Journal of Applied Phycology (2024) 36:1459–1484
https://doi.org/10.1007/s10811-023-03176-9

REVIEW

Nutritional and health promoting perspectives of *Monostroma* spp. (Chlorophyta): A systematic review

Sana Mansoor[1] · Khawaja Muhammad Imran Bashir[1,2] · Md. Mohibbullah[3] · Maria Dyah Nur Meinita[4] · Mohammed Nurul Absar Khan[5] · Jae-Hak Sohn[6,7] · Jae-Suk Choi[1]

Received: 29 July 2023 / Revised: 17 December 2023 / Accepted: 22 December 2023 / Published online: 22 January 2024

Abstract

Green seaweeds, particularly species of the genus *Monostroma*, have gained recognition for their health-promoting potential, attributed to their rich content of polysaccharides, polyphenols, carotenoids, flavonoids, vitamins, and macro- and micronutrients, all of which show a wide range of bioactive properties. This review encompasses a total of 72 articles, selected in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The compounds present in *Monostroma* spp., in addition to their nutritional and chemical compounds, are associated with a number of health-promoting activities. However, it is notable that among the literature reviewed for bio-functionalities, a considerable proportion of studies were conducted *in vitro* (66%), followed by *in vivo* studies (29%), with clinical trials accounting for a much smaller fraction (5%). The mechanisms underlying the health-beneficial effects in biological systems require further in-depth exploration and characterization to facilitate future translational research leading to clinical trials. These clinical trials are an essential step in advancing seaweed-based functional food ingredients into the industrial realm. As of now, research focusing on bioactive compounds derived from *Monostroma* is relatively scarce. This review serves as a resource, offering insights into the nutritional and functional properties of *Monostroma* species. It can be a valuable tool for food scientists and engineers as they embark on future research involving *Monostroma* and the development of seaweed-based food and nutraceutical products.

Keywords Bioactive compounds · Health-beneficial effects · *Monostroma* · Chlorophyceae · Nutrition · Seaweed · Sulfated polysaccharides

Introduction

Seaweeds have been used as traditional medicine and supplementary food items for centuries. At present, the commercial utilization of seaweeds is of great interest in the preparation of food products, health functional ingredients, cosmetics, and colorants (Boopathy and Kathiresan 2010). The genus *Monostroma* is extensively distributed throughout the world. It is predominantly consumed in Korea, Japan, China, South Australia, New Zealand, Brazil, and South America (Kavale et al. 2020). *Monostroma* is a marine green macroalga belonging to the family Monostromataceae and consists of

Sana Mansoor and Khawaja Muhammad Imran Bashir contributed equally to this work.

✉ Jae-Hak Sohn
jhsohn@silla.ac.kr

✉ Jae-Suk Choi
jsc1008@gnu.ac.kr

[1] Department of Seafood Science and Technology, The Institute of Marine Industry, Gyeongsang National University, Tongyeong 53064, Korea

[2] German Engineering Research and Development Center for Life Science Technologies in Medicine and Environment, Busan 46742, Korea

[3] Department of Fishing and Post Harvest Technology, Sher-e-Bangla Agricultural University, Dhaka 1207, Bangladesh

[4] Faculty of Fisheries and Marine Science, Jenderal Soedirman University, Purwokerto 53123, Indonesia

[5] Department of Fishing and Post Harvest Technology, Faculty of Fisheries, Chattogram Veterinary and Animal Sciences University, Chattogram 4202, Bangladesh

[6] Seafood Research Center, IACF, Silla University, Busan 49277, Korea

[7] Department of Food Biotechnology, College of Medical and Life Sciences, Silla University, Busan 46958, Korea

a single-cell thick sheet-like thallus (monostromatic). More than 32 species have been reported (Guiry and Guiry 2022), of which: *M. nitidum, M. latissimum, M. oxyspermum, M. undulatum, M. angicava, M. arcticum,* and *M. hariotii* are identified as more nutritious and of high commercial value (FAO 2021). Among the *Monostroma* species, *M. nitidum* is mainly cultivated in Korea, accounting for 6321 t wet weight in 2019 (Lüning and Pang 2003; FAO 2021). The global green seaweed production in 2019 was 35.82 million (wet) tonnes (FAO 2021), among which the production of *Monostroma* and *Ulva* together contributed 6748 (wet) tonnes with a commercial market value of $US 54.28 million (FAO 2021).

Lahteenmaki-Uutela et al. (2020) reported that because of their delicacy and quality, *Monostroma* seaweeds were accepted in novel food catalogues that have been maintained online by the European Commission. This finding is similar to the reports of Gubelit et al. (2015) and Garcia-Vaquero and Hayes (2016), who reported that *Monostroma* has great potential to be used in food products due to the presence of substantial amounts of protein and polyunsaturated fatty acids, as compared to other seaweeds. *Monostroma* spp. are often used in salads, jams, soups, spices, relishes, meat, and fish dishes in Brazil, China, Japan, and the Pacific Coast of America (Kavale et al. 2020; Kaur et al. 2023). Wang and Chiang (1994) reported the processing technology of "Hai-Tsai Jam" (sea vegetable jam) and a soup of *Monostroma* species mixed with eggs and scallion.

Monostroma spp. contain several bioactive compounds, including polysaccharides, chlorophyll-*a*, chlorophyll-*b*, carotenoids, phenolics, flavonoids, and levoglucosan (Gordillo et al. 2006; Zhang et al. 2008; Seedevi et al. 2015; Tsubaki et al. 2016; Liu et al. 2018a; Saco et al. 2018; Song et al. 2021; Gomes et al. 2022; Kaur et al. 2023). The amount of chlorophyll-*a* and chlorophyll-*b* found in *Monostroma* is comparable to that found in terrestrial plants (Choudhary et al. 2021) and is responsible for their specific green colour. Among the isolated polysaccharides, rhamnan sulfate (RS) has the potential to be used commercially and has been extensively studied against various disease models, confirming the health-functional activity.

Research interest in exploring *Monostroma* species as viable alternatives for protein and nutrition sources is increasing. This heightened focus is attributed to the presence of essential proteins and associated health benefits, as documented by Thiviya et al. (2022). To date, a very limited number of review articles have focused on the nutritional and health-promoting effects of *Monostroma* spp., where the life history (Masakazu 1969; Kaur et al. 2023) and biological activities of RS extracted from *M. nitidum* (Suzuki and Terasawa 2020) are currently available in the database. In addition, Bast (2011) produced a book focusing on cultivation, ecophysiology, phylogeography, and molecular systematics of members of the genus. However, to the best of our knowledge there has been no systematic review of the nutritional and health-promoting bio-functional properties of *Monostroma*. The present review systematically updates the current research on the nutritional properties, chemical compounds, and health-beneficial effects of *Monostroma* spp. to encourage further commercial utilization of these seaweeds in both food and pharmaceutical industries.

Materials and methods

A systematic literature search of articles published from 2000 to the present, covering the topics of nutritional and functional properties of *Monostroma* species, was conducted. The articles were primarily written in English. The analysis of the literature was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al. 2009; Negara et al. 2023). Articles were searched using PubMed, ScienceDirect, Wiley Online Library, SpringerLink, and Google Scholar databases. Additionally, references in each article were further reviewed to find any relevant studies. The key search used a comprehensive list of MeSH (Medical Subject Headings) terms, including terms such as "*Monostroma*" and "functionality" or "compounds" or "nutrition" or "effect" or "pharmacology". Additional search words included "antioxidant", "antimicrobial", "anti-hypertension", "immunomodulation", "seaweeds", "seaweeds *in vitro*", "seaweeds *in vivo*", and "seaweeds clinical". Original articles, conference papers, abstracts, theses, book chapters, and review articles were assessed and subjectively selected based on their relevance. Furthermore, articles were extracted and sorted using Mendeley to prevent duplicate citations (Chakniramol et al. 2022). After thorough screening, articles not fulfilling the inclusion criteria were discarded. The remaining articles were analysed and extracted, and the information included in this review.

After searching databases, a total of 130 articles were reviewed. In the final stage of screening using the PRISMA method, 72 studies were included in this review. Out of these 72 articles, 10 reported the nutritional properties, and 62 reported the health-functional properties of *Monostroma*.

Nutritional properties of *Monostroma* spp.

Many types of seaweeds are used as commercial ingredients in foods and pharmaceuticals and are considered a potential source for new food and drug development due to the presence of various macro- and micronutrients. The nutritional composition of seaweeds varies among species due to their dependence on growth conditions and environmental factors (Maehre et al. 2014; Ganesan et al. 2014; Pirian et al. 2018; Xu et al. 2023). *Monostroma* spp. contribute significantly to obtaining a high level of nutrition due to the abundance of

dietary proteins, carbohydrates, vitamins, fibres, lipids, peptides, and mineral content (McDermid and Stuercke, 2003; Risso et al. 2003). They are used in dietary supplements due to the presence of numerous vitamins, minerals, and trace elements (Arasaki and Arasaki 1983). The proximate composition of selected *Monostroma* spp. is shown in Table 1.

The carbohydrate content of *Monostroma* can range from 3.7–46.1% dry weight (DW; McDermid and Stuercke 2003; Risso et al. 2003; Gordillo et al. 2006; Kumar et al. 2014; Sufen et al. 2021), which is similar to that of many brown seaweeds (12.2–56.4% DW), as reported by Salehi et al. (2019) and Leandro et al. (2020). Among the *Monostroma* spp. studied, *M. nitidum* had the highest carbohydrate content (46.1% DW; Sufen et al. 2021), followed by *M. oxyspermum* (32.6% DW; McDermid and Stuercke 2003), *M. undulatum* (32.5% DW; Risso et al. 2003), *M. arcticum* (16.7% DW; Gordillo et al. 2006), and *M. latissimum* (8.3% DW; Kumar et al. 2014). Among the reported carbohydrates, a significant percentage is in the form of dietary fibre, which is indigestible but aids in digestion and helps control blood cholesterol. The fibre content of *Monostroma* species is reported to be 0.9–19.6% DW (Risso et al. 2003; Sufen et al. 2021), with *M. undulatum* having the highest fibre content of species assessed (19.6% DW; Risso et al. 2003), followed by *M. nitidum* (4.94% DW; Sufen et al. 2021). Chang and Wu (2008) developed seaweed noodles using *M. nitidum* powder, with or without eggs. They found that as the proportion of *M. nitidum* powder increased, there was a significant improvement in the extensibility, springiness, and breaking energy of freshly cooked noodles. Furthermore, the inclusion of seaweed powder had a noteworthy positive impact on the texture properties, cooking yield, and overall quality of the noodles, whether eggs were added or not.

Dietary fibre helps to maintain a positive environment in the gastrointestinal tract, thus providing beneficial effects on human health (Holdt and Kraan 2011; Salehi et al. 2019). Fibre also helps regulate the body's use of sugars, helping to maintain and control blood sugars. In general, dietary fibre suppresses the increase in blood glucose levels (Yu et al. 2014; Fuller et al. 2016). The related mechanisms include: i) delay in the transfer of carbohydrates from the stomach to the duodenum and ii) inhibition of carbohydrate digestion and absorption in the small intestine. The daily demand for dietary fibre in a meal for an average human is recommended to range between 25–30 g (EFSA 2010). Conversely, polysaccharides consist of long chains of monosaccharides, the simple carbohydrates, linked together by glycosidic bonds (Zhu et al. 2010). Seaweeds, in general, contain 40–50% polysaccharides (Torres et al. 2019), which are influenced by environmental and ecological conditions. Large quantities of polysaccharides are synthesized in green seaweeds.

The cell wall of *Monostroma* contains a significant amount of sulfated polysaccharides (Ulvan; Lee et al. 1998; Patel 2012) with a molecular weight of approximately $10x10^3$ to more than $1x10^6$ Daltons (Suzuki and Terasawa 2020). Rhamnan sulphate, a sulfated polysaccharide extracted from the cell wall of *M. nitidum*, is the main fibre component in this species (Suzuki and Terasawa 2020). Song et al. (2021) found that rhamnan sulphate contains approximately 59 ± 9% (w/w) carbohydrate and 31 ± 4% (w/w) sulfate. It consists of a long linear chain structure of α-1,3-linked l-rhamnose connected with α-1,2-linked branched chains, to which several sulfate groups are bound (Lee et al. 2010; Tako et al. 2017). Rhamnan sulphate is the most extensively studied polysaccharide from *Monostroma*, probably due to its numerous nutritional and health benefits (Wang et al. 2014; Tsubaki et al. 2016; Liu et al. 2018a). Nakamura et al. (2011) reported that the extracted polysaccharides from *M. nitidum* had 25% sulfate groups. Sulfate groups are an important structural element responsible for macrophage-stimulating activities (Jiang et al. 2013). Activated macrophages are not only produced because of cell-mediated immune responses but they can also be produced in response to innate stimuli following viral infections or stress (Mosser and Edwards 2008). Their role in host defence against intracellular pathogens behind several autoimmune diseases, including inflammatory bowel syndrome and rheumatoid arthritis, has been well reported (Gordon and Taylor 2005; Szekanecz and Koch 2007; Dale et al. 2008; Mosser and Edwards 2008; Zhang and Mosser 2008). Other polysaccharides reported from *M. nitidum* are low-degree-of-polymerization (low-DP) sulfated polysaccharides, named Mon-6, Mon-24, and Mon-30 (Kazłowski et al. 2012).

Table 1 Proximate composition of selected *Monostroma* spp.

Seaweeds	Proximate composition (% D.W.)						Reference
	Moisture content	Ash content	Lipids	Proteins	Carbohydrates	Fiber	
M. oxyspermum	92.3 – 93.5	21.9 – 22.9	3.7 – 3.9	9.4 – 9.8	31.0 – 32.6	-	McDermid & Stuercke 2003
M. undulatum	-	33.94 – 40.05	0.32 – 1.47	12.89 – 21.85	20.86 – 32.48	14.36 – 19.6	Risso et al. 2003
M. arcticum	-	-	-	0.74 – 1.94	13.3 – 16.7	-	Gordillo et al. 2006
M. latissimum	-	-	-	1.184 – 1.584	3.7 – 8.3	-	Kumar et al. 2014
M. nitidum	-	15.4	0.60 – 1.82	5.10 – 9.29	41.88 – 46.10	0.94 – 4.94	Sufen et al. 2021

The protein content of many green seaweeds is reported to be rather low compared to that of other seaweeds, but its presence with other nutrients promotes synergistic effects on animal and human health upon consumption (Leandro et al. 2020). *Monostroma* protein content ranges from 0.74–21.85% DW, where *M. undulatum* (Risso et al. 2003) has the highest protein content (21.85% DW), followed by *M. oxyspermum* (9.8% DW; McDermid and Stuercke 2003).

The lipid content of *Monostroma* ranges from 0.32–3.8% DW (McDermid and Stuercke 2003; Risso et al. 2003; Sufen et al. 2021). Seaweeds contain different polyunsaturated fatty acids (PUFAs) that essentially provide energy and help in developing the cell wall (Schmid et al. 2018). A higher lipid content has been reported in *M. oxyspermum* (3.9% DW; McDermid and Stuercke 2003) than in *M. undulatum* (1.47% DW; Risso et al. 2003), which corresponds to the increased level of PUFAs. Mohammed et al. (2021) explained that some seaweeds contain low-fat levels, thereby reducing their caloric content when ingested alone, or as a component with other food products. In addition to a relatively high lipid content, *M. oxyspermum* also has a higher caloric content (3300 cal g^{-1} ash-free DW) than other *Monostroma* species (McDermid and Stuercke 2003).

