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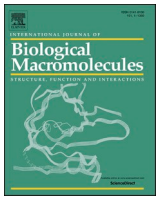

Review

Production and ecological function of fucoidans from marine algae in a changing ocean

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ABSTRACT

Fucoidans have multiple biological and biomedical functions, e.g., antibacterial, antiviral, immunomodulatory, inflammatory, and growth-promoting effects. Recent studies show that they also have essential ecological functions whereas our understanding in this field is very superficial. This study first reviewed the fucoidan content in algae and the highest content of 13.3 % in *Undaria pinnatifida* sporophyll and the lowest content of 0.1 % in *Alaria angusta* were found. Field investigation demonstrates that light, temperature, salinity, and nutrient can affect fucoidan production in algae; while more laboratory experiments need to be carried out to verify these conclusions. Brown algae can excrete 8–31 % of their net carbon fixation into seawater in the form of fucoidans. Fucoidans are highly recalcitrant to bacterial degradation, enabling the carbon within them to be stored for centuries. Therefore, fucoidans can play an essential role in carbon sequestration. Ocean afforestation with brown algae may be an effective approach to remove atmospheric CO_2 since fucoidans have a high carbon content while seldom need any nitrogen or phosphorus. Fucoidan production in a warming and CO_2 enriched ocean was also discussed. This study provides new insight into production and ecological functions of fucoidans, indicating their role in carbon sequestration and climate change alleviation.

1. Introduction

Fucoidan or fucose-rich sulfated polysaccharides (FSPs) is an expression used to describe a group of heterogeneous polysaccharides. Unlike other polysaccharide, e.g., cellulose, which has been in use for centuries, fucoidan is a relatively recently discovered and naturally occurring biopolymer. It was originally isolated by Harald Kylin, a researcher at Uppsala University in Sweden, from brown macroalgae in 1913 [1]. It was dubbed "fucoidin" and subsequently referred to as fucoidan according to IUPAC standards. Meanwhile, it is also known as fucan, fucosan, or sulfated fucan. The evolving term fucoidan covers a wide range of sulfated polysaccharides (FCSP) with a backbone of fucose (fucans), heterogeneous compositions (i.e., fucogalactans, xylofucoglucuromannan) and diverse origins [1]. Fucoidans mainly exist in brown seaweeds and Echinoderms (e.g., sea urchins, sea cucumbers and starfish). In addition, recent studies show that some diatoms also contain fucoidans [2].

Fucoidan occurs in the extracellular matrix of brown algae and marine invertebrates. Fucoidan, making up 23 % of cell wall dry weight, is the important component of cell wall [3], where it plays important biological functions, such as maintaining cell wall integrity, tissue hydration, regulating osmotic pressure, aiding in communications between cells, and serving as a defense mechanism for the organism [4]. In addition to biological functions, a lot of studies have demonstrated that fucoidans have huge biomedical potentials as a natural with less side effects drug candidate [5]. Examples include inflammatory, antitumour, antibacterial, antiviral, anticoagulant, antioxidant, neuroprotective, immunomodulatory, cardio-protection and growth-promoting effects [6]. Dietary supplementation of fucoidans shows significant therapeutic influences on aquatic organisms, livestock, poultry, and human [6]. Therefore, there are rising interests in fucoidan production and application.

In addition to multiple biological functions, recent studies show fucoidans have potential ecological functions. Fucoidans can be excreted into seawater as dissolved organic matter (DOM) by brown macroalgae. As brown algae excrete 18 to 62 % of their net primary production, they inject substantial amounts of fucoidan carbon into the 660 Gt dissolved organic carbon pool in the ocean [7–9]. Due to their recalcitrance to microbial degradation, fucoidans have been found to persist for centuries in the ocean [7]. In addition, fucoidans are adhesive and can form

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particles by aggregation. These particles can reach the deep oceans, as part of biological carbon pump [2,10]. Therefore, fucoidans can play an essential role in carbon sequestration in the forms of both dissolved organic carbon (DOC) and particle organic carbon (POC).

