while showing minimal effect on serotypes DENV-1, DENV-3, and DENV-4 [143]. The antiviral potential of *Gracilaria corticate* extract was demonstrated when tested against HSV-1 and HSV-2 [144]. Several marine sulfated polysaccharides, such as chondroitin sulfate from sharks, fucoidan from brown algae, iota-carrageenan from red algae, and sea cucumber sulfated polysaccharide (SCSP), inhibit SARS-CoV-2. At doses of 3.90–500 μg/mL, SCSP, fucoidan, and carrageenan all showed significant antiviral activities. The ability of SCSP to bind to S glycoprotein and obstruct SARS-CoV-2 host cell entrance was validated by an examination of pseudotyped viruses containing S-glycoprotein [145]. The antiviral potential of agar against dengue-2 virus was assessed in a study by Schulze et al. [146]. Based on these findings, sulfated polysaccharides from agar gel directly interact with the virus particle to suppress its hemagglutinating capabilities and prevent infection, as opposed to interacting with the host cells or erythrocytes [146]. Research findings indicate that carrageenan has a direct antiviral effect on certain enveloped viruses, rendering them incapable of infecting cells and minimizing viral replication. Herpes simplex viruses HSV-1 and HSV-2 have been successfully prevented by several carrageenan formulations [147]. The superiority of sulfated polysaccharides such as fucoidan and porphyrin implies that the structure of these polysaccharides may obstruct membrane fusion and the efficacy of the delivery mechanism. A review of minor alterations to the established delivery system regarding the level of sulfation, molecular weight, and resemblance to the β-carrageenan successor path may yield prospective antiviral options and suggest the conditions required to combat viral infections [148].

MAPs possess strong antiviral and antibacterial properties, showing potential in fighting infections and antibiotic-resistant pathogens. Compounds like carrageenan, fucoidan, and alginate effectively inhibit viruses, often by blocking viral entry or replication. Their activity is influenced by factors like molecular weight and sulfate content.

5.3. Anticancer Potential

Polysaccharides found in algae exhibit a range of biological actions, including immunomodulatory and anticancer effects. Algae also have a high nutritional value. By causing apoptosis, cell cycle arrest, anti-angiogenesis, and regulation of intestinal flora and immunological function, algal polysaccharides have anticancer effects. For example, various reports have suggested that clodosiphon fucoidan decreases the incidence of gastric cancer by preventing *Helicobacter pylori* from adhering to the mucus of the stomach tract [149,150]. The growth of melanoma B16 cells was dose-responsively inhibited by fucose-containing sulfated polysaccharides derived from *Sargassum henslowianum* and *F.*

vesiculosus [151]. When laminarin and fucoidan were used, the AO/EB (Acriding Orange/Ethidium Bromide) assay showed a substantial increase in apoptosis and necrosis, respectively. Necrotic cancer cell death was supported by the DNA fragmentation data [31]. Thus, laminarin and fucoidan are promising bioactive substances for anticancer treatment. Both fucoidan and laminarin exert anticancer effects through multi-faceted mechanisms that induce programmed cell death and halt tumour progression [31]. Fucoidan primarily triggers the mitochondrial-mediated intrinsic apoptotic pathway by upregulating pro-apoptotic proteins like Bax and cleaving executioner caspases, while simultaneously downregulating survival signals through the inhibition of the PI3K/Akt and ERK pathways [152,153]. It further suppresses cancer proliferation by inducing cell cycle arrest in the G0/G1 phase and enhances the body's immune response by activating N K cells and stimulating cytokines like IL-2 and IFN-γ [154]. Conversely, laminarin promotes apoptosis through both the extrinsic pathway, by activating death receptors like Fas, and the intrinsic pathway, by inhibiting survival signals such as IGF-IR [155]. Its anti-proliferative action is characterized by halting the cell cycle at the G2/M phase, preventing mitosis, and it demonstrates a direct, dose-dependent cytotoxic effect that effectively reduces overall cancer cell viability [156]. In conclusion, algal polysaccharides demonstrate significant anticancer potential through mechanisms such as apoptosis induction, cell cycle arrest, and anti-angiogenesis. Their ability to inhibit cancer cell growth and interfere with pathogenic adhesion, as seen with fucoidan and laminarin, highlights their promise as natural, bioactive agents in cancer prevention and therapy.