Monostroma undulatum had a higher ash content, varying between 33.92 and 40.05% on a dry weight basis (Risso et al. 2003), in comparison to *M. oxyspermum*, which had an ash content of 22.62% (McDermid and Suercke 2003). Following this, *M. nitidum* showed a lower ash content at 15.4% (Sufen et al. 2021). Ash contains macro- and micro-minerals or trace elements. Edible seaweeds contain most of the essential macrominerals (Ca, Mg, K, Na, and P) and microminerals (Fe, Cu, Mn, Zn, B, N, S, and I; Muñoz and Díaz 2022) required for growth and maintenance. Macrominerals are elements of essential cellular components and trace elements are natural inorganic ingredients that are required in very small quantities in the human body (<100 μg g^{-1}); however, both macro- and micro-minerals play a vital role in the biochemical responses of living organisms (Al-fartusie and Mohssan 2017). *Monostroma* spp. contain different minerals and polysaccharides which improve the viscosity and overall nutritional value of other foods they are added, for example, soup and jam (Kaur et al. 2023). Due to a high amount of iodine in *M. nitidum* (63.6 ± 2.5 μg g^{-1} of dry mass; Hou et al. 1997), with an appropriate cultivation management it can be recommended as a functional food for patients with iodine deficiency. The mineral composition of selected *Monostroma* spp. is presented in Table 2.

Among the reviewed literature, data on nitrogen (N; 2.58% DW) have only reported in *M. oxyspermum* (McDermid and Stuercke 2003), and data on chromium (Cr; 16.3 μg g^{-1}), iodine (I; 63 μg g^{-1}), nickel (Ni; 3.8 μg g^{-1}), and aluminum (Al; 20.4 μg g^{-1}) are only available for *M. nitidum* (Oza et al. 1983; Hou et al. 1997; Im et al. 2006). The

Table 2 Macro- and micro-nutrients reported in selected *Monostroma* spp.

Species	Macronutrients (% D. W.)							Micronutrients (μg g^{-1})										Reference
	P	Ca	K	Mg	Na	N	S	Fe	Zn	Mn	Cu	Cr	B	I	Ni	Al	Vit. C	
M. lastissimum	0.4	0.6	3.1	1.4	-	-	62.3	142	32	10	28	-	52	-	-	-	-	McDermid & Stuercke 2003
M. oxyspermum	0.35	0.58	3.14	1.36	-	2.68	6.23	142	32	10	28	-	52	-	-	-	1.3	McDermid & Stuercke 2003
M. undulatum	1.9-4.5	1.5-2.3	1.4-3.2	-	7.4-13.1	-	-	-	-	-	-	-	-	-	-	-	1.6-4.6	Risso et al. 2003
M. nitidum	0.12	5.3	5.28	1.26	5.55	-	79.7	106	20.9	4.6	4.1	16.3	-	63	3.8	20.4	-	Im et al. 2006; Oza et al. 1983; Hou et al. 1997

D.W.: Dry weight; *P*: Phosphorus; *Ca*: Calcium; *K*: Potassium; *Mg*: Magnesium; *Na*: Sodium; *N*: Nitrogen; *S*: Sulfur; *Fe*: Iron; *Zn*: Zinc; *Mn*: Manganese; *Cu*: Cupper; *Cr*: Chromium; *B*: Boron; *I*: Iodine; *Ni*: Nickel; *Al*: Aluminum; *Vit. C*: Vitamin C.

World Health Organization has set a guideline value of 50 μg L^{-1} for the total chromium content in food (WHO 2020). Trace amounts of trivalent chromium – Cr(III) - are required for normal body functions (Bashir et al. 2021). Cr content observed in *M. nitidum* (16.3 μg g^{-1}; Im et al. 2006) was higher than the one found in other food crops, including rice (2.18 ± 0.42 μg g^{-1}), water spinach (12.80 ± 0.16 μg g^{-1}), cabbage (0.41 ± 0.01 μg g^{-1}), and Chinese cabbage (0.55 ± 0.01 μg g^{-1}) (Xu et al. 2023).

With respect to macronutrients, *M. undulatum* contained the highest amount of phosphorus (P; 4.5% DW; Risso et al. 2003), followed by *M. latissimum* (0.4% DW; McDermid and Stuercke 2003). *Monostroma nitidum* contained the highest amount of calcium (Ca; 5.3% DW) and potassium (K; 5.28% DW), followed by *M. undulatum* (Risso et al. 2003). *Monostroma latissimum* contained the highest amount of magnesium (Mg; 1.4% DW; McDermid and Stuercke 2003) and *M. undulatum* contained the highest amount of sodium (Na; 13.11% DW; Risso et al. 2003). Among the micronutrients, *M. latissimum* contained the highest amounts of iron (Fe; 142 μg g^{-1}), zinc (Zn; 32 μg g^{-1}), manganese (Mn; 10 μg g^{-1}), copper (Cu; 28 μg g^{-1}), and boron (B; 52 μg g^{-1}) McDermid and Stuercke (2003). *Monostroma undulatum* contained the highest amount of vitamin C (4.55 μg g^{-1}) Risso et al. (2003). McDermid and Stuercke (2003) showed that *M. oxyspermum* powder had vitamin A (β-carotene), vitamin B_3 (Niacinamide), and vitamin C in measurable amounts of 70 IU g^{-1}, 0.70 μg g^{-1}, and 1.3 μg g^{-1}, respectively. Furthermore, different toxic elements such as Al, Pb, Cd, As, and Hg have been reported in some edible green seaweeds, including *Caulerpa* spp., *Codium fragile*, and *Ulva clathrata* (Muñoz and Díaz 2022) but, to date, not in any species of *Monostroma*.

The above studies showed that *Monostroma* spp. are a reliable source of fibre, proteins, carbohydrates, and water-soluble (B_1, B_2, B_3, and C) and fat-soluble (β-carotene with vitamin A activity and vitamin E) vitamins, highlighting the nutritional significance of *Monostroma* (Skrovankova 2011).

Bioactive compounds in selected species of *Monostroma*

Seaweeds have great potential as nutraceuticals and pharmaceuticals due to their rich content of bioactive compounds, including secondary metabolites such as chlorophylls, polysaccharides, levoglucosan, phenolics, carotenoids, and flavonoids. The primary bioactive compounds identified in *Monostroma* are detailed in Table 3.

Monostroma angicava contained sulfated polysaccharides Ls2-2 and RS (Mao et al. 2005; Liu et al. 2017, 2018a) and *M. nitidum* featured sulfated polysaccharide MS-1, low-DP (Mon-6 and Mon-30), RS, and levoglucosan (Luyen et al. 2006; Nakamura et al. 2011; Karnjanapratum and You

Table 3 Major bioactive components reported in selected *Monostroma* spp

Species	Polysaccharides							Chlorophyll		Carotenoids	Flavonoids	Levoglucosan	Polyphenols	Reference
	SP	SP Ls2-2	SP Ms-1	Low DP Mon-6	Low-DP Mon-24	Low-DP Mon-30	RS	*a*	*b*					
M. arcticum								•	•	•				Gordillo et al. 2006
M. angicava		•					•							Mao et al. 2005; Liu et al. 2017; Liu et al. 2018a
M. nitidum	•		•	•	•	•	•					•		Luyen et al. 2006; Nakamura et al. 2011; Karnjanapratum & You 2011; Kazlowski et al. 2012; Yamashiro et al. 2017; Cao et al. 2019; Song et al. 2021
M. latissimum							•	•		•	•			Zhang et al. 2008; Kumar et al. 2014; Wang et al. 2014; Tsubaki et al. 2016; Saco et al. 2018
M. oxyspermum	•													Seedevi et al. 2015
M. grevillei													•	Gomes et al. 2022
Monostroma sp.							•							Kaur et al. 2023

SP: Sulfated polysaccharide; *Low-DP*: Low-degree polymerisation sulfated polysaccharide; *RS*: Rhamnan sulphate

2011; Kazłowski et al. 2012; Yamashiro et al. 2017; Cao et al. 2019; Song et al. 2021). Levoglucosan, which easily hydrolyses to glucose using acid (Kitamura et al. 1991), can be utilized by various microorganisms, both eukaryotic and prokaryotic, as a carbon and energy source (Prosen et al. 1993; Nakahara et al. 1994; Zhuang et al. 2001; Khiyami et al. 2005). *Monostroma latissimum* contained RS, chlorophyll *a*, carotenoids, and flavonoids (Zhang et al. 2008; Kumar et al. 2014; Wang et al. 2014; Tsubaki et al. 2016; Saco et al. 2018). Additionally, *M. oxyspermum* contained sulfated polysaccharides (Seedevi et al. 2015) and *M. grevillei* contained polyphenols (Gomes et al. 2022).

Health-promoting effects of *Monostroma* spp.

Among the diverse bioactive compounds found in *Monostroma*, the sulfated polysaccharide called "rhamnan" holds significant importance due to its antioxidant, anti-viral, anti-thrombotic, and anti-coagulant activities (Zhang et al. 2008; Cao et al. 2019; Li et al. 2011). Arasaki and Arasaki (1983) have reported that *Monostroma* can combat goitre, hypertension, insomnia, stomach diseases, constipation, and digestive tract internal parasites owing to their content of vitamins, minerals, fibre, and trace elements. The following sections summarize the evidence for those bio-functionalities of selected *Monostroma* spp.

Antimicrobial properties

The *in vitro* studies have highlighted the anti-viral activity of extracts of selected *Monostroma* spp. against various viruses, including enterovirus 71 (EV71; Wang et al. 2018, 2020) and coronaviruses (SARS-CoV and SARS-CoV-2; Terasawa et al. 2020; Song et al. 2021). Moreover, *in vivo* anti-viral activity of *Monostroma* seaweeds has also been reported against EV71, Japanese encephalitis virus (JEV; Kazłowski et al. 2012), and influenza A virus (IFV-1; Terasawa et al. 2020). Kim and Lee (2008) reported the *in vitro* anti-bacterial properties of methanol extracts from *M. nitidum* against a broad spectrum of bacteria, including Gram-positive species such as *Bacillus subtilis*, *Micrococcus luteus*, *Staphylococcus aureus,* and methicillin-resistant *Staphylococcus aureus* CCAR and CCARM, as well as Gram-negative bacteria like *Escherichia coli*, *Enterobacter aerogenes*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Vibrio parahaemolyticus*, and *Edwardsiella tarda*. Lee et al. (2013) reported the bioactivity of *M. nitidum* ethanol and methanol extracts against *Helicobacter pylori*. In addition to anti-viral and anti-bacterial activities, *M. nitidum* methanol extracts have also shown anti-fungal activity against *Candida albicans* (Kim and Lee 2008). The *in vitro* antimicrobial activities of selected *Monostroma* spp. are listed in Table 4, while the *in vivo* studies are in Table 5, and the clinical studies are reported in Table 6.

Ethanol-extracted polysaccharides from *M. latissimum* showed antimicrobial activity (Wang et al. 2018). An *in vitro* cytopathic effect (CPE) assay was performed using African green monkey kidney cells (Vero cells) infected with EV71 strain BrCr-TR and found strong cytopathic inhibition (35, 45, 65, and 85% at 0.1 μg mL^{-1}, 1 μg mL^{-1}, 10 μg mL^{-1} and 100 μg mL^{-1} concentration, respectively), IC_{50} value of 461 μg mL^{-1}, cytotoxic concentration 50% (CC_{50}) value of <5000 μg mL^{-1}, and selectivity index (SI: CC_{50}/IC_{50}) value of >10000.0. The plaque reduction assay showed that pre-incubation of EV71 with extract at concentrations of 15.63 to 250 μg mL^{-1} markedly reduced the number of EV71 plaques and protected Vero cells from infection. For *in vivo* experiments, three-day-old neo-natal ICR mice were intra-peritoneally challenged with a 50% tissue culture infectious dose ($10^{5.5}$ $TCID_{50}$) of EV71, followed by intra-muscular injection of extract. Five days post challenge at 5 mg kg^{-1}, the viral titers strongly decreased in the heart (50%), brain (30%), intestine (33%), and muscle tissue (20%). The results of this study suggested polysaccharides from *M. latissimum* possess strong anti-EV71 activities both *in vitro* and *in vivo* with low toxicity.

Sulfated glucuronorhamnan from ethanol extracts of *M. nitidum* showed anti-viral activity against EV71 strain BrCr-TR (Wang et al. 2020). The IC_{50} values of cytopathic activity for pre-treatment of EV71 with the polysaccharide, pre-treatment of cells with the polysaccharide, and addition of the polysaccharide during and after virus adsorption were 256.91 ng mL^{-1}, 16.11, 2.90, and 1.68 μg mL^{-1}, respectively. The SI was above 84% during *in vitro* experiments. Similar to the study of Wang et al. (2018), three-day-old neo-natal ICR mice were intra-peritoneally challenged with $10^{5.5}$ $TCID_{50}$ of EV71 followed by an intra-muscular injection of the polysaccharide for the *in vivo* study. At 16 h post challenge with 10 μg mL^{-1}, the viral titers strongly decreased in the cell supernatant (64%). The *M. nitidum* extracts directly inactivated EV71 virions or inhibited some stages of the virus life cycle after adsorption.

Song et al. (2021) assessed the anti-viral activity of RS from water extracts of *M. nitidum* against SARS-CoV-2 S-protein binding activity (RBD; related to delta variants of SARS-CoV-2; expressed in Expi293F cells). The IC_{50} value was 1.6 μg mL^{-1}, and inhibition was 22 and 20% in the S-protein variants E484Q and L452R+E484Q, respectively, at 5 ng mL^{-1} RS. On the other hand, 1 μg mL^{-1} RS provided >80% viral entry inhibition (IC_{50}) for both the wild type (2.39 μg mL^{-1}) and delta variant (1.66 μg mL^{-1}). Furthermore, the isolated RS demonstrated a significant ability to bind the S-protein and neutralized the pseudotyped virus *in vitro*. This highlights its competiveness relative to

Table 4 Antimicrobial properties of *M. latissimum, M. nitidum,* and *M. oxyspermum* – *In vitro* studies