Due to their multiple biological and ecological functions, there are substantial concerns on fucoidans, with the relative publications exponentially increasing (Fig. 1A). Previous review articles focus on structure, extraction, biological and biomedical functions of fucoidans while their production and ecological functions are very fragmented (Fig. 1B). In this study, we review the distribution features of fucoidans in marine algae, their production in changing ocean environments, and ecological functions. We identify the key remaining challenges of fucoidan production, indicating future goals and directions. This study will make solid contribution to understanding the production and ecological function of fucoidans from marine algae in a changing ocean.

2. Bibliometric analysis

Literature search was conducted through Web of Science in May 2024 with the topic of "fucoidan". A total number of 3086 publications, including papers and books, were found. To identify the research focus and gap regarding fucoidans, bibliometric analysis was conducted with VOSviewer 1.6.20. Bibliometric maps of hot keywords were built. The minimum number of occurrences of a keyword is 200, with the binary counting method.

3. Structure of fucoidans in marine algae

Fucoidan is a polymer in which fucose forms the core monomeric module. Naturally occurring fucoidan usually has two types of chain. Type I chain is composed of α (1 → 3) linked fucose while type II chain is

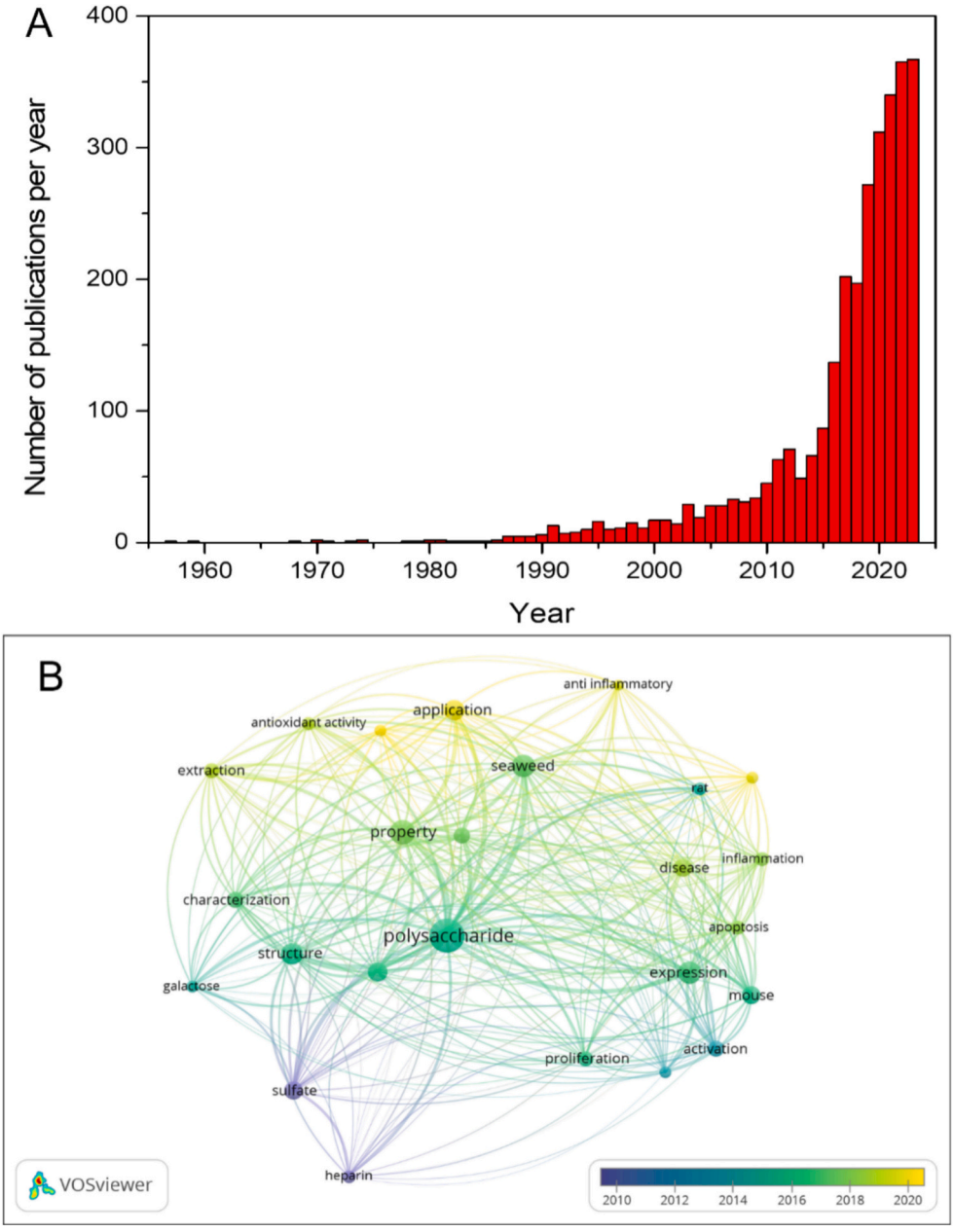

Fig. 1. Number of fucoidan publications (A) and bibliometric map of the studies based on co-occurrence of keywords (B). The size of the dot is proportional to the frequency that a certain keyword appears in the analyzed publications. The line between two dots means that these two keywords appeared in the same publication. The thicker the line, the more frequently the two keywords appeared in the same publications. The color represents the year when a certain keyword most frequently appeared in publications.

