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Algae-Derived Marine Oligosaccharides and Their Biological Applications

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The biological relevance of algae-derived marine oligosaccharides has potential significance in numerous applications of industrial biotechnology. Marine oligosaccharides are produced in algae naturally and/or by hydrolysis of derived polysaccharides. The potential of marine oligosaccharides is still unexplored, and these molecules, including their derivatives, are a versatile source of chemical diversity. In-depth knowledge on such molecules will provide novel insights, thus depicting their role in discovering mechanisms and the molecular functions within specific biological applications.

Keywords: algae, biofuels, biological applications, industrial biotechnology, marine oligosaccharides

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INTRODUCTION

The global algae population is responsible for approximately 40–50% of the photosynthesis each year that occurs on earth (Falkowski et al., 1998; Qin et al., 2012). Algae are an extremely diverse group with the substantial reservoir of biomolecules, physiological characteristics and molecular functions (Hallmann, 2015). Understanding the algal glycobiology by carbohydrate recognition phenomena and their biological properties forming complex glycans, that exhibits both bioactivity and structural function is essential (Trincone, 2015). Algae-derived marine oligosaccharides are low molecular weight carbohydrates that can be produced naturally or may originate from polysaccharides after chemical or enzymatic hydrolysis (Giordano et al., 2006; Trincone, 2013). The nature of interactions in these oligosaccharides and their conformations are more specific in considering them as therapeutic agents, or elicitors for the production of specific metabolites. In algae, the diversity of monosaccharides in these biomolecules with absolute configuration (D or L) of sugars and the α or β distinction of glycosidic linkages, and their position of substitutions remains essentially unexplored. Thus, the molecular size is characterized by the degree of polymerization (DP) defined as follows: DP with generally 20–25 or higher are defined as polymers while oligosaccharides contain between 2 and 10 residues (Courtois, 2009). Henceforth, algae-derived marine oligosaccharides have shown to be essential in numerous industrial applications such as biomedicine/pharmaceuticals, cosmetics, nutraceuticals, prebiotics, environmental protection, feed-based, wastewater management, algal-based biomaterials, and more (Kim and Rajapakse, 2005; Giordano et al., 2006; Ji et al., 2011; Kang et al., 2015).

Recently, marine oligosaccharides have gained attention in biological applications based on chemical and physical properties. Moreover, the composition and sequence analysis of marine oligosaccharides are still a challenging task because of their complexity in structures and heterogeneity. More research to understand the structural properties of these oligosaccharides are essential to utilize them efficiently. Mass spectrometry (MS) based studies provide the structural characterization of these oligosaccharides in more precise, reproducible and reliable manner (Stahl et al., 2002; Zaia, 2004; Mischnick, 2012; Lang et al., 2014). Thus, the differential liability of certain residues or chemical groups for the elucidation of the depolymerization mechanisms has to be further investigated with a multi-disciplinary approach for the fine structural analysis of algae-derived marine oligosaccharides. Thus, the sustainable ways to access these molecules is to understand the range of important functions in the biological systems, with an effort to unlock potential applications of these algae-derived marine oligosaccharides (Trincone, 2014; Ermakova et al., 2015).

ALGAE-DERIVED MARINE OLIGOSACCHARIDES

Recently, microalgae are recognized as a rich source of polysaccharides with high biodiversity serving numerous biological applications (Stengel et al., 2011; Barra et al., 2014). These algae-derived marine oligosaccharides are broadly classified into different classes depending upon their chemical diversity namely chitosan-, laminarin-, alginate-, fucoidan-, carrageenan- and ulvan- oligosaccharides. The study of structural details (such as ramification, substitution etc.) of well-defined molecular size oligosaccharides has gained attention by NMR chemical shifts assignments and mass spectrometry in combination (Duus et al., 2000; Lang et al., 2014; Préchoux and Helbert, 2014). Few biological applications of algae-derived oligosaccharides and their recent relevant advancements are illustrated in this review with keen foresight on future perspectives. Algae consists of carbohydrates such as glucose, starch and other polysaccharides used as potential bioactive ingredients in functional foods (Hamed et al., 2015). Besides these oligosaccharides are another group of carbohydrates with small DP containing 3–10 sugar units, ranging from disaccharides and/or carbohydrates with up to 20 residues with defined functions (Patel and Goyal, 2010).