5.4. Wound Healing and Tissue Regeneration

Marine-derived polysaccharides have been investigated as potential materials for wound dressings because of their favourable qualities of low toxicity, biocompatibility, and biodegradability. It also has various advantages, including the promotion of wound healing through the creation of a moist environment that encourages cell migration and proliferation. They can also provide a layer of protection to prevent additional wound damage and function as a barrier against external pollutants [157]. Alginates have special qualities that make them promising materials for modern biotechnologies, including the creation of wound dressings [158]. These qualities include high biological activity, biocompatibility, biodegradability, non-toxicity, lack of immunogenicity, high absorption capacity, hydrogel-forming ability, and low production costs. Alginate-based materials for wound dressings are typically used as foams, nanofibers, amorphous gels, membranes, and films [159]. Dressings made of alginate can be used on wounds that are infected or not, because they have the capacity to absorb fluids up to 20 times their weight [160]. Fucoidan-containing wound dressings have several properties that help speed up the healing process, such as encouraging the production of collagen, stimulating the growth of new hair follicles, lowering inflammatory reactions, minimizing scar formation, and encouraging angiogenesis [161]. Marine-derived polysaccharides such as alginate and fucoidan show strong potential in wound healing due to their biocompatibility, biodegradability, and ability to promote cell growth, absorb fluids, prevent infection, and stimulate collagen and angiogenesis, making them ideal for advanced wound dressings.

5.5. Antiviral Therapy

Viral infections are often driven by oxidative processes that aid viral replication and disrupt cell regulation. Marine algae offer a rich source of natural antiviral compounds, including sulfated polysaccharides, phlorotannins (from brown algae), and phycobiliproteins (from marine algae), all showing strong antiviral activity. To develop effective natural antivirals, research should prioritize understanding their mechanisms and exploring macroalgae

for their rapid growth and ease of cultivation [162]. A diverse array of antiviral polysaccharides derived from marine organisms exhibit their potential against numerous viral pathogens. Carrageenan, extracted from red algae *Gigartina skottsbergii* demonstrates broad-spectrum antiviral activity against influenza, dengue virus (DENV), herpes simplex viruses (HSV-1, HSV-2), human papillomavirus (HPV), human rhinovirus (HRV), and HIV [163]. Galactans from red algae species such as *Callophyllis variegate* and *Schizymenia binderi* exhibit efficacy against HSV, HIV, DENV, and hepatitis A virus (HAV). Similarly, alginates from brown algae like *Laminaria hyperborea* and *Macrocystis pyrifera* are active against HIV, influenza A virus (IAV), and hepatitis B virus (HBV) [164].

Other noteworthy examples include fucoidans from various brown algae, which inhibit HSV, HCMV, VSV, Sindbis virus, and HIV-1. Laminaran from *Fucus vesiculosus* and *Saccharina longicruris* also targets HIV [162,165]. Diatom-derived naviculan shows activity against HSV, while microalgal polysaccharides such as p-KG03 (*Gyrodinium impudicum*) and A1/A2 (*Cochlodinium polykrikoides*) offer protection against influenza and RSV [166]. Additionally, blue-green algae like *Arthrospira platensis* and *Nostoc flagelliforme* produce calcium spirulan and nostaflan, respectively, which are potent against multiple viruses, including HIV, mumps, measles, and cytomegalovirus [167]. This wide range of antiviral efficacy underscores the promise of marine-derived polysaccharides as natural antiviral agents. MAPs offer strong, broad-spectrum antiviral potential due to their ability to block virus activity and support immune defence. Their natural origin and sustainability make them ideal candidates for future antiviral therapies.