Species	Component	Microorganism	Method/Assay	Results	Reference
Anti-viral					
M. latissimum	PML	EV71	MTT, CPE assay, CC_{50} activity, Protein expressions	• No significant cytotoxicity observed at 0.1 – 5000 µg mL^{-1} in MTT assay. • IC_{50} of 461 µg mL^{-1} in CPE assay. • CC_{50} of >5000 µg mL^{-1}. • PML (12.5–50 µg mL^{-1}) treatment for 0.5 h significantly inhibited the PI3K/Akt pathways which interfere with EV71 replication thus significantly inhibiting the early stages of the EV71 life cycle. • PML (12.5–50 µg mL^{-1}) treatment for 0.5 h significantly reduced the activation of EGFR, however, did not significantly decrease the expression level of phosphorylated NF-κB protein. Therefore, the cellular EGFR/PI3K/Akt signaling pathway may be involved in the anti-EV71 activity of PML *in vitro.*	Wang et al. 2018
M. nitidum	SPsm	HSV-1	CC_{50}, IC_{50}, anti-HSV-1 activity, CPE assay	• The CC_{50} of 4100 µg mL^{-1}. • The IC_{50} of 0.4* and 3.7** µg mL^{-1} in Anti-HSV-I activity assay.	Lee et al. 2004
	CRS	HSV-2, IFV-A	CC_{50}, IC_{50}, activity, CPE assay	• Potent anti-viral activity against the HSV-2 virus, whereas the CRS had no influence on replication of the IFV-A virus. • The CC_{50} of >10,000 µg mL^{-1} for HSV-2 and IFV-A. • The IC_{50} of 0.87* and 40** µg mL^{-1} for HSV-2 and >1,000 µg mL^{-1} for the IFV-A.	Lee et al. 2010
	MWS	EV71	MTT, CPE, FCM, Confocal imaging, qRT-PCR	• The IC_{50} of 256.91 ng mL^{-1}, 16.11, 2.90, and 1.68 µg mL^{-1}, during pre-treatment. of EV71 with MWS, pre-treatment of cells with MWS, addition of MWS during and after virus adsorption, respectively, in CPE assay. • The IC_{50} of 0.90 and 256.91 µg mL^{-1} in plaque reduction assay and cellular EGFR/PI3K/Akt pathway activity, respectively.	Wang et al. 2020
	RP	SARS-CoV-2	Competitive SPR assay; RBD activity	• The IC_{50} of 1.6 µg mL^{-1} in a competition SPR assay. • The IC_{50} 750 ng mL^{-1} for heparin in a RBD activity.	Song et al. 2021
	RS	HSV-1, HSV-2, HCMV, MV, MuV, IFV-A, HIV, SARS-CoV, HAV-2, PV3, CVB-1, HRV14	CC_{50} , EC_{50}, $TCID_{50}$, SI, Time of addition experiment, Virus adsorption assay, Virus penetration assay	• The CC_{50} of 16000 ± 640, 16000 ± 640, 12000 ± 920, 16000 ± 640, 16000 ± 640, 17000 ± 2000, 9900 ± 780, 12000 ± 19000, 4300 ± 220, 16000 ± 640, 16000 ± 640, and 13000 ± 640 µg mL^{-1} for HSV-1, HSV-2, HCMV, MV, MuV, IFV-A, HIV, SARS-CoV, HAV-2, PV3, CVB-1, and HRV14, respectively. • The EC_{50} of 6.5 ± 0.49, 0.93 ± 0.18, 1.1 ± 0.18, 8.3 ± 0.57, 1.5 ± 0.19, 41 ± 6.4, 1.2 ± 0.15, 0.77 ± 0.17, 480 ± 42, >5000, 2600 ± 170, and 530 ± 29 µg mL^{-1} for HSV-1, HSV-2, HCMV, MV, MuV, IFV-A, HIV, SARS-CoV, HAV-2, PV3, CVB-1, and HRV14, respectively, when sample was added during viral infection. • The EC_{50} of 31 ± 2.8, 4.7 ± 0.35, 67 ± 9.9, 4300 ± 450, 51 ± 6.4, 310 ± 42, 1.2 ± 0.11, 0.99 ± 0.13, >1000, >5000, >5000, and >1000 µg mL^{-1} for HSV-1, HSV-2, HCMV, MV, MuV, IFV-A, HIV, SARS-CoV, HAV-2, PV3, CVB-1, and HRV14, respectively, when sample was added immediately after viral infection.	Terasawa et al. 2020
	Low-DP	JEV	MTT, Plaque assay	• The IC_{50} of 36.2 ± 5.8 µM in MTT assay. • The IC_{50} of 44.5 ± 5.7 µM in plaque assay.	Kazłowski et al. 2012
M. oxyspermum (Newly: Gayralia oxysperma)	ShR	HSV-1, HSV-2	MTT assay, Virus plaque reduction assay	• Potent antiherpetic activity with the IC_{50} of 0.27 ± 0.03 µg L^{-1} for HSV-1. • The IC_{50} of 0.036 ± 0.001 µg L^{-1} for HSV-2. • The SI value of >3704 for HSV-1 and >27,778 for HSV-2.	Cassolato et al. 2008
Anti-bacterial					

Table 4 (continued)

Species	Component	Microorganism	Method/Assay	Results	Reference
M. nitidum	Methanol extract	Gram-positive: *B. subtilis,* *M. luteus,* *S. aureus,* MRSA CCAR, MRSA CCARM, Gram-negative : *E. coli,* *E. aerogenes,* *K. pneumonia,* *P. aeruginosa,* *S. typhimurium,* *V. parahaemolytices,* *E. tarda*	Radial diffusion assay, MIC and MBCs values	• The inhibition zones of 8, 8, and 6 mm were observed for *B. subtilis,* MRSA CCAR 3561, and MRSA CCARM3089. • The extract was not effective against tested Gram negative bacteria.	Kim & Lee, 2008
	Ethanol and methanol extract	*H. pylori*	Antimicrobial activity by disk diffusion and MIC values; Urease inhibition assay	• Low activity. • 5.5 ± 0.1 at 1 mg/disk and 10.0 ± 0.1 at 3 mg/disk in disk diffusion method. • MIC value of 195 µg mL^{-1}. • The ethanol extracts showed the *H. pylori* urease inhibition activity of 2.11 ± 0.61, 3.32 ± 0.88, and 18.92 ± 3.77 % at 10, 100, and 1000 µg mL^{-1}, respectively. • The 80% methanol extracts showed the *H. pylori* urease inhibition activity of 9.00 ± 2.82, 12.50 ± 2.34, and 18.68 ± 2.93 % at 10, 100, and 1000 µg mL^{-1}, respectively.	Lee et al. 2013
Anti-fungal					
M. nitidum	Methanol extract	*C. albicans*	Anti-fungal assay	• No anti-fungal activity was observed.	Kim & Lee, 2008

PML: Sulphated Rhamnan polysaccharide from *M. latissimum; CPE*: Cytopathic effect; CC_{50}: Concentration required to reduce cell viability by 50%; *EV71*: Enterovirus 71; *MWS*: Water-soluble sulfated polysaccharide from *M. nitidum*; *FCM*: Flow cytometry; *qRT-PCR*: Real-time quantitative PCR; *RP*: Rhamnose polysaccharides; *SARS-CoV-2*: *Coronavirus 2; SPR*: Surface Plasmon resonance; *RBD*: S-protein binding activity; *SPs*: Sulfated polysaccharides; *HSV-1*: Anti-herpes simplex virus type 1; *CRS*: Crude rhamnan sulfate; *HSV-2*: Herpes simplex virus type 2; EC_{50}: Half maximal effective concentration; *SI*: Selectivity Index; *HSV-1*: Herpes simplex virus type 1; *MV*: Measles virus; *MuV*: Mumps virus; *PV3*: Poliovirus type 3; *CVB-1*: Coxsackievirus type B-1; *IFV-A*: Influenza A virus; *HCMV*: Human cytomegalovirus; *SARS-CoV*: Human coronavirus; *HAV-2*: Human adenovirus type 2; *HIV*: Human immunodeficiency virus; *HRV14*: Human rhinovirus type 14; $TCID_{50}$: 50% tissue culture infectious dose; *Low-DP*: Low-degree polymerization sulfated polysaccharides; *JEV*: Japanese encephalitis virus; *ShR*: Sulfated heterorhamnan; *MIC*: Minimum inhibitory concentration; *MRSA*: Methicillin Resistant *Staphylococcus aureus*; *MBCs*: Minimal bactericidal concentrations

* Sample was added to the medium during infection and throughout the incubation thereafter; ** Sample was added to the medium immediately after viral infection

Table 5 Antimicrobial properties of *M. latissimum* and *M. nitidum* – *In vivo* studies

Species	Component	Microorganism	Animal model	Results	Reference
Anti-viral					
M. latissimum	PML	EV71	SPF-ICR mice	• Viral titers in the heart (1.80 and 2.20 Log_{10} PEU mL^{-1}), brain (1.60 and 2.00 Log_{10} PEU mL^{-1}), intestine (1.50 and 4.00 Log_{10} PEU mL^{-1}), and muscle tissues (3.00 and 4.00 Log_{10} PEU mL^{-1}) after 5-days of post challenge at 5 or 10 mg kg^{-1} of PML. • Continuous increase in body weights of the infected ICR mice treated with PML (5 or 10 mg/kg) during the observation period.	Wang et al. 2018
M. nitidum	low-DP	JEV	6-8-week-old male C3H/HeN mice	• Higher positive effect on survivability in JEV-infected C3H/HeN mice. • High (>65%) anti-viral activity.	Kazłowski et al. 2012
	MWS	EV71	SPF-ICR mice	• Up to 64% decreased viral titers in brain, intestine, heart, and muscle tissue of EV71-infected mice after treatment with 10 µg mL^{-1} of MWS. • Obvious reduction in the level of virus VP1 protein in brain, heart, skeletal muscle and intestine of EV71-infected mice after treatment with 10 mg kg^{-1} of MWS.	Wang et al. 2020
	RS	IFV-A	5-week-old female BALB/c mice	• RS-treated mice showed approximately 20-25% reduction in body weight. • RS significantly reduced IFV-A production in the lungs by 50% and showed a viral titer reducing tendency in the bronchoalveolar lavage fluids 3 days after infection. • RS did not reduce lung viral titers but showed a reducing tendency for viral production 3 days after infection. • This indicates that RS exerted inhibitory effects on IFV-A replication in both immunocompetent and immunocompromised mice.	Terasawa et al. 2020

PML: Sulphated rhamnan polysaccharide from *M. latissimum; EV71*: Enterovirus 71; *SPF-ICR mice*: Specific-pathogen-free mice from the Institute of Cancer Research; CC_{50}: Concentration required to reduce cell viability by 50%; *MWS*: Water-soluble sulfated polysaccharide from *M. nitidum; RS*: Rhamnan sulfate; *IFV-A*: Influenza A virus; *Low-DP*: Low-degree polymerization sulfated polysaccharides; *JEV*: Japanese encephalitis virus

iota-carrageenan and fucoidans in their potential to combat COVID-19 (Kwon et al. 2020; Jin et al. 2020). Therefore, RS isolated from *M. nitidum* has the potential to be used as an anti-viral drug against coronaviruses. However, before considering the utilization of RS as a therapeutic and/or preventive anti-viral drug, it is imperative to undertake future investigations. These should encompass an exploration of the structure-activity relationship, an evaluation of bioavailability, an examination of the anti-viral activity of RS through *in vivo* and clinical trials, and a comprehensive toxicity analysis.

Lee et al. (2004) reported promising anti-viral activity of the sulfated polysaccharides from hot water extracts of *M. nitidum* against herpes simplex virus-1 (HSV-1). Vero cells for the HSV-1 and HF strains were grown in MEM supplemented with 5% FBS. The cytotoxicity of the polysaccharides was very low, with CC_{50}, IC_{50}, and SI values of 4100 µg mL^{-1}, 0.4 µg mL^{-1}, and 10000, respectively, for HSV-1 replication. Vero

Table 6 Antimicrobial properties of *M. nitidum* – Clinical studies

Species	Component	Microorganism	Subject	Results	Reference
Anti-bacterial					
M. nitidum	RS	Clostridia phylum Negativecutes class Acidaminococcales order Veillonelales order	Subjects with low defecation frequencies	• RS decreased Clostridia from 36.1 to 31.2%. • RS increased Negativecutes from 4.6 to 7.56%. • RS increased Acidaminococcales from 1.9 to 3.2%. • RS increased Veillonelales from 1.7 to 2.7%.	*Shimada et al.* 2021

RS: Rhamnan sulfate

cells were infected with HSV-l at a high titer of 10 PFU per cell, and after 8 h of infection, the anti-HSV-1 activity value for RS was 67 μg mL^{-1}. Therefore, RS from *M. nitidum* can be a potent anti-viral substance against HSV-1.

Sulfated polysaccharides from hot water extracts of *M. nitidum* had anti-viral activity against IFV-A and HSV-2 (Lee et al. 2010). Vero cells for the herpes simplex virus-2 (HSV-2) strain UW258 were grown in MEM supplemented with 5% FBS, and MDCK cells for the IFV-A, strains A/NWS/33 and H1N1, were grown in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% FBS. The polysaccharides showed low inhibitory effects, where CC_{50} of >10000 μg mL^{-1} was observed for both Vero and MDCK cells. The IC_{50} for HSV-1 was 0.87 μg mL^{-1} during infection and throughout the incubation period and 40 μg mL^{-1} after viral incubation. The IC_{50} value for IFV-A was >1000 μg mL^{-1} in both cases. The SI value decreased by more than 97.5% during infection and throughout the incubation period compared with that after viral incubation for HSV-2. Hence, polysaccharides from *M. nitidum* extracts may be useful as preventive agents for HSV-2 infection.

Rhamnan sulfate isolated from the hot water extract of *M. nitidum* was orally administered to IFV-infected immuno-competent (5-FU (-)) and immuno-compromised (5-FU (+)) mice, which suppressed viral proliferation (Terasawa et al. 2020). Female BALB/c mice were intra-nasally infected with 2 x 10^5 PFU of virus in 50 μL of phosphate-buffered saline (PBS). Oral administration of RS was performed 30 min after viral infection at a dose of 5 mg day^{-1} twice a day from seven days before virus inoculation to seven days after virus inoculation. Viral particles were not detected in the RS-treated 5-FU (-) mice, but the virus was still detected in the control mice and the 5-FU (+) mice after seven days of infection. Moreover, RS suppressed viral replication in both lungs at 18% and bronchoalveolar lavage fluids (BALFs) at 58% after seven days of infection compared with the control group. Not only those findings but also the CC_{50}, EC_{50}, and CC_{50}/EC_{50} values prove that RS from *M. nitidum* provided anti-viral properties against enveloped viruses [HSV-1, HSV-2, human cytomegalovirus (HCMV), measles virus (MV), mumps virus (MuV), IFV-A, human immunodeficiency virus (HIV), and SARS-CoV] and non-enveloped viruses [human adenovirus type (HAV), human rhinovirus type 14 (HRV14), poliovirus type 3 (PV3), and coxsackievirus type B (CVB)].

Oral administration of RS (in a cellulose white capsule) from hot water extracts of *M. nitidum* showed anti-bacterial activity against bacteria such as *Clostridia*, Negativecutes, Acidaminococcales, and Veillonelales in a clinical study (Shimada et al. 2021). Seventy-three healthy Japanese male and female volunteers (20-65 years old) participated in this study. Each participant ingested one capsule per day for two weeks. After two weeks, *Clostridia* bacteria decreased in fecal matter (36.1 ± 13.0% at 0 weeks vs. 31.2 ± 12.6% at 2 weeks). This is helpful for humans because *Clostridia* spp. produce medium-length fatty acids that increase water absorption into cells of the gastrointestinal tract and subsequently dry up faeces, causing constipation. Rhamnan sulfate increased Negativicutes class bacteria (4.6 ± 5.0% at 0 weeks vs. 7.5 ± 5.0% at 2 weeks). In the Negativicutes, they detected four orders, and two of these orders, Acidaminococcales (1.9 ± 3.0% at 0 weeks vs. 3.2 ± 3.6% at 2 weeks) and Veillonellales (1.7 ± 2.3% at 0 weeks vs. 2.7 ± 2.5% at 2 weeks), were significantly increased by the application of RS. The increase in these bacteria is positively related to a reduction in constipation.

Kim and Lee (2008) studied the anti-fungal activity of *M. nitidum* methanol extracts against *C. albicans*; however, no significant activity was observed in this case. Hence, future research could focus on the anti-fungal activity of other *Monostroma* spp. The above studies indicated that *Monostroma* extracts and purified compounds such as RS from selected *Monostroma* spp. have great potential as anti-viral and anti-bacterial agents. Thus, comprehensive research studies using animal models and subsequent clinical trials are needed to further understand these properties.

Antioxidant properties

The defence mechanism of organisms against free radical attack is typically mediated by antioxidants (Arshad et al.