composed of altering α (1 → 3) and α (1 → 4) linked fucose (Fig. 2A, B). In addition to these two common types, two new types of chain have been found recently. For instance, *Laminaria longipes* contains altering α (1 → 3) and α (1 → 4) linked fucose, with small amounts of disaccharide1,4-linked fragments and 3-sulfated fucose residues (Fig. 2C). *Tauya basicrassa* has1,6-linked galactose backbone with branches at C3 and C4, terminal fucose and galactose residues and fragments from 1,3-; 1,4-; and 1,2-fucose residues (Fig. 2D). Fucoidan is made up primarily of L-fucose and sulfated ester groups with minor amounts of D-xylose, glucuronic acid, D-galactose and D-mannose [14]. Acetyl groups and uronic acid are also components of the polymer [15]. The sulfate component is frequently substituted at either the C2 or C4 positions of L-fucopyranosyl residues and randomly at C3 [16]. Molecular weight of fucoidans varies largely (3.2–3374.9 kDa), with the lowest in *Lessonia vadosa* and the highest in *Sargassum hemiphyllum* (Table 1). Fucales has the largest range of 19.8–3374.9 kDa while Dictyotales has the narrowest range of 21–179 KDa. Molecular weight of fucoidans in the orders of Desmarestiales, Scytothamnales and Naviculales has not been reported yet (Table 1), which needs to investigated in future study.

Chemical structure of fucoidans is species specific and different species of brown seaweeds show variable monomeric composition, glycosidic linkage, and sulphation pattern [5]. Fucose is considered as the most important monosaccharide component for fucoidans. Its proportion (mol %) reaches 86–91.7 % in Scytothamnales and 32.89–90 % in Ectocarpales. Furthermore, it reaches 100 % in *Laminaria longipes* of Laminariales (Table 1). On the other hand, it has a very low proportion of 1.1 % in *Durvillaea antarctica* of Fucales, suggesting dramatic differences among orders or species (Table 1). In terms of sulfate content (% DW), the highest (62 %) and lowest (1.18 %) contents are respectively found in *Saccharina japonica* and *Lessonia trabeculata*, both from Laminariales. Ectocarpales has a narrower range of sulfate content (6.4–34 %) compared to other orders in Phaeophyceae. In addition to taxonomic differences, fucoidan also shows complex seasonal variation in their structure. For instance, the proportion of fucose in fucoidan in summer is significantly higher than in spring for *Saccharina sculpera* while the proportions of galactose and glucosamine show an opposite tendency [77]. The content of sulfate in fucoidan *S. sculpera* also increases in