Studies on oligosaccharides were characterized by antioxidant and antitumor effects demonstrates immunostimulation functions (Lordan et al., 2011) and prebiotic functional foods (Iji and Kadam, 2013). *In vitro* antioxidant assays by three marine oligosaccharides from alginate-, chitosan-, and fucoidan-based derivatives exhibits their structural significance including scavenging activities (Wang et al., 2007). Low molecular weight alginate-derived oligosaccharide (ADO) and chito-oligosaccharide (COS) were purified from alginate and chitosan with polyanionic and polycationic properties, confirmed the anti-UVR activity, a potential commercial UVR protector application in the domain of functional foods (He et al., 2013). The alginate oligosaccharides derived from seaweeds may serve as growth elicitors for few microalgae like *Chlamydomonas reinhardtii, Nannochloropsis oculata* enhancing biomass (Yokose et al., 2009), along with increased levels of essential fatty acids in *C. reinhardtii* (Yamasaki et al., 2012). Seaweed-derived oligosaccharides were able to perform set of actions, such as antifungal and antibacterial precursors, defense enzymes and active natural products aiming toward enhanced pathogen protection (Weinberger et al., 2010; Vera et al., 2011). Our focus is to understand the significance of algae-derived marine oligosaccharides, thus directly and/or indirectly depicting their role in discovering mechanisms and the molecular functions within specific biological applications.

APPLICATIONS

Functional Foods

The algal biodiversity provides wide range of derived oligosaccharides used as prebiotics such as fructo-, galacto-, xylo-, mannano-, glyco- and isomalto-oligosaccharides in human and animal nutrition (Ouwehand et al., 2005; Bosscher et al., 2006). Marine macroalgae or seaweeds are rich sources of bioactive compounds namely polysaccharides, tannins, and diterpenes that are crucial as functional ingredients (O'sullivan et al., 2010) and will be regarded as key element of nutrition in the future (Milinki et al., 2011). Functional oligosaccharides have been regarded as keen constituent in prebiotics as sweeteners, fiber, humectants, etc. (Patel and Goyal, 2010). Thus, carbohydrates derived from algae are regarded as alternatives in future due to their inherent prebiotic properties as functional foods.

Environmental Protection

The potential of growth-enhancing properties in these natural biomolecules provides new insights on their metabolic changes, increasing stress tolerance and triggering disease response pathways (Khan et al., 2009; Kurepin et al., 2014; Stadnik and Freitas, 2014). Algae-derived oligosaccharides will stimulate growth by enhancing carbon and nitrogen assimilation in terrestrial plants and trees, thereby increasing basal metabolism, and cell division along with level of essential oils and/or biomolecules such as alkaloids, terpenoids, terpenes, and phenylpropanoid compounds (PPCs), which triggers protection against pathogens (González et al., 2012). In principle, the dual beneficial effect by the oligo-alginates and oligo-carrageenans leading to the simultaneous activation of growth and defense against pathogens in plants involve specific binding of these oligosaccharides to receptors involved in signal transduction (Castro et al., 2011; Vera et al., 2011).

Nutraceuticals

Nutraceuticals are essential to protect human body against damage caused by reactive oxygen species (ROS), which can destroy macromolecular machinery such as DNA, membrane lipids, and proteins, lead to health disorders namely diabetes mellitus, neurodegenerative, inflammatory diseases, and cancer (Kim, 2013). Chitosan and its oligosaccharides has gained considerable attention due to their biological activities and potential applications in the pharmaceutical, agricultural and environmental industries (Xia et al., 2011). Studies demonstrate these marine organisms are potential resources of such novel molecules and their derivatives (chitosan, chitosan oligosaccharides, β-carotene, astaxanthin, fucoidans, and phlorotanins) acting as anticancer agents, and the mechanism of these marine-derived compounds varies depending upon the nature of cancer inhibitory pathways (Janak et al., 2010; Kim, 2010). Recently, Raman and Doble (2015) showed that marine dietary fiber, κ-Carrageenan from marine red algae, *Kappaphycus alvarezii* used as a functional food to prevent colon carcinogenesis. Alginate oligosaccharides (AOs) obtained from enzymatic treatment of abundant alginate showed antioxidant activities which involves radical scavenging as natural antioxidant, has profound applications in the food industry (Falkeborg et al., 2014). Alginate-derived oligosaccharides exerts inhibitory effect on neuro-inflammation and promotes microglial phagocytosis, a potential nutraceutical agent for neurodegenerative diseases such as Alzheimer's disease (AD; Zhou et al., 2015).