Table 7 Antioxidant properties of selected *Monostroma* spp. – *In vitro* studies

Species	Component	Cell line	Method/Assay	Results	Reference
M. arcticum	Crude extract	-	SOD, GsR, APX, CAT, and Ascorbate activity	• SOD activity of 1,004 U mg^{-1} TSP. • GsR activity of 1.581,004 U mg^{-1} TSP. • APX activity of 0.97 U mg^{-1} TSP. • CAT activity of 27.11 U mg^{-1} TSP. • Ascorbate activity of 1.63 U mg^{-1} TSP.	Aguilera et al. 2002
M. oxyspermum (newly: G. oxysperma)	SP	-	TAC, DPPH• and ABTS• scavenging activity, Reducing power assay	• TAC activity of 33.2–66.29% at concentration of 50–250 g mL^{-1}, respectively, with a maximum inhibition of 66.29% at 250 g mL^{-1}. • DPPH• scavenging activity of 22.39-68.19% at concentrations of 10–160 g mL^{-1}, respectively, with the highest activity of 66.83% at 160 g mL^{-1}. • ABTS• scavenging activity of 25.37–76.81% at concentrations of 25–125 g mL^{-1}, respectively. • The reducing power of sulfated polysaccharide was 1.02–15.81% at 50–400 g mL^{-1}, respectively.	Seedevi et al. 2015
M. hariotii	Phenolic compounds and carotenoids	-	DPPH• scavenging activity, Phenolic and carotenoid content	• DPPH• scavenging activity of 5.1%. • Phenolic content of 75.7 µg GAE g^{-1}. • Carotenoid content of 36.3 µg β-carotene g^{-1}.	Bernardi et al. 2016
M. nitidum	Methanol and aqueous extracts	-	O_2^-•, HO•, H_2O_2, and DPPH• scavenging assays, TPC	• O_2^-• scavenging activity of 6.82 ± 1.32%, 56.82 ± 3.24%, 6.67 ± 1.49%, and 7.69 ± 0.53% for 20ME, 70ME, 20AE, and 70AE, respectively. • HO• scavenging activity of 74.64 ± 1.68%, 34.37 ± 2.92%, and 53.59 ± 0.96% at 20ME, 70ME, and 20AE, respectively. • H_2O_2 scavenging activity of 62.36 ± 2.215%, 21.58 ± 2.97%, 45.78 ± 1.10%, and 30.29 ± 0.42% at 20ME, 70ME, 20AE, and 70AE, respectively. • DPPH• scavenging activity of 27.90 ± 0.34%, 20.86 ± 0.89%, 66.28 ± 1.06%, and 30.67 ± 3.63% at 20ME, 70ME, 20AE, and 70AE, respectively. • Total phenolic content of 5.49 ± 1.075 mg g^{-1}, 15.62 ± 1.04 mg g^{-1}, 1.70 ± 0.68 mg g^{-1}, and 1.18 ± 0.60 mg g^{-1} at 20ME, 70ME, 20AE, and 70AE, respectively.	Heo et al. 2005
	Algal polysaccharides	-	DPPH• scavenging, Ferrous ion chelating, and H_2O_2 scavenging activity, Reducing power assay	• DPPH• scavenging activity of 6.4 ± 0.4%, 19.8 ± 0.6%, and 11.6 ± 0.4% in non-digested, A_{250} and B_{500} digested samples, respectively. • Reducing power of 1.0 ± 0.4%, 6.5 ± 0.4%, and 9.8 ± 0.7% in non-digested, A_{250} and B_{500} digested samples, respectively. • Inhibition of the hemoglobin-catalyzed peroxidation of linoleic acid at 11.7 ± 0.8%, 67.4 ± 1.1%, and 43.4 ± 0.6% in non-digested, A_{250} and B_{500} digested samples, respectively. • Ferrous ion chelating effect of 7.3 ± 0.1%, 69.1 ± 0.4%, and 73.8 ± 0.1% in non-digested, A_{250} and B_{500} digested samples, respectively. • H_2O_2 scavenging activity of 3.3 ± 1.0%, 30.5 ± 2.8%, and 31.7 ± 0.4% in non-digested, A_{250} and B_{500} digested samples, respectively. • STP content of 91.0 ± 1.9%, 169.9 ± 2.5%, and 213.5 ± 12.3% in non-digested, A_{250} and B_{500} digested samples, respectively.	Wu and Pan 2004
	Ethanol extract	-	DPPH• scavenging and AChE inhibitory activity	• DPPH• scavenging activity of 54.1 ± 6.7% at 40 µg mL^{-1}. • AChE inhibitory activity of 23.4 ± 2.4% at 10 µg mL^{-1}.	Jeon et al. 2012
	Sulfated polysaccharide	-	SOD assay	• SOD activity of 579-650% at 200 µg mL^{-1}.	Hoang et al. 2015
	Flavonoid	-	DPPH• scavenging and Ferrous ions chelating activity	• DPPH• scavenging activity of >18%. • Ferrous ion chelating capacity of 32%.	Lin et al. 2021

SOD: Superoxide dismutase; *U*: units; *CAT*: Catalase; *TSP*: Total soluble protein; *GsR*: Glutathione reductase; *APX*: Ascorbate peroxidase; *SP*: Sulfated polysaccharide; *DPPH•*: 2,2-diphenylpicrylhydrazyl radical; *TAC*: Total antioxidant capacity; *ABTS•*: 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid; O_2^-•: Superoxide anion radical, *HO•*: Hydroxyl radical; H_2O_2: Hydrogen peroxide; *TPC*: Total phenolic content; *20ME*: Methanol extract at room temp; *70ME*: Methanol extract at 70 °C; *20AE*: Aqueous extract at room temp; *70AE*: Aqueous extract at 70 °C; *AChE*: Acetylcholinesterase; *STP*: Soluble total polyphenol content

Table 8 Antioxidant properties of *M. nitidum* – *In vivo* studies

Species	Component	Animal model	Results	Reference
M. nitidum	CSP	SD rats	• Significant increase in UGT1A1 and UGT1A6 mRNA levels in liver. • Significant decrease in CYP1A1 mRNA levels in liver.	Charles et al. 2007

CSP: Crude seaweed polysaccharides; *SD*: Sprague-Dawley

2014). Bioactive compounds and polysaccharides from various *Monostroma* spp. have shown promising antioxidant activities determined through α,α-diphenyl-β-picrylhydrazyl (DPPH) radical scavenging activity (Aguilera et al. 2002; Wu and Pan 2004; Bernardi et al. 2016), ferrous ion chelating activity, H_2O_2 scavenging activity (Wu and Pan 2004), enzymatic activities [superoxide dismutase (SOD) assay, glutathione reductase (GR) assay, ascorbate peroxidase (APX) assay, catalase (CAT), ascorbate; Aguilera et al. 2002; Hoang et al. 2015)], phenolic content, carotenoid content (Bernardi

Table 9 Anti-obesity activity and anti-hypercholesterolemia properties of *M. angicava* and *M. nitidum* – *In vitro* studies

Species	Component	Cell line	Method/Assay	Results	Reference
M. angicava	SP Ls2-2	HepG2 and insulin-resistant HepG2 cells	MTT assay, Glucose consumption assay, TG, TC levels, mRNA expressions of genes related to glucose and lipid metabolism	• Strong anti-diabetic activity. • No significant cytotoxicity up to 500 µg mL^{-1}. • 36% increase in the glucose consumption level of Ls2-2 at 200 µg mL^{-1} was observed, as compared to the control. • Significantly reduced TG and TC levels at concentrations of 25-100 µg mL^{-1}. • Ls2-2 treatment groups stimulated the expressions of AMPKα2, GLUT2 and HL however, inhibited the expressions of PEPCK and ACC2.	Liu et al. 2017
M. nitidum	Methanol and aqueous extracts	-	α-glucosidase inhibitory efficacy	• Poor α-glucosidase inhibitory activities (less the10% with both extracts) at 1 mg mL^{-1}.	Ko et al. 2011
	SP	HepG2 cells	Cellular TG and cholesterol content, qRT-PCR	• 33-36% reduced cholesterol content at 200 µg mL^{-1}. • 31-43% reduced TG content at 200 µg mL^{-1}.	Hoang et al. 2015
	RS	HCAEC	LDL permeability, Apoptosis rate, Immunostaining	• Significant increase in HS coverage. • Barrier formation and resulting 5-fold decrease in monolayer permeability to both water and LDL.	Cancel and Tarbell 2013
		HUVECs, HAoSMCs, HCAEC	Proliferation and migration assays, LDL permeability assay, Immunostaining of HS, Western blot	• Reduced proliferation and migration of endothelial cells. • Enhanced barrier function of endothelial cells, preventing deposition of LDL. • A maintained barriers function even in the presence of glycocalyx-degrading enzymes. • Potent inhibitor of NF-kB pathway activation in endothelial cells by TNF-α.	Patil et al. 2022

SP: Sulfated polysaccharide; *HepG2*: Human hepatocellular carcinoma cells; *HUVECs*: Human umbilical endothelial cells; *HAoSMCs*: Human aortic smooth muscle cells; *HCAEC*: Human coronary artery endothelial cells; *HS*: Heparin sulphate - a major gycocalyx component; *RS*: Rhamnan sulphate; *LDL*: Low-density lipoprotein; *NF-kB*: nuclear factor kappa light chain enhancer of activated B cells; *TNF-α*: Tumor necrosis factor alpha

Table 10 Anti-obesity activity and anti-hypercholesterolemia properties of *M. angicava* and *M. nitidum* – *In vivo* studies

Species	Component	Animal model	Results	Reference
M. angicava	SP: Ls2-2	Male SD rats	• 36% increase in glucose consumption level at 200 µg mL^{-1}. • TG and TC levels decreased by 33% and 30% at 50 µg mL^{-1}, respectively.	Liu et al. 2017
M. nitidum	Crude Rhamnan sulfate extract	Male Wister rats	• Significantly inhibited increment of plasma glucose levels. • 30 mg dL^{-1} prohibition of plasma glucose level after 30 min in rats.	Kamimura et al. 2010
	RS	DIO – Zebrafish model	• Oral administration of 250 µg g^{-1}, BW day^{-1} attenuated body weight gain, dyslipidemia (plasma TG and LDL-C content) and hepatic steatosis in DIO. • 11% decrease in weight gain. • 21.5% decrease in plasma TG. • 23.5% decreased in plasma LDL-C.	Zang et al. 2015
		HFD-fed NSY/HOS mice, a type 2 diabetes mellitus strain	• RS increased the fecal volume in mice and calorie excretion with decreased plasma lipids. • 7.41% decrease in body weight. • 26.50% decrease in Plasma TG. • 11.93% decrease in TC.	Shimada et al. 2021
		HFD-fed ApoE-/- mice	• No change in plasma TG content in both male and female mice. • Reduced vascular inflammation and atherosclerosis in both sexes of mice but stronger therapeutic effect in female mice. • Significant decrease in cholesterol plasma levels in female mice but not in male. • 45.2% decrease in lipid deposition in female and 36.4% in male mice.	Patil et al. 2022

RS: Rhamnan sulphate; *SP*: Sufated polysaccharide; *DOI*: Diet-induced obesity; *TG*: Triglyceride; *LDL-C*: Low-density lipoprotein cholesterol; *SD*: Sprague-Dawley; *TC*: Total cholesterol; *HFD*: High-fat diet

et al. 2016) and reducing power assay (Wu and Pan 2004). The *in vitro* antioxidant activities of some *Monostroma* spp. are listed in Table 7, and *in vivo* studies are presented in Table 8. To the best of our knowledge, no clinical study on the antioxidant activity of *Monostroma* has been reported yet.

The tripotassium phosphate extracts of *M. arcticum* (Aguilera et al. 2002) showed SOD, GR, APXs, CAT activity, and ascorbate content of 1004 U mg^{-1} TSP, 1.58 U mg^{-1} TSP, 0.97, U mg^{-1} TSP, 27.11 U mg^{-1} TSP, and 1.63 U mg^{-1} TSP, respectively. Therefore, *M. arcticum* extract can be used as a source of potent antioxidants of natural origin. Bernardi et al. (2016) identified antioxidants, such as phenolic compounds and carotenoids, in *M. nitidum*. The methanol extracts of *M. nitidum* showed a DPPH-radical scavenging

Table 11 Anti-obesity activity and anti-hypercholesterolemia properties of *M. latissimum* and *M. nitidum* – Clinical studies

Species	Component	Subject	Results	Reference
M. latissimum	SP	Adult males with high cholesterol levels	• No change in serum HDL-C level however, LDL-C significantly reduced compared with the control. • RS maintained a low ratio of LDL-C/HDL-C, thus could prevent lifestyle-related diseases, such as obesity and hyperlipidemia.	Nishikawa et al. 2006 (in Japanese)
M. nitidum	SP	Adult males with high cholesterol levels	• *M. nitidum* SP suppressed elevated blood glucose and LDL-C levels, thus preventing obesity.	Nishikawa et al. 2006 (in Japanese)
	RS	Healthy adults	• Significant deduction of blood glucose level was observed 30 min (42 mg dL^{-1}) after intake to 120 min (3 mg dL^{-1}) after intake.	Kamimura *et al.* 2010

SP: Sulphated polysaccharide; *RS*: Rhamnan sulphate; *LDL-C*: Low-density lipoprotein cholesterol; *HDL-C*: High-density lipoprotein cholesterol

Table 12 Anti-coagulant and anti-thrombotic properties of selected *Monostroma* spp. – *In vitro* studies

Species	Component	Cell line	Methods/assays	Results	Reference
M. oxyspermum	SP	-	APTT and PT assay	• An activity of 7.13 IU and 1.26 IU at 25 g mL^{-1} was observed in APTT and PT assay, respectively.	Seedevi et al. 2015
M. latissimum	Sulfated rhamnan and its five degraded fragments with different molecular weights	-	APTT, PT, and TT assay	• Inhibited intrinsic and common pathways of coagulation and thrombin activity and conversion of fibrinogen to fibrin. • RS did not inhibit extrinsic pathway of coagulation as no effect of anticoagulant on PT was observed. • 200 s clotting time at 120 µg mL^{-1} in APTT assay. • 120 s clotting time at 50 µg mL^{-1} in TT assay.	Zhang et al. 2008
	SP with high rhamnose content	-	APTT and TT assay	• 200 s clotting time at 20 µg mL^{-1} in APTT assay. • 120 s clotting time at 10 µg mL^{-1} in TT assay. • High APTT and TT activities mediated by heparin cofactor II.	Mao et al. 2009
	Purified SP - PML	-	APTT, PT, and TT assay	• 200 s clotting time at 16 µg mL^{-1} in APTT assay. • 120 s clotting time at 16 µg mL^{-1} in TT assay. • 15.7 ± 2.6 s clotting time at 16 µg mL^{-1} in PT assay.	Li et al. 2011
	LMWP	-	APTT assay	• Higher activity at higher LMWP concentration. • Lower bleeding risk as compared to heparin. • 200 s clotting time at 50 µg mL^{-1} in APTT assay. • High APTT activity mediated by heparin cofactor II.	Li et al. 2012

Table 12 (continued)

Species	Component	Cell line	Methods/assays	Results	Reference
M. angicava	SP - PF2	-	APTT, PT and TT assay, Fibrin(ogen)olytic activity and thrombolytic activity	• 200 s clotting time at 150 µg mL^{-1} in APTT assay. • 120 s clotting time at 100 µg mL^{-1} in TT assay. • 16.1 ± 2.3 s clotting time at 150 µg mL^{-1} in PT assay. • Clot lytic rate of 26.49% at 10 mg mL^{-1}.	Li et al. 2017
	SP- Ls2-2	-	APTT, PT, and TT assay	• 200 s clotting time at 50 µg mL^{-1} in APTT assay. • 120 s clotting time at 200 µg mL^{-1} in TT assay.	Liu et al. 2017
	SPm	-	APTT, PT, and TT assay, Fibrin(ogen)olytic activity and thrombolytic activity	• 200 s clotting time at 50 µg mL^{-1} in APTT assay. • 120 s clotting time at 100 µg mL^{-1} in TT assay. • Markedly different PT as compared to that of heparin. • SPm showed a lack of prolongation effect in PT assay. • Clot lytic rate (%) of 38.26 ± 0.54% at 16 mg mL^{-1}.	Liu et al. 2018b
	MSP, MSP4	-	APTT, PT, and TT assay, Fibrin(ogen)olytic activity and thrombolytic activity	• 200 s clotting time at 100 µg mL^{-1} in APTT assay. • 120 s clotting time at 100 µg mL^{-1} in TT assay. • MSP failed to prolong PT at the tested concentrations, showing no inhibition of the extrinsic pathway of coagulation. • High fibrin(ogen)olytic and thrombolytic activities. • Clot lytic rate (%) of 34.29 ± 1.68 and 20.79 ± 1.17 was observed at 20 mg mL^{-1} in MPS and MSP4 treatments, respectively.	Liu et al. 2018c

Table 12 (continued)