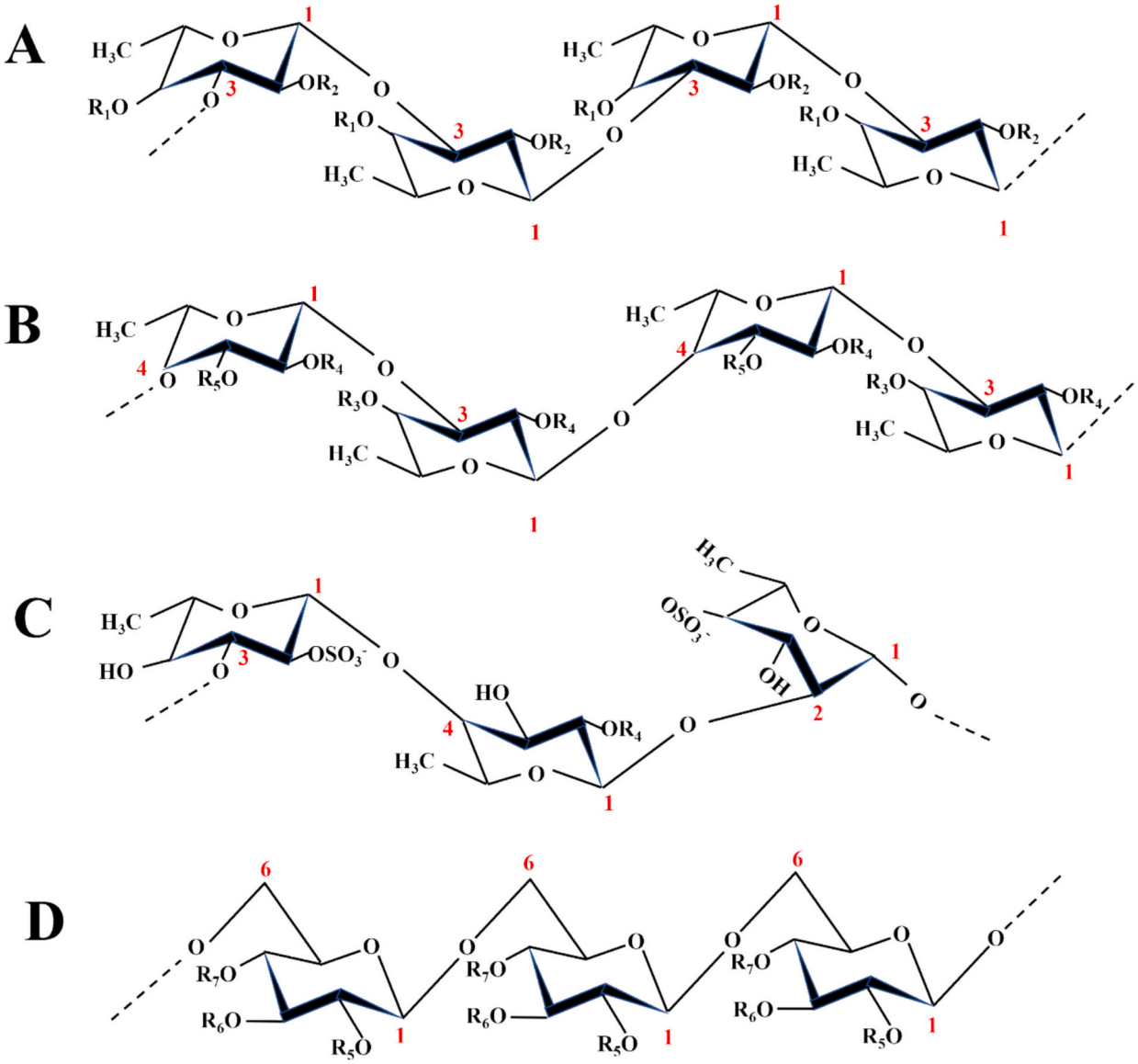

Fig. 2. Diverse structures of fucoidans in algae. (A) *Laminariales* [11]; (B) Fucales [11]; (C) *Laminaria longipes* [12]; (D) *Tauya basicrassa* [13]. R_1 = H, SO_3Na, $COCH_3$, Fuc, short fucose chains; R_2 = H, SO_3Na, Fuc, Xyl, short fucose chains; R_3 = H, SO_3Na, $COCH_3$, Fuc, Xyl, short fucose chains; R_4 = H, SO_3Na; R_5 = H, SO_3Na, $COCH_3$; R_6 = H, SO_3Na, $COCH_3$, Gal.