5.6. Anti-Diabetic and Anti-Obesity Effects

Fucoidan has demonstrated potential efficacy in mitigating obesity via many mechanisms identified in laboratory research. Research using 3T3-L1 cells demonstrated a reduction in the expression of several genes associated with adipogenesis, including AAP2, ACC, and PPARγ. It also decreased the quantities of deleterious reactive oxygen species (ROS), curtailed fat formation in cells, and facilitated the catabolism of fats [168]. Additionally, fucoidan reduced the overall process of adipogenesis, which is the formation of fat cells [169]. In other laboratory tests without using cell lines, fucoidan was able to block the activity of enzymes like pancreatic lipase, α-amylase, and α-glucosidase, which are responsible for breaking down fats and carbohydrates. These actions suggest that fucoidan may help in managing obesity by both reducing fat storage and limiting fat and carbohydrate absorption in the body [170].

Marine polysaccharides such as alginate, ulvan, carrageenan, galactofucan, and laminarin have shown significant potential in managing obesity and diabetes through various biochemical and cellular mechanisms. Alginate, derived from brown algae, promotes satiety by forming a gel in the stomach, thereby reducing gastric emptying and fat absorption. It also inhibits digestive enzymes like pancreatic lipase and slows glucose diffusion, supporting glycemic control [14]. Carrageenan, sourced from red algae, regulates lipid metabolism and reduces fat accumulation in cells, while also exhibiting inhibitory effects on α-glucosidase, contributing to lowered glucose absorption [171]. These diverse mechanisms highlight the potential of marine polysaccharides as multi-target therapeutic agents in combating obesity and type 2 diabetes.

5.7. Neuroprotective Effects

Marine polysaccharides such as alginate, ulvan, carrageenan, galactofucan, and laminarin exhibit promising neuroprotective effects through diverse biochemical mechanisms. Alginate has been found to reduce oxidative stress, inhibit neuroinflammation, and stabilize mitochondrial function, thereby preserving neuronal health [172]. Ulvan protects

neurons from oxidative damage, reduces apoptosis, and helps regulate neurotransmitter levels, which are crucial for normal brain signalling [173]. Carrageenan demonstrates anti-inflammatory properties by suppressing the release of pro-inflammatory cytokines such as IL-6 and TNF-α, which are often elevated in neurodegenerative conditions [174]. Collectively, these marine-derived polysaccharides target multiple pathways, including antioxidant defence, anti-inflammatory response, enzyme inhibition, and neurotrophic support, offering a multifaceted approach to neuroprotection.

5.8. Antibacterial Coatings and Medical Implants

MAPs have attracted growing attention as bio-based materials for producing antibacterial coatings on medical devices because of their biocompatibility, biodegradability, and natural antimicrobial properties [175]. Drawn from brown, red, and green seaweeds, polysaccharides including alginate, carrageenan, fucoidan, and ulvan have shown great promise in avoiding bacterial colonization on implant surfaces [176]. Research on polysaccharide-based strategies to combat antimicrobial resistance, a global threat causing healthcare-associated infections, is being devoted to developing effective antibacterial coatings. Polysaccharides, essential building blocks and renewable resources, have significant biological potential for antibacterial activities [176]. By functionalizing these natural polymers with metallic nanoparticles such as silver or zinc oxide, their antibacterial activity can be improved and tissue integration and wound healing supported at the same time [177].

Various naturally derived polysaccharides exhibit promising antibacterial and antimicrobial properties, making them valuable in biomedical and pharmaceutical applications (Figure 4). Ulvan, extracted from green algae, shows strong antimicrobial activity against *Enterobacter cloacae*, *Aeromonas hydrophila*, and *Pseudomonas fluorescens*. Fucoidan, a sulfated polysaccharide from brown seaweeds, is known for its antibacterial effects against *S. aureus* and *Vibrio alginolyticus* [178]. Carrageenans provide effective antibacterial action with excellent biocompatibility, targeting organisms such as *Staphylococcus aureus* and *Listeria monocytogenes* [179]. Alginate (ALG) exhibits strong antibacterial activity with low cytotoxicity, effectively targeting *Staphylococcus aureus* and *Escherichia coli* [180]. Meanwhile, laminarin displays bactericidal activity along with wound-healing properties, especially against *E. coli*. These findings underscore the therapeutic potential of these polysaccharides in combating bacterial infections and enhancing wound care [79].