Species	Component	Cell line	Methods/assays	Results	Reference
M. nitidum	SP with high rhamnose content	-	APTT and TT assay	• Potent thrombin inhibitor mediated by heparin cofactor II. • Mildly inhibitor of coagulation factor Xa by potentiating antithrombin III. • 200 s clotting time at 15 µg mL^{-1} in APTT assay. • 120 s clotting time at 50 µg mL^{-1} in TT assay.	Mao et al. 2008
	Sulfated rhamnan	-	APTT and TT assay	• 22.7% relative activity in APTT assay. • 173% relative activity in TT assay.	Yamashiro et al. 2017
	Purified Sulfated Polysaccharide – MS1	-	APTT, PT, and TT assay, Fibrin(ogen)olytic activity and thrombolytic activity, Factor Xa activity	• > 200 s clotting time at 25 µg mL^{-1} in APTT assay. • > 120 s clotting time at 50 µg mL^{-1} in TT assay. • Lack of prolongation effect in PT assay. • Inhibited both intrinsic/common pathways of coagulation and thrombin activity or conversion of fibrinogen to fibrin.	Cao et al. 2019
	RS	HUVEC	Measurement of thrombin and factor Xa activity, TF and VWF expression	• Significantly enhanced inhibition of thrombin and factor Xa in the presence of antithrombin as well as heparin. • Inhibited tissue factor expression and VWF release from the endothelial cells treated with or without lipopolysaccharide, TNF-α, or thrombin. • 5% suppressed TNF-α expression at 100 µg mL^{-1}. • 50% suppressed VWF release in 100 µg mL^{-1}.	Okamoto et al. 2019

RS: Rhamnan sulphate; *APTT*: Activated partial thromboplastin time; *TT*: Thrombin time; *PT*: Prothrombin time; *SP*: Sulfated polysaccharides; *LMWP*: Low molecular weight sulphated rhamnan; *MSP*: Monostroma sulfated polysaccharides; *SPm*: Seaweed polysaccharide; *HUVEC*: Human umbilical vein endothelial cells; *VWF release*: von Willebrand factor release; *TNF-α*: Tumor necrosis factor alpha

Table 13 Anti-coagulant activity and anti-thrombotic properties of *M. nitidum* and *M. angicava* – *In vivo* studies

Species	Component	Animal model	Results	Reference
M. nitidum	Purified Sulfated Polysaccharide – MS-1	Male SD rats	• Moribund and bleeding after intravenous injection was not observed. • Prolonged clotting time showing absorption. • > 200 s clotting time at 10 mg kg^{-1} in APTT assay. • > 120 s clotting time at 50 µg mL^{-1} in TT assay. • No prolongation effect observed in PT assay at 2.5 mg/kg. • Platelet aggregation was significantly reduced at 10 mg kg^{-1}.	Cao et al. 2019
M. angicava	SF – PF2	SD rats	• Clot lytic rate of 26.49% at 10 mg mL^{-1}. • High fibrin(ogen)olytic activity and thrombolytic activity.	Li et al. 2017
	SF – Ls2-2	Male SD rats	• Increased clot lytic rate from 24.09 % to 38.11% with increasing dose from 10 mg mL^{-1} to 20 mg mL^{-1}.	Liu et al. 2017
	SPm	Male SD rats	• High fibrin(ogen)olytic and thrombolytic activities. • D-dimer 0.28 ± 0.05 mg L^{-1}, PAI-1 0 U mL^{-1}, and FDP 4.67 ± 0.38 µg mL^{-1} was observed at 8 mg mL^{-1}.	Liu et al. 2018b
	Polysaccharides – MSP	Male SD rats	• 200 s clotting time at 16 mg mL^{-1} in APTT assay. • 70 s clotting time in TT assay. • Clot lytic rate of 34.29 ± 1.68% at 20 mg $mL^{-1.}$	Liu et al. 2018c

SF: Sulfated polysaccharide; *SD*: Sprague-Dawley; *MSP*: *Monostroma* sulfated polysaccharides; *SPm*: Seaweed polysaccharide; *APTT*: Activated partial thromboplastin time; *TT*: Thrombin time; *PT*: Prothrombin time; *PAI-1*: Plasminogen activator inhibitor 1; *FDP*: Fibrin(ogen) degradation products

activity of 5.1%, a phenolic content of 75.7 µg GAE g^{-1}, and a carotenoid content of 36.3 µg g^{-1}, suggesting potential antioxidant activity of these extracts. However, the reported concentration of these compounds in fresh vegetables, such as spinach and broccoli, is much higher than that in *Monostroma* spp. Spinach (*Spinacia oleracea* L.) hot water extracts, for instance, had a total phenolic content of 1.5 mg GAE g^{-1}, while ethanol extracts contained 0.5 mg GAE g^{-1}

Table 14 Anti-inflammatory properties of *M. nitidum* – *In vitro* studies

Species	Component	Cell line	Method/Assay	Results	Reference
M. nitidum	Sulfated polysaccharides – MF1, MF2	HepG2 cells	Real-time qPCR, iNOS, TNF-α, IL-6, IL-8 and visfatin expression	• Reduced iNOS expression from 7 fold to 1.5 fold at 100 µg mL^{-1}. • Reduced TNF-α expression from 6 fold to 1.5 of at 100 µg mL^{-1}. • Reduced IL-6 expression from 4.5 fold to 1 fold at 100 µg mL^{-1}. • Reduced IL-8 expression 3.5 fold to 1.5 fold at 100 µg mL^{-1}. • 21% and 33% reduced visfatin expression at 20 µM.	Hoang et al. 2015
	Ethanol extracted polysaccharides	LPS-induced murine RAW264.7 macrophages	NO assay, Western blot, NF-kB activity via ELISA	• NO secretion levels were 3.11 µM (67.4% inhibition) at 400 µg mL^{-1}. • Maximum NO secretion at 10 µg mL^{-1} (7 µM) then a constant reduction in NO activity till 400 µg mL^{-1} (3 µM).	Wu et al. 2016
	RS	-	PT assay, vWF release and TF expression, thrombin and factor Xa activity	• No prolongation effect observed in PT assay at 2.5 mg kg^{-1}. • Reduced TF activity from 100% to 5% and next to 0% when the dose increased from 3 µg mL^{-1}. • Reduced vWF release activity: 50% at 3 µg mL^{-1} and in a dose-dependent manner.	Okamoto et al. 2019

RS: Rhamnan sulfate; *TNF*: Tumor necrosis factor; *iNOS*: Inducible nitric oxide synthase; *IL*: Interleukin; *NO*: Nitric oxide; *NF-kB*: Nuclear factor kappa light chain enhancer of activated B cells; *ELISA*: Enzyme-linked immunosorbent assay; *PT*: Prothrombin time; vWF: von Willebrand Factor Antigen; *TF*: Transcription factors; *real-time qPCR*: Real-time quantitative PCR

Table 15 Anti-inflammatory properties of *M. nitidum* – *In vivo* studies

Species	Component	Animal model	Results	Reference
M. nitidum (formally: *Porphyra crispata)*	Purified RS	10-week-old SPF BALB/c male mice	• Suppressed elevated plasma levels of liver damage markers. • Significantly suppressed neutrophil infiltration into the lung, liver, and jejunum tissues. • No significant reduction in glycocalyx. • Increased levels of syndecan-4, one of the glycocalyx components. • Provides protection against LPS induced inflammation.	Terasawa et al. 2022

RS: Rhamnan sulfate; *SPF*: Specific-pathogen-free; *BALB/c mice*: Bagg Albino mice; *LPS*: Lipopolysaccharide

(Ko et al. 2014). In contrast, methanol extracts of broccoli (*Brassica oleracea* var. Italia) have been reported to have a total phenolic content of 35.5 mg GAE g^{-1} (Hwang and Lim 2014). Similarly, both spinach and broccoli extracts have displayed a DPPH-radical scavenging activity exceeding 50% (Guo et al. 2001; Huang et al. 2005).

Lin et al. (2021) stated that pulsed microwave-assisted extraction of *M. nitidum* has antioxidant potential. A DPPH-radical scavenging activity and the ferrous ion chelating activity of 18% and 30% were measured, respectively. Hoang et al. (2015) evaluated the antioxidant activity of sulfated polysaccharides from *M. nitidum*. The SOD values ranged from 82 – 93% at a polysaccharide dose of 200 µg mL^{-1}. In addition, the algal polysaccharide extract (APE) from the water extracts of *M. nitidum* showed 26.9% DPPH-radical scavenging activity, 75.2% ferrous ion chelating activity, 31.5% H_2O_2 scavenging activity, and a 10.3% reducing power effect (Wu and Pan 2004), indicating potent antioxidant activity.

The antioxidant capacity of natural products, such as compounds extracted from *Monostroma* spp., is attributed to the presence of polysaccharides, phenolic compounds, flavonoids, and carotenoids. These bioactive compounds are naturally occurring in both terrestrial and aquatic plants (Hayase and Kato 1984). The antioxidant activity of *M. nitidum* has been found to be comparable to that of the brown seaweed, *Hizikia fusiformis* (Lee et al. 1996). These findings highlight the robust antioxidant capacities of certain species of *Monostroma*, with the majority of studies conducted *in vitro*, except for one *in vivo* study (Charles et al. 2007). In addition, culture conditions and/or environment can influence antioxidant activity in seaweeds. Thus, further *in vivo*, and clinical studies are required to verify the antioxidant properties of the isolated substances from *Monostroma* spp., especially sulfated polysaccharides, since it is likely these will vary with the environmental conditions.

Table 16 Immunomodulatory properties of *M. nitidum* and *M. oxyspermum* – *In vitro* studies

Species	Component	Cell line	Method/Assay	Results	Reference
M. nitidum	Crude polysaccharide	AGS, HeLa, and Raw 264.7 cells	Cell proliferation assay, NO and PGE2 production assay, RT-PCR	• 80% and 64% growth inhibition of AGS cells and HeLa cells, respectively. • Induced NO (>40 µM) and PGE2 (>11 ng mL^{-1}) production, respectively.	Karnjanapratum & You 2011
M. oxyspermum (currently: *G. oxysperma*)	Sulfated heterorhamnan	U87MG cells	MTT assay, Cell cycle analysis, Real-time PCR	• Increased numbers of cells in the G1 phase with concomitant increase of the mRNA levels of p53 and p21. • Dose-dependent reduction in viable cells.	Ropellato et al. 2015

AGS cells: Human gastric carcinoma cell line; *HeLa*: Human cervical cancer cell line; *U87MG cells*: Human glioblastoma cells; *NO*: Nitric oxide; *PGE2*: Prostaglandin E2; *RT-PCR*: Reverse transcription-polymerase chain reaction; *MTT*: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide

Table 17 Immunomodulatory properties of *M. angicava* and *M. nitidum* – *In vivo* studies

Species	Component	Animal model	Results	Reference
M. angicava	Rhamnose containing sulphated polysaccharide	BALB/c mice	• Rapid recovery of the counts of leukocytes, thrombocytes and erythrocytes post irradiation. • Significantly increased polysaccharides in the spleen index, natural killer cytostatic activity and the transformation response of splenic lymphocytes.	Mao et al. 2005
M. nitidum	Fermented *Tilapia* by-products and oligosaccharide-containing mixture	Male SAMP8 mice	• Supplementation of 824 or 1648 mg/kg BW/day doses effectively reduced BUN and lactate concentration and increased the lactate ratio and liver glycogen content post-exercise.	Chen et al. 2021

BALB/c: Bagg Albino mice; *SAMP8*: Senescence-accelerated mouse prone-8; *BUN*: Blood urea nitrogen concentration

Anti-obesity and anti-hypercholesterolemia properties

The *in vitro* anti-obesity and anti-hypercholesterolemia properties of *Monostroma* are listed in Table 9, the *in vivo* studies are provided in Table 10, and the clinical studies are presented in Table 11.

Hoang et al. (2015) evaluated the *in vitro* anti-hypolipidemic activity of sulfated polysaccharides (SPs) from ethanol extracts of *M. nitidum* using lipid-loaded hepatocytes (HepG2 cells). The SPs at 100 µg mL^{-1} markedly increased the total cholesterol (TC) and triglyceride (TG) content from 29–45% and from 30 – 47%, respectively. On the other hand, when the SP dose was increased to 200 µg mL^{-1}, the TC and TG content increased from 36 – 40% and from 20 – 40%, respectively (Dir et al. 2009; Zha et al. 2012; Matloub et al. 2013). The hypercholesterolemia mechanisms induced by SPs (200 µg mL^{-1}) in cultured hepatocytes increased the mRNA expression levels of CYP7AI and low-density lipoprotein-receptor (LDL-R) from 2.4 – 5.4 times and from 13.5 – 21.5 times, respectively.

The anti-obesity activity of RS from *M. nitidum* on diet-induced obese (DIO) female zebrafish, *Danio rerio* (AB strain), was investigated by Zang et al. (2015). Rhamnan sulphate (250 µg g^{-1} BW per day) administration for two weeks decreased fish body weight, plasma TG level, and plasma low-density lipoprotein-cholesterol (LDL-C) level by 11, 21.5, and 23.5%, respectively, but fasting blood glucose did not decrease. These findings indicated that RS supplementation improved dyslipidemia but not glucose intolerance. Furthermore, RS administration down-regulated the hepatic expression of *cebpa, pparg, srebf1,* and *acacb*, which are key regulators involved in the lipid synthesis pathway, indicating the purported curative properties of RS against dyslipidemia and hepatic steatosis.

Sulfated polysaccharides from hot water extracts of *M. nitidum* were used to treat diseases such as thrombosis and obesity (Shimada et al. 2021). Six-month-old NSY/HOS (type 2 diabetes mellitus strain) mice were fed a high-fat diet (HFD) supplemented with RS (250 mg g^{-1} body weight; BW) for four weeks to induce obesity. After four weeks of feeding, RS revealed a tendency to suppress body weight, plasma TG, and TC content by 7.5, 26.5, and 12%, respectively. Furthermore, RS significantly suppressed fasting blood glucose by 21.5%; however, faecal weight and calories increased by 16.67 and 16%, respectively. Thus, RS from *M. nitidum* has therapeutic properties capable of improving constipation issues, and thereby subsequently decreasing blood lipids and body weight.

Liu et al. (2017) studied the effect of a sulfated polysaccharide (Ls2-2) isolated from *M. angicava* in Sprague–Dawley (SD) rats. The *in vivo* glucose consumption levels were increased by 36% at 200 µg mL^{-1} administration of Ls2-2. The glucose consumption levels at 50 µg mL^{-1} and 100 µg mL^{-1} Ls2-2 showed a significant increase. Compared to the model group, TG levels were reduced by 30, 33, and 32% at 25, 50, and 100 µg mL^{-1} Ls2-2, respectively. Furthermore, the effects of Ls2-2 on glucose consumption, TG, and TC were better than those of metformin, which is used to lower blood sugar in type 2 diabetics (Maruthur et al. 2016). Therefore, *M. angicava* extracts could potentially be used as fibrinolytic and thrombolytic agents.

Kamimura et al. (2010) reported that oral administration of RS isolated from *M. nitidum* resulted in glycemic responses. For this study, Wister male rats were fed 2 g of glucose, sucrose, maltose, or soluble starch per kg BW with *M. nitidum* powder (200 mg kg^{-1} BW) or RS (approximately 50 mg kg^{-1} BW). The test material successfully prohibited (90%) the enhancement of plasma glucose levels after 120 min of administration compared with 30 min of administration. The effects of *M. nitidum* powder and RS on post-prandial enhancement in healthy human blood glucose levels were also evaluated (Kamimura et al. 2010). For the clinical trial, fifteen healthy volunteer men were selected for the oral glucose load test (OGTT). A significant decrease in the blood glucose level

was found (87.5% after 120 min of administration compared with 30 min of administration). The human blood plasma level was 88 mg dL^{-1} after 30 min of administration and 42 mg dL^{-1} after 60 min of administration. Hence, RS from *M. nitidum* can be used as a tool to help control diabetes.