Cosmetics

Natural cosmetics and personal care products that incorporate marine-based extracts are being increasingly demanding due to their natural origin, and the potential for new marine-derived compounds and extracts are immensely poised for accelerated development in the cosmeceutical industry (Thomas and Kim, 2013; Kim, 2014). Matrix metalloproteinase enzymes (MMPs) are closely associated with wrinkle formation and play an important role in the digestion of extracellular matrix components. These MMPs activity are inhibited by marine-derived chitooligosaccharides, flavonoids, polyphenols, and fatty acids (Zhang and Kim, 2009). Chitosan and its derivatives, especially chitooligosaccharides, also show antioxidant activity that offers protection against free radicals play a significant role in protecting the skin aging from oxidative damage (Harish Prashanth and Tharanathan, 2007). Brown algae-derived active oligosaccharides having unique functional properties are good hydrocolloids used for thickening and stabilizing emulsion in cosmetic formulations (Wijesinghe and Jeon, 2011).

Biomedicine

Recently, chitooligosaccharides (COS) have gained attention in the pharmaceutical and medicinal applications, due to their higher solubility and toxicity, along with physiological effects such as antioxidant, anticancer, antidiabetic, antimicrobial, hypoglycemic, anti-Alzheimer's, anticoagulant, and hypocholesterolemic properties (Kim and Mendis, 2006). Chitosan oligosaccharides (COS) is effective agents for lowering blood cholesterol and pressure, controlling arthritis, and enhancing antitumor properties (Kim and Rajapakse, 2005). Ulvan or ulvan-derived oligosaccharides significantly lowers total and LDL-cholesterol, and reduces triglyceride content in serum, meanwhile increases HDL-cholesterol (Pengzhan et al., 2003). The carrageenan oligosaccharides from *Kappaphycus striatum* activates the immune system by exerting antitumor effect (Yuan et al., 2006). Carrageenan possesses promising activity both *in vitro* and *in vivo*, showing potential as therapeutic agents (Pangestuti and Kim, 2014) and also well known for their medicinal effects with vast array of bioactivities such as cholesterol-lowering effects, anticoagulant, immunomodulatory activity, antiviral, and antioxidant properties. Since oligosaccharides and their derivatives are water-soluble, non-toxic and biodegradable, they might be beneficial biomaterials in diseases such as diabetes and obesity (Qin et al., 2006).

FUTURE PERSPECTIVES

The advancements in algae biotechnology has significant role for innovative and sustainable renewables wherein the manipulation and targeting of bioactive ingredients among these organisms has to fit the increasingly niche product specifications. Our knowledge on the algae-derived oligosaccharides has been increased substantially and many research advancements are published in this decade on their chemical structure diversity and their biological applications. Understanding the basic biology of these derivatives using -omics technology, biochemistry and applied biotechnology through screening and characterization of bioactive molecules, developing -omics tools to reconstruct metabolic pathways, and low-cost production of algae-derived oligosaccharides will focus upon driving bioproduct discovery and optimization in algal systems. Further analytical studies of oligosaccharides, together with molecular investigations will enhance our understanding on the mechanisms of their biological action. Henceforth, these insights on cellular and molecular mechanisms of algae-derived oligosaccharides will ultimately result in futuristic green cell-factories.

CONCLUSIONS

Glycobiology is the understanding of structure and function relationship of carbohydrates and their derivatives playing fundamental role in range of complex biological processes associated with molecular and cellular communication, disease and immunology, and developmental biology. Thus, understanding glycomics is the complex information conveyed by these biomolecules the paucity of structural information and may provide genuine candidates for complete carbohydrate characterization. Henceforth, understanding the molecular mechanisms of these algae-derived oligosaccharides in various biological applications are essential and the diversity in their chemical structures and -omics studies will provide insights toward unrevealing metabolic functions, the amicable solution of marine resources to next generation sustainables.

AUTHOR CONTRIBUTIONS

All the authors contributed equally toward the preparation of the manuscript. PJ was involved in overall contribution of the manuscript such detailing and final editing. AN and KS contributed equally in drafting the manuscript.

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