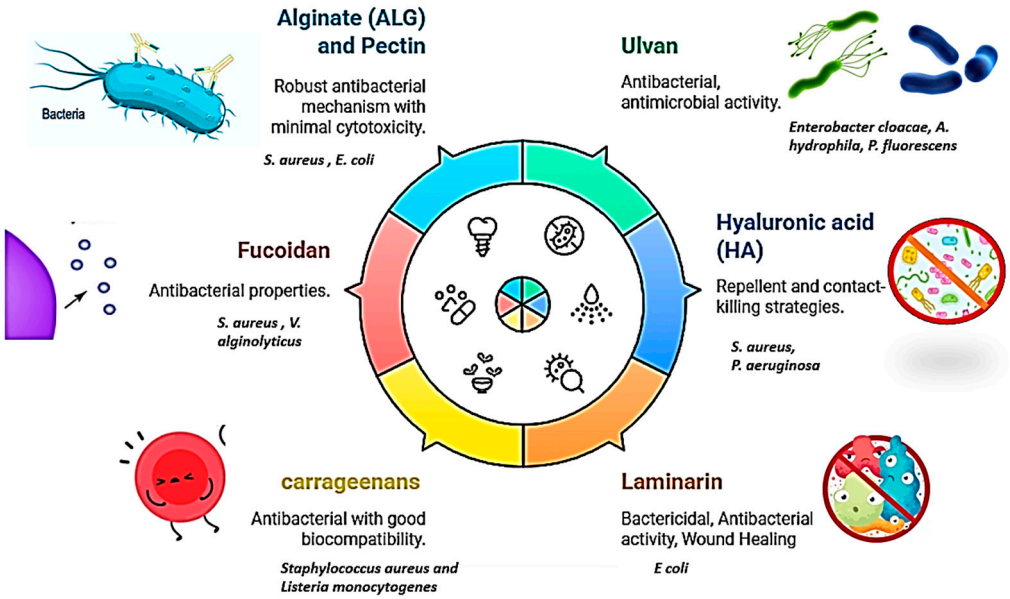


Figure 4. Marine algal polysaccharide-based materials and their antibacterial mechanism.

5.9. Anticoagulant and Antithrombotic Agent

Marine algal polysaccharides, such as fucoidan, carrageenan, alginate, and ulvan, have emerged as promising natural anticoagulant and antithrombotic agents. These sulfated polysaccharides possess structural similarities to heparin, a widely used anticoagulant, enabling them to inhibit key enzymes in the coagulation cascade, like thrombin and factor Xa [63,181]. Fucoidan, derived from brown algae, is particularly notable for its strong anticoagulant activity, attributed to its high sulfate content and unique molecular structure [182]. Carrageenan, from red algae, and ulvan, from green algae, also demonstrate clot-preventing properties by enhancing antithrombin activity and reducing platelet aggregation [183]. These natural compounds are biocompatible, biodegradable, and exhibit low toxicity, making them attractive alternatives to synthetic anticoagulants. Their dual role in preventing blood clot formation and dissolving existing clots positions them as valuable candidates in cardiovascular disease management and biomaterial surface modifications for blood-contacting devices [23].

6. Molecular Mechanisms Underlying the Biomedical Activities of Marine Macroalgae Polysaccharides

Seaweed is one of the major producers of biomass and has an active metabolite that can treat tumours. The most common polysaccharides in cancer management are sulfide polysaccharides, fucoidans, carageenans and ulvans from various algae species, which are known to have chemoprotective effects in vitro and in vivo [134]. The underlying anticancer mechanisms of algae polysaccharides include the induction of apoptosis, the suspension of the cell cycle, the modulation of the transmission signalling pathways, the suppression of migration and angiogenesis, and the activation of immune responses and antioxidant systems. VEGF/VEGFR2, TGFR/Smad/Snail, TLR4/ROS/ER, CXCL12/CXCR4, TGFR/Smad7/Smurf2, PI3K/AKT/mTOR, PBK/TOPK and -catenin/Wnt are among the main cell signaling pathways modulated by the algal polysaccharides. These pathways serve as checkpoints for normal cellular growth and are regulated by multiple extracellular stimuli [184,185].