Table 1
Overview of published fucoidan content in different algae species. Sori means a cluster of sporangia. Slash means data unavailable.

Species	Location	Part of thallus	Crude content (%DW)	Purified content (%DW)	Fucose content (mol %)	Sulfate content (%DW)	Molecular weight (kDa)	References
Phaeophyceae/Desmarestiales								
Desmarestia viridis	Russia	Whole plant	0.51	/	63	12.5	/	Shevchenko et al. [17]
Phaeophyceae/Dictyotales								
Dictyota dichotoma	Russia	Whole plant	1.02	/	52	2.0	/	Shevchenko et al. [17]
Dictyota divaricata	Vietnam	Whole plant	0.32	/	43–61	11.2–18.3	/	Shevchenko et al. [17]
Dictyopteris plagiogramma	Brazil	Whole plant	6–10	/	42	4	/	Percival et al. [18]
Dictyopteris polypodioides	Lebanon	Whole plant	/	<1	38–48	13	/	Sokolova et al. [19]
Lobophora variegata	Brazil	Whole plant	/	/	25	~3	/	Medeiros et al. [20]
Padina australis	Vietnam	Whole plant	/	1.9	60	21.9	179	Yuguchi et al. [21]
Padina boryana	Viatnam	Whole plant	0.25	/	61	18.2	/	Shevchenko et al. [17]
Padina gymnospora	Brazil	Whole plant	/	/	36–39	3–6	/	Silva et al. [22]
Padina pavonica	England	Whole plant	5.0	/	2.0–12.5	3–17	/	Mian and Percival [23]
Padina sp.	Malaysia	Whole plant	2.1	/	/	/	/	Lim et al. [24]
Padina tetrastomatica	India	Whole plant	6	/	68–73	~3–~6	/	Karmakar et al. [25]
Spatoglossum asperum	India	Whole plant	/	4.4 ± 0.2	61	21	/	Palanisamy et al. [26]
Spatoglossum schroederi	Brazil	Whole plant	/	/	27–53	~28–~37	21–21.5	Queiroz et al. [27]
Stoechospermum marginatum	India	Whole plant	9	/	96	13	40	Adhikari et al. [28]
Phaeophyceae/Ectocarpales								
Adenocystis utricularis	Argentina	Whole plant	2.9–10.8	/	60–84	8–34	6.5–19	Ponce et al. [29]
Dictyosiphon foeniculaceus	Germany	Whole plant	12.3	2.0	38.7	8.8	194	Bittkau et al. [30]
Leathesia difformis	Argentina	Whole plant	2.9–6.4	/	68–90	6.4–7.1	38–51	Feldman et al. [31]
Nemacystus decipiens	China	Whole plant	18.25 ± 0.09	/	32.89–40.33	20.26–22.03	676–1076	Li et al. [32]
Papenfussiella lutea	New Zealand	Whole plant	11.5	/	55.0	/	/	Wozniak et al. [33]
Scytosiphon lomentaria	Argentina		1.6		70	18.6	11.8	Ponce et al. [34]
Phaeophyceae/Fucales								
Ascophyllum mackaii	South Africa	Whole plant	5.0	/	29.2 ± 0.3	22.4 ± 0.2	162	Qu et al. [35]
Ascophyllum nodosum	Wales	Whole plant	6.5–8.9	/	35–46	6–22	1274–1486	Fletcher et al. [36]
Ascophyllum nodosum	Canada	Whole plant	1.1	/	/	22.3 ± 2.1E-5	1323	Rioux et al. [37]
Cystoseira barbata	Tunisia	Whole plant	5.45 ± 0.51	/	45	23	/	Sellimi et al. [38]
Cystoseira compressa	Tunisia	Whole plant	/	5.2 ± 0.45	62	15	/	Hentati et al. [39]
Durvillaea antarctica	China	Whole plant	14.21 ± 1.03	/	1.1	/	482	He et al. [40]
Durvillaea potatorum	Australia	Whole plant	6.28 ± 0.25	/	12.2 ± 0.7	12.4 ± 1.4	/	Lorbeer et al. [41]
Fucus evanescens	Russia	Sterile tissue	10.0	/	69.0 ± 5.3	/	/	Skriptsova et al. [42]
Fucus evanescens	Russia	Fertile tissue	17.6	/	76.6 ± 5.9	/	/	Skriptsova et al. [42]
Fucus serratus	Wales	Whole plant	4.2–7.5	/	18–28	30–40	1336–2024	Fletcher et al. [36]
Fucus serratus	Russia	Whole plant	7.2	/	46.6	31.8	/	Bilan et al. [43]
Fucus vesiculosus	Wales	Whole plant	8.1–12.2	/	26–39	9–35	1184–1789	Fletcher et al. [36]
Fucus vesiculosus	Canada	Whole plant	1.4	/	/	19.0 ± 3.3E-5	877	Rioux et al. [37]
Hizikia fusiforme	China	Whole plant	/	2.7	38	12	25.9–959	Li et al. [44]
Himanthalia elongata	Spain	Whole plant	0.7–17.9	/	17	6	/	Mateos-Aparicio et al. [45]
Himanthalia lorea	England	Whole plant	18.0	/	2.5–14.0	2–29	/	Mian and Percival [23]
Hormophysa cuneiformis	Vietnam	Whole plant	16.1	/	33–79	18–35	/	Bilan et al. [46]
Marginariella boryana	New Zealand	Reproductive	12.3	/	72.0	/	/	Wozniak et al. [33]
Marginariella boryana	New Zealand	Vegetative	2.1	/	44.8	/	/	Wozniak et al. [33]