These findings indicate that certain *Monostroma* spp. have nutritional applications against hyperlipidemia and have beneficial anti-glycemic and anti-obesity properties.

Anti-coagulant and anti-thrombotic properties

Different sulfated polysaccharides from *Monostroma* species have shown effective anti-coagulants (Li et al. 2011, 2012, 2017; Liu et al. 2017, 2018b, 2018c), anti-thrombin and platelet aggregation activities. The *in vitro* (Table 12) and *in vivo* (Table 13) anti-coagulant and anti-thrombotic activities of selected *Monostroma* spp. have been extensively reported; however, to the best of our knowledge, these studies have not yet been proven clinically.

The formation of thrombi due to enhanced platelet aggregation is known to cause artery thrombosis (Vanhoutte et al. 2009; Sprague and Khalil 2009). Sulfated polysaccharides from ethanol extracts of *M. angicava* showed thrombolytic activity (Li et al. 2017). The clotting time in SD rats was more than 200 s at 150 µg mL^{-1} in the activated partial thromboplastin time (APTT) assay and 120 s at 100 µg mL^{-1} in the thrombin time (TT) assay. In addition, the clot lytic rate of algal sulfated polysaccharides at 10 mg mL^{-1} was up to 26.49%, and at 20 mg mL^{-1}, it was markedly higher (25%) than that in the control. This study showed that sulfated polysaccharides from *M. angicava* have high fibrinolytic and thrombolytic activity.

Liu et al. (2017) found that sulfated polysaccharides, Ls2-2 (molecular weight 58.4 kDa), from ethanol extracts of *M. angicava* have antithrombotic activity. The clotting time in SD rats was more than 200 s at 50 µg mL^{-1} in the APTT assay and 120 s at 200 µg mL^{-1} in the TT assay. In addition, the *in vitro* thrombolytic experiment showed that the clot lytic rate of polysaccharides increased from 24.09 - 38.11% when the dose increased from 10 to 20 mg mL^{-1}. Later, in another study, Liu et al. (2018b) observed a 10-fold higher anti-coagulation effect of sulfated polysaccharides from *M. angicava* than heparin (used to treat and prevent blood clots in medical procedures). Sulfated polysaccharides in male SD rats showed a clotting time of more than 200 s at 50 µg mL^{-1} in the APTT assay and 120 s at 100 µg mL^{-1} in the TT assay. In addition, *in vivo* experiments showed clotting times of more than 200 s and 70 s at 16 mg kg^{-1} in APTT and TT assays, respectively. The clot lytic rate of seaweed polysaccharides was 38.26%. Furthermore, in a follow-up study, Liu et al. (2018c) showed sulfated polysaccharides (24–240 kDa) from ethanol extracts of *M. angicava* to have strong anti-coagulant activities evaluated through *in vitro* and *in vivo* experiments. In this case, sulfated polysaccharides in male SD rats showed a clotting time of more than 200 s at 100 µg mL^{-1} *in vitro* and 200 s at 16 mg kg^{-1} *in vivo* in the APTT assay. However, the TT assay showed a clotting time of more than 120 s at 100 µg mL^{-1} *in vitro* and a clot lytic rate of 34.29 ± 1.68% at 20 mg mL^{-1} *in vivo*. The above studies indicate that the sulfated polysaccharides of *M. angicava* have promising anti-coagulant properties and could effectively be used as a potential drug or food supplement for health promotion and treatment of thrombotic disease. However, a thorough investigation of the relationship between the anti-coagulant properties of these sulfated polysaccharides and their chemical structure is essential for understanding their biological characteristics. Additionally, the utilization of computational modelling techniques, such as artificial neural networks, could facilitate the identification of new polysaccharides with notable anti-coagulant activity among various *Monostroma* spp.

The APTT and TT assays for assessing the intrinsic coagulant activity of RS from water extracts of *M. latissimum* showed a clotting time of 200 s at 120 µg mL^{-1} in the APTT assay and 120 s at 50 µg mL^{-1} in the TT assay (Zhang et al. 2008). Mao et al. (2009) evaluated the anti-coagulant activity of sulfated rhamnan from the water extract of *M. latissimum*. The clotting time of sulfated polysaccharides (200 s and 120 s) became excessively saturated at a high concentration level of 20 µg mL^{-1} in the APTT assay and 10 µg mL^{-1} in the TT assay. Sulfated polysaccharides showed a considerable effect on the amidolytic activity of thrombin (dose increased to 100 µg mL^{-1} and thrombin activity decreased to 7%) in the presence of heparin cofactor II, which was strong like heparin. Sulfated polysaccharides also had a considerable effect on the amidolytic activity of thrombin (dose increased to 10^3 µg mL^{-1}, resulting in a 20% decreased activity) when combined with anti-thrombin III. Li et al. (2011) reported that low molecular weight (513 kDa) active polysaccharides from *M. latissimum* hot water extracts showed clotting times exceeding 200 s at 150 µg mL^{-1} in the APTT assay and over 120 s at 100 µg mL^{-1} in the TT assay.

In a follow-up study, Li et al. (2012) reported that a low molecular weight polysaccharide (3.4 kDa) derived from *M. latissimum* had strong anti-coagulant properties. Inhibition of thrombin activity by this polysaccharide was examined by amidolytic anti-factor thrombin and coagulation factor Xa assays in the absence and presence of heparin cofactor II (70 nmol L^{-1}) and anti-thrombin III (50 nmol L^{-1}). APTT activity by the polysaccharides slowly increased, and the clotting time was more than 200 s at 50 µg mL^{-1}. The polysaccharides had a considerable effect on the amidolytic activity of thrombin (dose increased to 1 µg mL^{-1} and thrombin activity decreased to 5%). The polysaccharides weakly inhibited the amidolytic activity of thrombin in a dose-dependent manner when heparin cofactor II or anti-thrombin was

absent. However, polysaccharides exhibited a considerable effect on thrombin inhibition through a heparin cofactor II-dependent pathway, and the ability to inhibit thrombin was stronger (dose increased to 1 µg mL^{-1} and thrombin activity decreased to 42%) than that of heparin. The above studies highlight that the sulfated polysaccharide of *M. latissimum* can be a potent anti-coagulant agent and promising thrombin inhibitor mediated by heparin cofactor II. However, this requires further detailed investigation as candidates for use in food supplements or ingredients in the pharmaceutical industry.

Sulfated rhamnan from water extracts of *M. nitidum* showed excessively saturated (200 s and 120 s) clotting times at high concentrations of 15 µg mL^{-1} in the APTT assay and 50 µg mL^{-1} in the TT assay (Mao et al. 2008). The polysaccharides had a considerable effect on the amidolytic activity of thrombin (dose increased to 1 µg mL^{-1} and thrombin activity decreased to 7%) in the presence of heparin cofactor II. The polysaccharides weakly inhibited the amidolytic activity of thrombin in a dose-dependent manner when heparin cofactor II or anti-thrombin was absent. The polysaccharides had a considerable effect on the amidolytic activity of thrombin (dose increase to 1 µg mL^{-1} and thrombin activity decrease to 30 - 38%) in the presence of anti-thrombin III.

The RS from water extracts of commercially cultured *M. nitidum* showed potential anti-coagulant activity (Yamashiro et al. 2017). The relative activity of RS (75 µg mL^{-1} and 150 µg mL^{-1}) in the APTT, TT and PT assays, ranged from 60 - 78%, 138 - 170%, and 120 - 123%, respectively, and was comparable to that of heparin (100%). Hence, the RS from *M. nitidum* may prolong the extrinsic and common pathways of coagulation by inhibiting thrombin activity. In another study by Okamoto et al. (2019), RS (100 µg mL^{-1}) from hot water extracts of *M. nitidum* significantly suppressed tissue factor (TF) expression (5%) and von Willebrand factor (VWF) release (50%) compared with heparin. Tumor necrosis factor (TNF)-α (a major pro-inflammatory cytokine) and thrombin (coagulation factor) significantly induced the expression of RS (100 µg mL^{-1}) by TF activity (0% and 50%) and VWF release (45% and 80%) in activated endothelial cells. The sulfated polysaccharide in the above studies showed potent anti-coagulant and thrombin inhibiting activities mediated by heparin cofactor II, suggesting that some *Monostroma* species can be effective in helping to prevent the development of venous thrombosis.

Anti-inflammatory properties

The *in vitro* and *in vivo* anti-inflammatory activities of selected extracts of *Monostroma* spp. are presented in Tables 14 and 15, respectively; however, to the best of our knowledge, these studies have not yet been proven clinically.

Crude RS from *M. nitidum* extracts prevents endothelial inflammation and regulates the onset of thrombotic disorders (Okamoto et al. 2019). The isolated RS strongly decreased TF expression (from 100% to near zero at doses above 3 µg mL^{-1}) and slightly suppressed TNF-α-induced VWF release (decreasing from 100 to 50% with increasing RS concentration). Hence, RS from *M. nitidum* may be a potential candidate for food supplementation possessing anti-thrombotic and anti-inflammatory effects. However, additional research at *in vivo* and clinical stages is necessary before incorporating these extracts into food applications.

The ethanol extracts of *M. nitidum* showed promising anti-inflammatory activity (Hoang et al. 2015). In lipid-loaded hepatocytes, the mRNA expression of iNOS, interleukin (IL)-6, and IL-8 decreased by 79.5, 63.6, and 66.7%, respectively, at a 200 µg mL^{-1} dose of sulfated polysaccharides. Furthermore, at dosage of 20 µM, a 33% reduction in visfatin, a pro-inflammatory gene expression, was noted. Therefore, it is likely that the lipid-lowering effect of the sulphated polysaccharides can be achieved by reducing elevated levels of pro-inflammatory mediators and visfatin mRNA expression. This suggests that sulfated polysaccharides from *M. nitidum* may assist in reducing the elevated expression of pro-inflammatory molecules, such as iNOS, IL-6, IL-8, and visfatin.

Overall, RS and other sulfated polysaccharides from various *Monostroma* species have shown strong attenuation of inflammatory injury in cultured vascular endothelial cells suggesting that polysaccharides extracted from *Monostroma* spp. could be a potential anti-inflammatory agent for cellular inflammation. Future *in vitro*, *in vivo* and clinical research is needed to verify their pharmacological properties.

Immunomodulatory properties

The *in vitro* and *in vivo* immunomodulatory properties of selected *Monostroma* spp. are presented in Tables 16 and 17, respectively; however, to the best of our knowledge, these studies have not yet been proven clinically.

Sulfated polysaccharides from ethanol extracts of *M. nitidum* have shown promising anti-cancer and immunomodulatory activities (Karnjanapratum and You 2011). The immunomodulatory effects of crude sulfated polysaccharides were determined by measuring the proliferation rate of Raw 264.7 cells. The cytotoxic effect of the crude polysaccharides at a concentration of 6.25 µg mL^{-1}, as measured by Raw 264.7 cell proliferation, was considerably improved and exhibited a significant potency to induce nitric oxide (NO; > 40 µM) and prostaglandin E2 (PGE2) production (> 11 ng mL^{-1}) compared with lipopolysaccharide (LPS; 42 µM and 12 ng mL^{-1}). A human gastric carcinoma cell line (AGS cells) and a human cervical cancer cell line (HeLa cells) were used in the colorimetric assay to determine the anti-cancer activity.

Growth inhibition of AGS and HeLa cells was found at 80% and 64% in 125 µg mL^{-1} of crude sulfated polysaccharide. These findings suggest that crude polysaccharides from *M. nitidum* could function as anti-cancer and immunomodulatory agents.

Chen et al. (2021) studied the anti-fatigue activity of sulfated polysaccharides from *M. nitidum* using a senescence-accelerated male mouse prone-8 (SAMP8) animal model. Polysaccharides from hot water extracts of *M. nitidum* were supplemented with a mixture of fermented *Tilapia* by-products and provided to mice. Blood samples were collected 30 min after the last feed. Blood was collected after 20 min during the post swimming rest period (10 min at 30°C temperature water). The blood urea nitrogen (BUN) concentration of the training group was significantly lower (25 mg dL^{-1}) than that of the non-training group (30 mg dL^{-1}). The lactate concentrations were 20.4%, 25.2%, and 25.7% in the mixed-dose groups of 412, 824, and 1648 mg kg-1 BW per day, respectively. The results showed that 824 mg kg^{-1} BW per day and 1648 mg kg^{-1} BW per day doses of the mixture with exercise training (ET) could significantly increase the liver glycogen level (10 to 11 mg g^{-1}) compared with the non-training group (7 mg g^{-1} liver).

Present and future prospects for applied research using various *Monostroma* spp.

Monostroma spp. have been included in the Novel Food Catalogue of the European Commission as macroalgal species owing to their delicacy and quality (Lahteenmaki-Uutela et al. 2020). Research on the nutritional and functional activities of *Monostroma* spp. is progressively increasing. *Monostroma* spp. contain carbohydrates, fibre, polysaccharides, protein, and minerals, making them suitable for use as a valuable food supplement. However, nutritional properties of various species of *Monostroma* are influenced by environmental and ecological conditions (Torres et al. 2019); thus, the nutritional properties of *Monostroma* species from different countries may vary significantly. It is worth noting that even the same species can exhibit substantial differences in its metabolic profile when found in distinct geographical location. Furthermore, the nutritional properties of only a limited number of *Monostroma* species have been explored. Therefore, unexplored *Monostroma* species, such as *M. angicava,* and *M. grevillei* should be considered for future study, and their nutritional properties should be explored.

Some of the *Monostroma* species have exhibited significant bio-functional activities, including anti-viral, antimicrobial, anti-inflammatory, anti-glycemic, anti-obesity, anti-thrombotic, anti-coagulant, antioxidant, anti-cancer, anti-fatigue, and immunomodulatory activities (Zhang et al. 2008; Kamimura et al. 2010; Karnjanapratum and You 2011; Hoang et al. 2015; Zang et al. 2015; Cao et al. 2019; Okamoto et al. 2019; Terasawa et al. 2020; Chen et al. 2021; Shimada et al. 2021). However, despite the use of novel and precise analytical techniques such as GC-MS, LC-MS, HRMS, and updated databases to explore new compounds in seaweeds, including edible algae (Vaghela et al. 2022, 2023), only a limited number of articles have addressed the phytochemical characterization of *Monostroma* species. Therefore, there is a need to focus on the intense phytochemical characterization of *Monostroma* spp. in future research.

The anti-viral activity against different enveloped (SARS-CoV, HIV, HSV, HCMV, MV, MuV, IFV, and HIV) and non-enveloped (EV71, HAV, PV, CVB, and HRV) viruses has been addressed by *in vitro* studies of *M. latissimum* and *M. nitidum* (Lee et al. 2004, 2010; Kazłowski et al. 2012; Wang et al. 2018, 2020; Terasawa et al. 2020; Song et al. 2021). The IC_{50}, CC_{50}, EC_{50}, NA inhibition assay, and plaque assay results were mainly considered to determine the anti-viral activity (Lee et al. 2004; Wang et al. 2018; Terasawa et al. 2020; Wang et al. 2020). However, virus-binding (attachment) assays and penetration assays have not been conducted, which could be considered in future studies.

Anti-obesity and anti-hypercholesterolemia activities of *M. angicava* and *M. nitidum* were extensively addressed by *in vitro*, *in vivo*, and clinical studies (Kamimura et al. 2010; Ko et al. 2011; Cancel and Tarbell 2013; Hoang et al. 2015; Zang et al. 2015; Liu et al. 2017; Shimada et al. 2021; Patil et al. 2022). A total of 14 articles reported the anti-coagulant and anti-thrombotic effects of selected *Monostroma* spp. Remarkable results were noted *in vitro* and *in vivo* settings, sometimes approximately 10-fold higher than those of conventional medicine (Liu et al. 2018b). However, only a limited number of studies have reported anti-bacterial (Kim and Lee 2008; Lee et al. 2013; Shimada et al. 2021), anti-fungal (Kim and Lee 2008), and antioxidant properties of selected *Monostroma* species.