Macrophages are crucial players in the innate immune system, serving diverse functions such as phagocytosis, antigen presentation, and T cell modulation [186]. A polysaccharide derived from the red algae *Porphyra haitanensis* has been shown to enhance phagocytosis in the RAW264.7 macrophage cell line [84]. Macrophages are highly versatile cells that can adapt to various microenvironmental cues, enabling them to maintain immune homeostasis in both normal and disease states [187]. These cells are capable of phagocytosing pathogens, dead cells, and other foreign materials, as well as secreting an array of cytokines, chemokines, and growth factors that can profoundly influence the immune response [157].

A polysaccharide extracted from brown algae *Hizikia fusiforme* has shown that RAW264.7 macrophages increase the production of nitrogen oxides (NOs) and the expression of induced nitrogen oxide synthesis (iNOS) [188]. Polysaccharides extracted from *Laminaria japonica* show significant macrophage stimulation and enhanced cytokine production, such as tumour necrosis factor (TNF), IL-1, IL-6 and IL-10. This polysaccharide has a positive effect on the phosphorylation of signal-regulated extracellular kinase (ERK1/2), JNK1/2 and P38 [189]. The maturation of dendritic cells plays an important role in the function of the immune system and the adaptive immune system. Recent research has shown that Fucoidan of *Fucus evanescens* induces stimulation and maturation of dendritic cells [190]. The study suggests that the maturation of dendritic cells caused by fucoidan is mediated by the production of TNF- and involves signal transmission through p38, phosphoinositide-3 and glycogen synthase kinase 3. Jeong et al. [190] reported that fu-

coidan of marine algae has the effect of cytoprotection on the viability and size of dendritic cells against 5-fluorouracil. 5FU is considered as an important chemoprotective drug for cancer treatment. This study suggests that fucoidan can maintain cancer patients' immunity. Natural killer cells (NKs) also play an important role in immune modulation activity because they are able to secrete cytokines, lymph nodes, and tissues that expand in human cells during increased immune tolerance [191]. Fucoidan of *Ascophyllum nodusum*, *Macrocystis pyrifera*, *Undaria pinnatifida* and *Fucus vesuculosus* promoted the activation of mouse NK cells. Among them, *Undaria pinnatifida* fucoidan showed the strongest effect as a result of the expansion of NK cells [192].

It was also shown that carrageenan is strongly associated with serum proteins used in cell cultures, especially fetal serum proteins, and that they may be involved in its mechanism of action. Two mouse macrophage cell lines (RAW 264.7 and 23ScCr), human colon epithelial cell lines NCM 460, and human colon cells were used to identify several receptors, including toll-like receptors and B cell lymphoma/leukemia B cell protein 10 (BCL10) that can bind to carrageenan [193]. Both receptors can stimulate NF-β transmission pathways and then activate pro-inflammatory genes and cytokines. In addition, the characteristic of preventing the interaction of certain proteins and receptors binding to these proteins and inhibiting the interaction with other proteins and receptors, as well as the stabilization properties (gel, thickness and binding), suggest that they can be used to bind to drugs with various effects, such as bactericides or cytotoxic drugs [194,195].

Red algae *Gracilariopsis lemaneiformis* (Gp. *lemaneiformis*) has anti-tumour activity, while polysaccharides of Gp. *lemaneiformis* (PGL) have been shown to have anticancer activity [196]. PGL inhibited the growth of three human cancer cell lines by suppressing cell proliferation, reducing cellular function, and altering cell morphology in a time- and concentration-dependent manner. Transcriptome analysis showed that PGL could regulate 758 genes involved in apoptosis, cell cycle, nuclear division, and cell death. In addition, the study demonstrated that PGL induces apoptosis and cell cycle suppression, and modulates the expression of A549 cell-line-related genes [197]. Marine polysaccharides show antiviral effects by disrupting key stages of the viral life cycle. They prevent virion binding to host cells via electrostatic interference, block penetration and uncoating by hindering conformational viral changes, and impair transcription and replication by targeting viral enzymes post-entry. Some can even directly deactivate virions prior to infection. Their effectiveness is closely tied to their structural features and is specific to certain viral types [67,198].