(*continued on next page*)

Table 1 (*continued*)

Species	Location	Part of thallus	Crude content (%DW)	Purified content (%DW)	Fucose content (mol %)	Sulfate content (%DW)	Molecular weight (kDa)	References
Nizamuddinia zanardinii	Iran	Whole plant	3.6–13.15	/	26.0–41.7	11.6–29.6	444–1184	Alboofetileh et al. [47]
Pelvetia canaliculata	France	Whole plant	13.9	/	82	29	/	Mabeau et al. [48]
Sargassum aquifolium	Vietnam	Whole plant	/	/	14–41	6–29	/	Bilan et al. [49]
Sargassum binderi	Malaysia	Whole plant	6.2	/	/	/	/	Lim et al. [24]
Sargassum binderi	Malaysia	Whole plant	/	/	60	7.7	47.9	Lim et al. [50]
Sargassum cinereum	India	Whole plant	/	/	66	4	/	Somasundaram et al. [51]
Sargassum crassifolium	Vietnam	Whole plant	/	1.4	56	27.5	230	Yuguchi et al. [21]
Sargassum duplicatum	Viatnam	Whole plant	0.32	/	40–59	32.3–38.2	/	Shevchenko et al. [17]
Sargassum feldmannii	Viatnam	Whole plant	0.46	/	39–72	21.0–25.3	/	Shevchenko et al. [17]
Sargassum filipendula	Indonesia	Whole plant	4.5–6.1	/	/	/	/	Laeliocattleya et al. [52]
Sargassum fusiforme	China	Whole plant	3.94–11.24	/	38.02–61.44	3.40–14.79	26.63–69.15	Liu et al. [53]
Sargassum glaucescens	China	Whole plant	4.20	/	13.42 ± 1.40	15.28 ± 2.15	/	Wang and Chen [54]
Sargassum hemiphyllum	China	Whole plant	2.72 ± 0.18	/	/	44.11 ± 0.01	22.40–3374.86	Li et al. [55]
Sargassum hemiphyllum	China	Whole plant	4.69 ± 1.05	/	31.3	/	/	Wang et al. [56]
Sargassum henslowianum	China	Whole plant	6.25	4.08	19.3	11.45	567.7	Lin et al. [57]
Sargassum horneri	China	Whole plant	4.80	/	7.30 ± 2.23	14.08 ± 1.32	/	Wang and Chen [54]
Sargassum latifolium	Saudi Arabia	Whole plant	/	/	10–16	16–22	70–130	Asker et al. [58]
Sargassum mcclurei	Vietnam	Whole plant	2.7	1.0	27.2–58.5	16.8–35.0	/	Duc Thinh et al. [59]
Sargassum muticum	Vietnam	Whole plant	/	1.22	52–67	18.4–48.6	/	Usol'tseva et al. [60]
Sargassum oligocystum	Vietnam	Whole plant	/	0.87–1.54	/	16.4–34.0	/	Men'shova et al. [61]