One study reported the anti-cancer and immunomodulatory activity of *M. nitidum* with remarkable inhibition in AGS and HeLa cells (Karnjanapratum and You 2011). However, it remains unconfirmed whether this anti-cancer activity results from the cytotoxic effect. Future studies on the anti-cancer activities of *Monostroma* can be extended with various cancer cell lines, elucidating the molecular mechanisms underlying their preventive effects in culture conditions. Rhamnan sulfate and other sulfated polysaccharides from *M. nitidum* attenuate inflammatory injury in vascular endothelial cells *in vitro* (Hoang et al. 2015). This provides a comprehensive research scope at *in vivo* and clinical levels to identify the potential anti-inflammatory compounds from *Monostroma* species.

While numerous bioactivities have been assessed through *in vitro* studies, there is a considerable scope for further

research involving animal models and subsequent clinical trials. Addressing this gap is crucial to elucidate the potential bioactivities of the studied *Monostroma* spp., facilitating translational research. This, in turn, could open avenues for utilizing these species in food supplements and medicinal applications.

Conclusion

This study highlights that amongst the various species of *Monostroma*, *M. nitidum* is the most extensively studied species, offering a valuable source of substances with extensive nutritional and functional properties. *Monostroma* species have been utilized both as ingredient in traditional medicines and as a source of dietary substances. Many bioactive compounds, including polysaccharides (such as 'RS' and low molecular weight polysaccharides), phenolics, flavonoids, chlorophyll, levoglucosan, and carotenoids, have been extracted from several *Monostroma* spp. and harnessed for their use in both food and medicine. The nutritional and functional attributes of some *Monostroma* spp. underscores their potential for commercial application. However, ensuring the sustainable management of oceanic resources presents challenges concerning the preservation of nutritional quality and bioactive components. This knowledge forms the basis for the development of functional ingredients for pharmaceuticals and functional foods. This review involved an analysis of previous studies focusing on the nutritional properties and activities of *Monostroma* seaweeds, thereby providing valuable insights and guidelines for future research aimed at expanding the application of some *Monostroma* spp. It is worth noting that while studies have explored the properties of some *Monostroma spp. in vitro*, only a limited number of investigations have conducted *in vivo* and clinical trials. Therefore, further research in *in vivo* and clinical settings should be pursued to fully understand their bioactivities. Furthermore, conducting a thorough toxicity analysis of the isolated compounds would contribute to the enhanced utilization of extracts from *Monostroma* spp. in food applications.

Authors' contributions Conceptualization: S.M., K.M.I.B. and J.-S.C.; Methodology: S.M. and K.M.I.B.; Formal analysis and investigation: S.M. and K.M.I.B.; Writing – original draft preparation: S.M., K.M.I.B. and J.-S.C.; Writing – review and editing: K.M.I.B., M.M., M.D.N.M., M.N.A.K., J.-H.S. and J.-S.C; Funding acquisition: J.-S.C.; Resources: J.-S.C.; Supervision: J.-S.C. All authors have read and agreed to the published version of the manuscript.

Funding This research was supported by the Korea Institute of Marine Science & Technology Promotion (KIMST) funded by the Ministry of Oceans and Fisheries (PJT200885).

Data availability The data supporting the findings of this study are available upon request from the corresponding author.

Declarations

Competing interests The authors declare no competing interests.

References

Aguilera J, Dummermuth A, Karsten U, Schriek R, Wienck C (2002) Enzymatic defences against photooxidative stress induced by ultraviolet radiation in Arctic marine macroalgae. Polar Biol 25:432–441

Al-fartusie FS, Mohssan SN (2017) Essential trace elements and their vital roles in human body. Indian J Adv Chem Sci 5:127–136

Arasaki S, Arasaki T (1983) Low calorie, high nutrition vegetables from the sea to help you look and feel better. Japan Publication, Tokyo.

Arshad MA, Khurshid U, Ahmad S, Ijaz S, Rashid F, Azam R (2014) Review on methods used to determine antioxidant activity. Int J Multidiscip Res Dev 1:41–46

Bashir KMI, Lee H-J, Mansoor S, Jahn A, Cho M-G (2021) The effect of chromium on photosynthesis and lipid accumulation in two chlorophyte microalgae. Energies 14:2260

Bast F (2011) *Monostroma*: The jeweled seaweed for future: Cultivation methods, ecophysiology, phylogeography and molecular systematics. Lambert Academic Publishing, Moldova

Bernardi J, de Vasconcelos ERTPP, Lhullier C, Gerber T, Neto CP, Pellizzari FM (2016) Preliminary data of antioxidant activity of green seaweeds (Ulvophyceae) from the Southwestern Atlantic and Antarctic maritime islands. Hidrobiológica 26:233–239

Boopathy SN, Kathiresan K (2010) Anticancer drugs from marine flora: An overview. J Oncol 2010:214186

Cancel LM, Tarbell JM (2013) Rhamnan sulfate enhances the endothelial glycocalyx and decreases the LDL permeability of human coronary artery endothelial cells in vitro. FASEB J 27:896.3–896.3

Cao S, He X, Qin L, He M, Yang Y, Liu Z, Mao W (2019) Anticoagulant and antithrombotic properties in vitro and in vivo of a novel sulfated polysaccharide from marine green alga *Monostroma nitidum*. Mar Drugs 17:247

Cassolato JEF, Noseda MD, Pujol CA, Pellizzari FM, Damonte EB, Duarte MER (2008) Chemical structure and antiviral activity of the sulfated heterorhamnan isolated from the green seaweed *Gayralia oxysperma*. Carbohydr Res 343:3085–3095

Chakniramol S, Wierschem A, Cho M-G, Bashir KMI (2022) Physiological and clinical aspects of bioactive peptides from marine animals. Antioxidants 11:1021

Chang HC, Wu LC (2008) Texture and quality properties of Chinese fresh egg noodles formulated with green seaweed (*Monostroma nitidum*) powder. J Food Sci 73:S398–S404

Charles AL, Chang CK, Wu ML, Huang TC (2007) Studies on the expression of liver detoxifying enzymes in rats fed seaweed (*Monostroma nitidum*). Food Chem Toxicol 45:2390–2396

Chen Y-J, Kuo C-Y, Kong Z-L, Lai C-Y, Chen G-W, Yang A-J, Lin L-H, Wang M-F (2021) Anti-fatigue effect of a dietary

supplement from the fermented byproducts of Taiwan Tilapia aquatic waste and *Monostroma nitidum* oligosaccharide complex. Nutrients 13:1688
Choudhary B, Chauhan OP, Mishra A (2021) Edible seaweeds: A potential novel source of bioactive metabolites and nutraceuticals with human health benefits. Front Mar Sci 8:740054
Dale DC, Boxer L, Liles WC (2008) The phagocytes: Neutrophils and monocytes. Blood 112:935–945
Dir I, Stark AH, Chayoth R, Madar Z, Arad SM (2009) Hypochlolesterolemic effects of nutraceuticals produced from the red microalga *Porphyridium* spp. in rats. Nutrients 1:156–167
EFSA European Food Safety Authority (2010) Scientific opinion on dietary reference values for carbohydrates and dietary fibre. EFSA J 8:1462
FAO (Food and Agriculture Organization of the United Nations) (2021) Fishery and Aquaculture Statistics. Global production by production source 1950-2019. Accessed from https://www.fao.org/fishery/en/statistics on 27 July 2023.
Fuller S, Beck E, Salman H, Tapsell L (2016) New horizons for the study of dietary fiber and health: A review. Plant Foods Hum Nutr 71:1–12
Ganesan K, Kumar KS, Rao PS, Tsukui Y, Bhaskar N, Hosokawa M, Miyashita K (2014) Studies on chemical composition of three species of *Enteromorpha*. Biomed Prev Nutr 4:365–369
Garcia-Vaquero M, Hayes M (2016) Red and green macroalgae for fish, animal feed and human functional food development. Food Rev Int 32:15–45
Gomes L, Monteiro P, Cotas J, Gonçalves AMM, Fernandes C, Gonçalves T, Pereira L (2022) Seaweeds' pigments and phenolic compounds with antimicrobial potential. Biomol Concepts 13:89–102
Gordillo FJL, Aguilera J, Jimenez C (2006) The response of nutrient assimilation and biochemical composition of Arctic seaweeds to a nutrient input in summer. J Exp Bot 57:2661–2671
Gordon S, Taylor PR (2005) Monocyte and macrophage heterogeneity. Nat Rev Immunol 5:953–964
Gubelit Y, Makhutova O, Sushchik N, Kolmakova A, Kalachova G, Gladyshev M (2015) Fatty acid and elemental composition of littoral "green tide" algae from the Gulf of Finland, the Baltic Sea. J Appl Phycol 27:375–386
Guiry MD, Guiry GM (2022) AlgaeBase (2022). World-wide electronic publication, National University of Ireland, Galway. http://www.algaebase.org; accessed 17 December 2023.
Guo J-T, Lee H-L, Chiang S-H, Lin F-I, Chang C-Y (2001) Antioxidant properties of the extracts from different parts of broccoli in Taiwan. J Food Drug Anal 9:96–101
Hayase F, Kato H (1984) Antioxidative components of sweet potatoes. J Nutr Sci Vitaminol 30:37–46
Heo S-J, Cha S-H, Lee K-W, Cho SK, Jeon Y-J (2005) Antioxidant activities of Chlorophyta and Phaeophyta from Jeju island. Algae 20:251–260
Hoang MH, Kim J-Y, Lee JH, You SG, Lee S-J (2015) Antioxidative, hypolipidemic, and anti-inflammatory activities of sulfated polysaccharides from *Monostroma nitidum*. Food Sci Biotechnol 24:199–205
Holdt SL, Kraan S (2011) Bioactive compounds in seaweed, functional food applications and legislation. J Appl Phycol 23:543–597
Hou X, Chai C, Qian Q, Yan X, Fan X (1997) Determination of chemical species of iodine in some seaweed. Sci Total Environ 204:215–221
Huang D-J, Chen H-J, Lin C-D, Lin Y-H (2005) Antioxidant and antiproliferative activities of water spinach (*Ipomoea aquatica* Forsk) constituents. Bot Bull Acad Sinica 46:99–106
Hwang JH, Lim SB (2014) Antioxidant and anti-inflammatory activities of broccoli florets in LPS-stimulated RAW 264.7 cells. Prev Nutr Food Sci 19:89–97
Im Y-G, Choi J-S, Kim D-S (2006) Mineral contents of edible seaweeds collected from Gijang and Wando in Korea. Korean J Fish Aquat Sci 39:16–22
Jeon Y-E, Yin X-F, Lim S-S, Chung C-K, Kang I-J (2012) Antioxidant activities and acetylcholinesterase inhibitory activities from seaweed extracts. J Korean Soc Food Sci Nutr 41:443–449
Jiang Z, Ueno M, Nishiguchi T, Avu R, Isaka S, Okimura T, Yamaguchi K, Oda T (2013) Importance of sulfate groups for the macrophage-stimulating activities of ascophyllan isolated from the brown alga *Ascophyllum nodosum*. Carbohydr Res 380:124–129
Jin W, Zhang W, Mitra D, McCandless MG, Sharma P, Tandon R, Zhang F, Linhardt RJ (2020) The structure-activity relationship of the interactions of SARS-CoV-2 spike glycoproteins with glucuronomannan and sulfated galactofucan from *Saccharina japonica*. Int J Biol Macromol 163:1649–1658
Kamimura Y, Hashiguchi K, Nagata Y, Saka T, Yoshida M, Makino Y, Amano H (2010) Inhibitory effects of edible green algae *Monostroma nitidum* on glycemic responses. J Jap Soc Nutr Food Sci 57:441–445
Karnjanapratum S, You S (2011) Molecular characteristics of sulfated polysaccharides from *Monostroma nitidum* and their in vitro anticancer and immunomodulatory activities. Int J Biol Macromol 48:311–318
Kaur M, Kala S, Bast Parida A, F, (2023) Concise review of green algal genus *Monostroma* Thuret. J Appl Phycol 35:1–10
Kavale MG, Italiya B, Veeragurunathan V (2020) Scaling the production of *Monostroma* sp. by optimizing culture conditions. J Appl Phycol 32:451–457
Kazłowski B, Chiu YH, Kazłowski K, Pan C-L, Wu C-J (2012) Prevention of Japanese encephalitis virus infections by low-degree-polymerisation sulfated saccharides from *Gracilaria* sp. and *Monostroma nitidum*. Food Chem 133:866–874
Khiyami MA, Pometto AL, Brown RC (2005) Detoxification of corn stover and corn starch pyrolysis liquors by *Pseudomonas putida* and *Streptomyces setonii* suspended cells and plastic compost support biofilms. J Ag Food Chem 53:2978–2987
Kim IH, Lee J-W (2008) Antimicrobial activities against methicillin-resistant *Staphylococcus aureus* from macroalgae. J Ind Eng Chem 14:568–572
Kitamura Y, Abe Y, Yasui T (1991) Metabolism of levoglucosan (1,6-anhydro-α-D-glucopyranose) in microorganisms. Ag Biol Chem 55:515–521
Ko S-C, Lee S-H, Kang S-M, Ahn G, Cha S-H, Jeon Y-J (2011) Evaluation of α-glucosidase inhibitory activity of Jeju seaweeds using high throughput screening (HTS) technique. J Mar Biosci Biotechnol 5:33–39
Ko SH, Park JH, Kim SY, Lee SW, Chun SS, Park E (2014) Antioxidant effects of spinach (*Spinacia oleracea* L.) supplementation in hyperlipidemic rats. Prev Nutr Food Sci 19:19–26
Kumar IN, Barot M, Kumar R (2014) Phytochemical analysis and antifungal activity of selected seaweeds from Okha coast, Gujarat, India. J Coast Life Med 2:535–540
Kwon PS, Oh H, Kwon S-J, Jin W, Zhang F, Fraser K, Hong JJ, Linhardt RJ, Dordick JS (2020) Sulfated polysaccharides effectively inhibit SARS-CoV-2 in vitro. Cell Discov 6:50
Lahteenmaki-Uutela A, Rahikainen M, Camarena-Gomez MT, Piiparinen J, Spilling K, Yang B (2020) European Union legislation on macroalgae products. Aquac Int 29:487–509
Leandro A, Pacheco D, Cotas J, Marques JC, Pereira L, Gonçalves AMM (2020) Seaweed's bioactive candidate compounds to food industry and global food security. Life 10:140
Lee B-B, Choi J-S, Moon HE, Ha Y-N, Kim MS, Cho KK, Choi IS (2013) Inhibition of growth and urease of *Helicobacter pylori by* Korean edible seaweed extracts. Bot Sci 91:515–522
Lee BH, Choi BW, Chun J-H, Yu B-S (1996) Extraction of water soluble antioxidants from seaweeds. J Ind Eng Chem 7:1069–1077

Lee JB, Yamagaki T, Maeda M, Nakanishi H (1998) Rhamnan sulfate from cell walls of *Monostroma latissimum*. Phytochemistry 48:921–925

Lee JB, Hayashi K, Maeda M, Hayashi T (2004) Antiherpetic activities of sulfated polysaccharides from green algae. Planta Med 70:813–817

Lee JB, Koizumi S, Hayashi K, Hayashi T (2010) Structure of rhamnan sulfate from the green alga *Monostroma nitidum* and its anti-herpetic effect. Carbohydr Polym 81:572–577

Li H, Mao W, Zhang X, Qi X, Chen Y, Chen Y, Xu J, Zhao C, Hou Y, Yang Y, Li N, Wang C (2011) Structural characterization of an anticoagulant-active sulfated polysaccharide isolated from green alga *Monostroma latissimum*. Carbohydr Polym 85:394–400