Overall, these polysaccharides, especially those derived from seaweeds, demonstrated promising potential for inhibiting viral replication and transcription, offering new avenues for antiviral therapy. Sulfated polysaccharides, fucoidans, carrageenan, and ulvan, from several algal species that have been identified in vitro and in vivo, are the most commonly used polysaccharides in cancer care. Algal polysaccharides have been found to have anticancer properties that involve induction of apoptosis, cell cycle arrest, modulation of transduction signalling pathways, suppression of migration and angiogenesis, and boosting of the antioxidant and immune systems [66].

7. Interaction with Cellular Receptors, Signal Transduction Pathways, and Immune Cells

MAPs interact with the immune system to activate various signalling pathways and induce immune responses. This activation involves molecular events, including the stimulation of the Akt, ERK1/2, JNK1/2, and PI3K pathways, as well as the engagement of receptors such as CR3, SR, and TLR-4. MAPs trigger the production of cytokines, such as IFN, IL, and TNF-α, leading to immune system activation. These interactions demonstrate the potential of MAPs to modulate immune responses, highlighting their significance in

immunotherapy and defence against foreign invaders. Fucoidan extracted from various marine sources, such as *Ascophyllum nodosum*, *Macrocystis pyrifera*, *Undaria pinnatifida*, and *Fucus vesiculosus*, enhances the activation of mouse NK cells, with *Undaria pinnatifida* fucoidan exhibiting the most potent effects by expanding NK cell populations. Additionally, sulfated polysaccharides from marine materials have been shown to inhibit the adhesion of Helicobacter pylori and reduce biofilm formation. Researchers have suggested that these polysaccharides likely influence the infectious process involving *H. pylori* through their actions on cells of both innate and adaptive immunity [4,165,192]. MAPs have shown the ability to support the immune system by activating important signalling pathways and promoting the production of immune-related molecules. They can enhance the activity of natural killer cells, reduce harmful bacterial adhesion, and help regulate immune responses. These properties suggest their potential use in improving immunity and protecting against infections.

8. Challenges and Future Directions

MAPs offer immense potential for biomedical applications; however, their extraction poses significant challenges. The structural diversity and complexity of these polysaccharides make their extraction and purification difficult, often necessitating the use of harsh chemicals and energy-intensive processes that can diminish their yield and bioactivity [13,17]. Additionally, the high variability in polysaccharide composition across different algal species complicates the standardization of extraction protocols [199]. To address these challenges, future research should focus on developing efficient and sustainable extraction techniques. Emerging methods, such as enzyme-assisted extraction, supercritical fluid extraction, and the use of green solvents, offer promising alternatives that can improve yield and maintain bioactivity while reducing environmental impact. Advancing our understanding of the molecular mechanisms underlying the extraction process and optimizing the large-scale cultivation of specific algal strains will also be crucial for harnessing the full biomedical potential of MAPs [200].

In biomedical applications, MAPs present both promise and challenges. Standardization and quality control are essential for ensuring consistency across different extraction methods and sources. Understanding their bioavailability and pharmacokinetics is crucial for optimizing their therapeutic efficacy. Biocompatibility and safety must be thoroughly assessed for clinical use. Mechanistic insights into their actions are necessary for the development of targeted therapies. Clinical translation requires rigorous validation in large-scale trials. Cost-effective production methods are required to achieve scalability. Exploring synergistic effects with other biomaterials could enhance the therapeutic outcomes. Overcoming these challenges requires interdisciplinary collaboration and has the potential to revolutionize biomedical therapeutics (Table 3). One significant challenge lies in optimizing the extraction and purification methods to enhance the yield and purity while minimizing the environmental impact and production costs [199].