Li H, Mao W, Hou Y, Gao Y, Qi X, Zhao C, Chen Y, Chen Y, Li N, Wang C (2012) Preparation, structure and anticoagulant activity of a low molecular weight fraction produced by mild acid hydrolysis of sulfated rhamnan from *Monostroma latissimum*. Bioresour Technol 114:414–418

Li N, Liu X, He X, Wang S, Cao S, Xia Z, Xian H, Qin L, Mao W (2017) Structure and anticoagulant property of a sulfated polysaccharide isolated from the green seaweed *Monostroma angicava*. Carbohydr Polym 159:195–206

Lin Y-P, Wu S-C, Huang S-L (2021) Effects of microwave-assisted extraction on the free radical scavenging and ferrous chelating abilities of *Monostroma nitidum* extract. J Mar Sci Technol 21:611–617

Liu X, Hao J, He X, Wang S, Cao S, Qin L, Mao W (2017) A rhamnan-type sulfated polysaccharide with novel structure from *Monostroma angicava* Kjellm (Chlorophyta) and its bioactivity. Carbohydr Polym 173:732–748

Liu X, Cao S, Qin L, He M, Sun H, Yang Y, Liu X, Mao W (2018a) A sulfated heterorhamnan with novel structure isolated from the green alga *Monostroma angicava*. Carbohydr Res 466:1–10

Liu X, Wang S, Cao S, He X, Qin L, He M, Yang Y, Hao J, Mao W (2018b) Structural characteristics and anticoagulant property in vitro and in vivo of a seaweed sulfated rhamnan. Mar Drugs 16:243

Liu X, Du P, Liu X, Cao S, Qin L, He M, He X, Mao W (2018c) Anticoagulant properties of a green algal rhamnan-type sulfated polysaccharide and its low-molecular-weight fragments prepared by mild acid degradation. Mar Drugs 16:445

Lüning K, Pang S (2003) Mass cultivation of seaweeds: Current aspects and approaches. J Appl Phycol 15:115–119

Luyen HQ, Frampton DMF, Park NG, Hong YK (2006) Microalgal growth enhancement by levoglucosan isolated from the green seaweed *Monostroma nitidum*. J Appl Phycol 19:175–180

Maehre HK, Malde MK, Eilertsen KE, Elvevoll EO (2014) Characterization of protein, lipid and mineral contents in common Norwegian seaweeds and evaluation of their potential as food and feed. J Sci Food Agric 94:3281–3290

Mao W, Li Y, Wu L, Wang H, Zhang Y, Zang X, Zhang H (2005) Chemical characterization and radioprotective effect of polysaccharide from *Monostroma angicava* (Chlorophyta). J Appl Phycol 17:349–354

Mao WJ, Fang F, Li HY, Qi XH, Sun HH, Chen Y, Guo SD (2008) Heparinoid-active two sulfated polysaccharides isolated from marine green algae *Monostroma nitidum*. Carbohydr Polym 74:834–839

Mao W, Li H, Li Y, Zhang H, Qi X, Sun H, Chen Y, Guo S (2009) Chemical characteristic and anticoagulant activity of the sulfated polysaccharide isolated from *Monostroma latissimum* (Chlorophyta). Int J Biol Macromol 44:70–74

Maruthur NM, Tseng E, Hutfless S, Wilson LM, Suarez-Cuervo C, Berger Z (2016) Diabetes medications as monotherapy or metformin-based combination therapy for type 2 diabetes: A systematic review and meta-analysis. Ann Intern Med 164:740–751

Masakazu T (1969) Culture studies on the life history of some species of the genus *Monostroma*. Rep Seaweed Res Inst Fac Sci Hokkaido Univ 6:1–56

Matloub AA, El-Sherbini M, Borai IH, Ezz MK, Aly HF, Fouad GI (2013) Assessment of anti-hyperlipidemic effect and physcochemical characterization of water soluble polysaccharides from *Ulva fasciata* Delile. J Appl Sci Res 9:2983–2993

McDermid KJ, Stuercke B (2003) Nutritional composition of edible Hawaiian seaweeds. J Appl Phycol 15:513–524

Mohammed HO, O'Grady MN, O'Sullivan MG, Hamill RM, Kilcawley KN, Kerry JP (2021) An assessment of selected nutritional, bioactive, thermal and technological properties of brown and red Irish seaweed species. Foods 10:2784

Moher D, Liberati A, Tetzlaff J, Altman DG (2009) Preferred reporting items for systematic reviews and meta-analyses. The PRISMA statement. Plos Med 6:1000097

Mosser DM, Edwards JP (2008) Exploring the full spectrum of macrophage activation. Nat Rev Immunol 8:958–969

Muñoz II, Díaz NF (2022) Minerals in edible seaweed: Health benefits and food safety issues. Crit Rev Food Sci Nutr 62:1592–1607

Nakahara K, Kitamura Y, Yamagishi Y, Shoun H, Yasui T (1994) Levoglucosan dehydrogenase involved in the assimilation of levoglucosan in *Arthrobacter* sp. I-552. Biosci Biotechnol Biochem 58:2193–2196

Nakamura M, Yamashiro Y, Konishi T, Hanasiro I, Tako M (2011) Structural characterization of rhamnan sulfate isolated from commercially cultured *Monostroma nitidum* (Hitoegusa). J Jap Soc Nutr Food Sci 58:245–251

Negara BFSP, Bashir KMI, Park Y, Shim KB, Kim J-S, Park SY, Lee J-S, Sohn J-H, Choi J-S (2023) Alaska pollock (*Gadus chalcogrammus*) proteins and hydrolysed polypeptides: A systematic review of their potential bioactivities. Int J Food Sci Technol 58:1695–1711

Nishikawa M, Mitsui M, Umeda K, Kitaoka Y, Takahashi Y, Tanaka S (2006) Effect of sulfated polysaccharides extracted from sea alga (*Monostroma latissium* and *Monostroma nitidum*) on serum cholesterol in subjects with borderline or mild hypercholesterolemia. J New Remed Clinics 55:1763–1770

Okamoto T, Akita N, Terasawa M, Hayashi T, Suzuki K (2019) Rhamnan sulfate extracted from *Monostroma nitidum* attenuates blood coagulation and inflammation of vascular endothelial cells. J Nat Med 73:614–619

Oza RM, Joshi HV, Parekh RG, Chauhan VD (1983) Preliminary observations on a *Monostroma sp.* From the Okha coast. Gujrat. Indian J Mar Sci 12:115–117

Patel S (2012) Therapeutic importance of sulfated polysaccharides from seaweeds: Updating the recent findings. 3 Biotech 2:171–185

Patil NP, Gómez-Hernández A, Zhang F, Cancel L, Feng X, Yan L, Xia K, Takematsu E, Yang EY, Le V, Fisher ME, Gonzalez-Rodriguez A, Garcia-Monzon C, Tunnell J, Tarbell J, Linhardt RJ, Baker AB (2022) Rhamnan sulfate reduces atherosclerotic plaque formation and vascular inflammation. Biomaterials 291:121865

Pirian K, Jeliani ZZ, Sohrabipour J, Arman M, Faghihi MM, Yousefzadi M (2018) Nutritional and bioactivity evaluation of common seaweed species from the Persian Gulf. Iran J Sci Technol Trans A 42:1795–1804

Prosen EM, Radlein D, Piskorz J, Scott DS (1993) Microbialutilization of levoglucosan in wood pyrolysate as a carbon and energy source. Biotechnol Bioeng 42:538–541

Risso S, Escudero C, de Portela M, Fajardo M (2003) Chemical composition and seasonal fluctuations of the edible green seaweed, *Monostroma undulatum*, Wittrock, from the Southern Argentina coast. Arch Latinoam Nutr 53:306–311

Ropellato J, Carvalho MM, Ferreira LG, Noseda MD, Zuconelli CR, Goncalves AG, Ducatti DR, Kenski JC, Nasato P, Winnischofer SM (2015) Sulfated heterorhamnans from the green seaweed *Gayralia oxysperma*: Partial depolymerization, chemical structure and antitumor activity. Carbohydr Polym 117:476–485

Saco JA, Sekida S, Mine I (2018) Characterization of photosynthesis and growth of *Monostroma latissimum* (Ulvophyceae) collected from the intertidal area in Kochi, Japan. Kuroshio Sci 12:89–99

Salehi B, Sharifi-rad J, Seca AML, Pinto DCGA (2019) Current trends on seaweeds, looking at chemical. Molecules 24:4182
Schmid M, Kraft LGK, van der Loos LM, Kraft GT, Virtue P, Nichols PD, Hurd CL (2018) Southern Australian seaweeds, A promising resource for omega-3 fatty acids. Food Chem 265:70–77
Seedevi P, Moovendhan M, Sudharsan S, Vasanthkumar S, Srinivasan A, Vairamani S, Shanmugam A (2015) Structural characterization and bioactivities of sulfated polysaccharide from *Monostroma oxyspermum*. Int J Biol Macromol 72:1459–1465
Shimada Y, Terasawa M, Okazaki F, Nakayama H, Zang L, Nishiura K, Matsuda K, Nishimura N (2021) Rhamnan sulphate from green algae *Monostroma nitidum* improves constipation with gut microbiome alteration in double-blind placebo-controlled trial. Sci Rep 11:13384
Skrovankova S (2011) Seaweed vitamins as nutraceuticals. Adv Food Nutr Res 64:357–369
Song Y, He P, Rodrigues AL, Datta P, Tandon R, Bates JT, Bierdeman MA, Chen C, Dordick J, Zhang F (2021) Anti-SARS-CoV-2 activity of rhamnan sulfate from *Monostroma nitidum*. Mar Drugs 19:685
Sprague AH, Khalil RA (2009) Inflammatory cytokines in vascular dysfunction and vascular disease. Biochem Pharmacol 78:539–552
Sufen Z, Ziyu H, Tingting D (2021) Analysis and evaluation of nutrient contents in *Monostroma nitidum* in Naozhou sea area, Zhanjiang. J Trop Biol 12:473–480
Suzuki K, Terasawa M (2020) Biological activities of rhamnan sulfate extract from the green algae *Monostroma nitidum* (Hitoegusa). Mar Drugs 18:228
Szekanecz Z, Koch AE (2007) Macrophages and their products in rheumatoid arthritis. Curr Opin Rheumatol 19:289–295
Tako M, Yamashiro Y, Teruya T, Uechi S (2017) Structure–function relationship of rhamnan sulfate isolated from commercially cultured edible green seaweed, *Monostroma nitidum*. Am J Appl Chem 5:38–44
Terasawa M, Hayashi K, Lee JB, Nishiura K, Matsuda K, Hayashi T, Kawahara T (2020) Anti-influenza A virus activity of rhamnan sulfate from green algae *Monostroma nitidum* in mice with normal and compromised immunity. Mar Drugs 18:254
Terasawa M, Hiramoto K, Uchida R, Suzuki K (2022) Anti-inflammatory activity of orally administered *Monostroma nitidum* rhamnan sulfate against lipopolysaccharide-induced damage to mouse organs and vascular endothelium. Mar Drugs 20:121
Thiviya P, Gamage A, Gama-Arachchige NS, Merah O, Madhujith T (2022) Seaweeds as a source of functional proteins. Phycology 2:216–243
Torres MD, Flórez-Fernández N, Domínguez H (2019) Integral utilization of red seaweed for bioactive production. Mar Drugs 17:314
Tsubaki S, Oono K, Hiraoka M, Onda A, Mitani T (2016) Microwave-assisted hydrothermal extraction of sulfated polysaccharides from *Ulva* spp. and *Monostroma latissimum*. Food Chem 210:311–316
Vaghela P, Das AK, Trivedi K, Anand KGV, Shinde P, Ghosh A (2022) Characterization and metabolomics profiling of *Kappaphycus alvarezii* seaweed extract. Algal Res 66:102774
Vaghela P, Trivedi K, Anand KGV, Nayak J, Vyas D, Ghosh A (2023) Aqueous homogenate of fresh *Ulva lactuca* for ameliorating nutrient deficiency – A nutraceutical alternative to using whole seaweeds. Algal Res 74:103211
Vanhoutte PM, Shimokawa H, Tang EH, Feletou M (2009) Endothelial dysfunction and vascular disease. Acta Physiol 196:193–222
Wang L, Wang X, Wu H, Liu R (2014) Overview on biological activities and molecular characteristics of sulfated polysaccharides from marine green algae in recent years. Mar Drugs 12:4984–5020
Wang S, Wang W, Hao C, Yunjia Y, Qin L, He M, Mao W (2018) Antiviral activity against enterovirus 71 of sulfated rhamnan isolated from the green alga *Monostroma latissimum*. Carbohydr Polym 200:43–53
Wang S, Wang W, Hao C, Yunjia Y, Qin L, He M, Mao W (2020) A sulfated glucuronorhamnan from the green seaweed *Monostroma nitidum*: Characteristics of its structure and antiviral activity. Carbohydr Polym 227:115280
Wang WL, Chiang YM (1994) Potential economic seaweeds of Hengchun Peninsula. Taiwan. Econ Bot 48:182–189
WHO (2020) Chromium in drinking-water. Background document for development of WHO Guidelines for drinking-water quality (WHO/HEP/ECH/WSH/2020.3). World Health Organization, Geneva, Switzerland. Available online: chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://apps.who.int/iris/bitstream/handle/10665/338062/WHO-HEP-ECH-WSH-2020.3-eng.pdf?sequence=1&isAllowed=y (accessed on 07 September 2023).
Wu SC, Pan CL (2004) Preparation of algal-oligosaccharide mixtures by bacterial agarases and their antioxidative properties. Fish Sci 70:1164–1173
Wu G-J, Shiu S-M, Hsieh MC, Tsai GJ (2016) Anti-inflammatory activity of a sulfated polysaccharide from the brown alga *Sargassum cristaefolium*. Food Hydrocoll 53:16–23
Xu S, Yu C, Wang Q, Liao J, Liu C, Huang L, Liu Q, Wen Z, Feng Y (2023) Chromium contamination and health risk assessment of soil and agricultural products in a rural area in southern China. Toxics 11:27
Yamashiro Y, Nakamura M, Yogi T, Teruya T, Konishi T, Uechi S, Tako M (2017) Anticoagulant activity of rhamnan sulfate isolated from commercially cultured *Monostroma nitidum*. Int J Biomed Mater Res 5:37–43
Yu K, Ke MY, Li WH, Zhang SQ, Fang XC (2014) The impact of soluble dietary fibre on gastric emptying, postprandial blood glucose and insulin in patients with type 2 diabetes. Asia Pac J Clin Nutr 23:210–218
Zang L, Shimada Y, Tanaka T, Nishimura N (2015) Rhamnan sulphate from *Monostroma nitidum* attenuates hepatic steatosis by suppressing lipogenesis in a diet-induced obesity zebrafish model. J Funct Foods 17:364–370
Zha XO, Xiao JJ, Zhang HN, Wang JH, Pan LH, Yang XF, Luo JP (2012) Polysaccharides in *Laminaria japonica* (LP): Extraction, physicochemical properties and their hypolipidemic activities in diet-induced mouse model of atherosclerosis. Food Chem 134:244–252
Zhang HJ, Mao WJ, Fang F, Li HY, Sun HH, Chen Y, Qi XH (2008) Chemical characteristics and anti-coagulant activities of a sulfated polysaccharide and its fragments from *Monostroma latissimum*. Carbohydr Polym 71:428–434
Zhang X, Mosser DM (2008) Macrophage activation by endogenous danger signals. J Pathol 214:161–178
Zhu T, Heo HJ, Row KH (2010) Optimization of crude polysaccharides extraction from *Hizikia fusiformis* using response surface methodology. Carbohydr Polym 82:106–110
Zhuang XL, Zhang HX, Tang JJ (2001) Levoglucosan kinase involved in citric acid fermentation by *Aspergillus niger* CBX-209 using levoglucosan as sole carbon and energy source. Biomass Bioenergy 21:53–60