Improving scalability and sustainability of the extraction process is crucial for the widespread application of MAPs in biomedical contexts [201]. Further research is needed to fully understand the complex mechanisms underlying the therapeutic effects of marine algal polysaccharides. This entails exploring their interactions with biological systems at the molecular level and elucidating their modes of action in various biomedical applications. Additionally, efforts to develop innovative delivery systems and formulations to enhance the bioavailability and efficacy of MAPs in vivo represent an exciting avenue for future research. Addressing these challenges and advancing our understanding of MAPs will unlock their potential as valuable resources for improving human health and well-being [13,17,29].

Table 3. Commercial and experimental products based on marine algal polysaccharides.

Polysaccharide	Product/Brand Name	Biomedical Use	Formulation Type	Status	Approved/ In Trials	References
Alginate	AlgiMatrix®	3D cell culture scaffold, Multicellular tumor spheroid (MCTS) assays, organogenesis studies (hepatocytes, cardiomyocytes), co-culture models	Porous sponge matrix	Commercial	Approved (research use)	[202,203]
Alginate	Algisite™ M	Wound healing, exudate absorption, high-throughput drug screening, and 3D stem cell differentiation	Calcium alginate dressing	Approved	CE Marked	
Carrageenan	Carraguard®	Vaginal microbicide (anti-HIV)	Gel	Clinical trial completed	Phase III (discontinued)	[204]
Carrageenan	Iota-Carrageenan nasal spray	Cold & flu treatment relieves nasal symptoms through antiviral action rather than affecting blood vessels or glands.	Nasal spray	Commercial	Approved (EU/OTC)	[205,206]
Fucoidan	Maritech® Fucoidan	Effectively reduced osteoarthritis symptoms such as pain and stiffness. Immunity, inflammation, and oncology support	Capsule, powder	Commercial	Approved (nutraceutical)	[128]
Fucoidan	Fucoidan wound dressings	Wound healing, angiogenesis	Hydrogel, biofilm	In development	Preclinical	[207]
Fucoidan	Fucoidan-cisplatin nanoparticle	Cancer drug delivery	Nanoparticle system	Experimental	In vitro/in vivo	[208]
Ulvan	Ulvans in wound healing scaffolds	Antioxidant, antimicrobial, promotes wound healing by maintaining moisture and absorbing exudate.	Ulvan-based hydrogel film	Experimental	In vitro	[133]
Ulvan	Ulvan–chitosan hydrogels	Skin regeneration, tissue engineering	Injectable hydrogel	Experimental	Preclinical	[209,210]
Laminarin	Laminarin microparticles	Drug delivery, immune modulation	Microparticle system	Experimental	In vitro	[211]
Laminarin	Laminarin in vaccine adjuvants	Immune adjuvant	Injectable vaccine adjuvant	Experimental	In vivo (animal models)	[212]
Laminarin	Agar-based wound dressings	Wound healing, moist environment	Film/dressing	Experimental	Preclinical	[213]
Laminarin	Agar-based hydrogels for drug release	Controlled drug delivery	Hydrogel	Experimental	In vitro/in vivo	[214]

9. Conclusions

Marine algae hold significant importance in their natural environments and are gaining increasing attention in the realm of green technology. The growing interest in both the scientific community and industry stems from rapid advancements in modern biotechnology. MAPs offer a vast array of biomedical applications and have demonstrated significant potential as therapeutic agents. Their immunomodulatory effects, antiviral and antibacterial activities, anticancer potential, and role in wound healing and tissue regeneration underscore their versatility and importance in medical research. Furthermore, elucidation of the molecular mechanisms underlying these activities provides valuable insights into their therapeutic benefits, paving the way for the development of novel treatments and therapies. With ongoing advancements in extraction techniques and a deeper understanding of their biochemical composition, MAPs hold promise in addressing various health challenges and improving patient outcomes in the future. In summary, the multifaceted properties of MAPs make them promising candidates for biomedical applications. Their diverse range of therapeutic benefits, coupled with ongoing research efforts to uncover their mechanistic insights, positions them as valuable resources in the pursuit of innovative medical treatments. As we continue to explore and harness the potential of these compounds, they stand poised to play a pivotal role in shaping the future of healthcare by offering hope for improved patient care and well-being.

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