Sargassum pallidum	Russia	Sterile tissue	6.8	/	45.6 ± 4.0	/	/	Skriptsova [62]
Sargassum pallidum	Russia	Fertile tissue	8.6	/	51.7 ± 4.7	/	/	Skriptsova [62]
Sargassum pallidum	Russia	Whole plant	1.2–7.0	/	/	/	/	Skriptsova [62]
Sargassum polycystum	China	Whole plant	3.41 ± 0.77	/	46.0	/	/	Wang et al. [56]
Sargassum ringgoldianum	China	Whole plant	0.95 ± 0.02	/	/	/	/	Li et al. [32]
Sargassum siliquosum	China	Whole plant	5.08 ± 1.17	3.61 ± 0.83	47.5	19.5	107.3	Wang et al. [56]
Sargassum stenophyllum	Brazil	Whole plant	0.4	0.38	52–60	19–28		Duarte et al. [63]
Sargassum swartzii	Vietnam	Whole plant	/	/	50–56	15–28	/	Ly et al. [64]
Sargassum tenerrimum	India	Whole plant	3.1	/	73	2	/	Sinha et al. [65]
Sargassum trichophyllum	Japan	Whole plant	/	/	80	23	19.8	Lee et al. [66]
Sargassum thunbergii	China	Whole plant	/	8.67	55	/	373	Luo et al. [67]
Sargassum vachellianum	China	Whole plant	5.5 ± 0.25	/	65	12	/	Jesumani et al. [68]
Seirococcus axillaris	Australia	Whole plant	1.24 ± 0.18	0.92	13.4 ± 1.6	9.79 ± 2.5	/	Lorbeer et al. [41]
Silvetia babingtonii	Russia	Sterile tissue	16.1	/	71.0 ± 6.1	/	/	Skriptsova [62]
Silvetia babingtonii	Russia	Fertile tissue	24.7	/	79.9 ± 5.5	/	/	Skriptsova [62]
Stephanocystis crassipes	Russia	Whole plant	2.2–5.8	/	/	/	/	Skriptsova [62]
Turbinaria conoides	India	Whole plant	8.8	/	54	4	/	Chattopadhyay et al. [69]
Turbinaria decurrens	India	Whole plant	/	5.32 ± 0.31	59.3	23.51 ± 0.32	/	Manikandan et al. [70]
Turbinaria ornata	Vietnam	Whole plant	/	0.6	83	32	/	Ermakova et al. [71]
Turbinaria turbinata	Malaysia	Whole plant	/	/	61	/	233.5–495.5	Monsur et al. [72]
Phaeophyceae/Laminariales								
Alaria angusta	Russia	Whole plant	1.4	0.1–1.1	52.7–74.8	9.5–24.0	/	Menshova et al. [73]
Alaria fistulosa	Russia	Frond	0.7	/	/	15.8	/	Usov et al. [74]
Alaria fistulosa	Russia	Midrib	0.6	/	/	/	/	Usov et al. [74]
Alaria fistulosa	Russia	Sporophyll	7.8	/	/	19.6	/	Usov et al. [74]
Alaria fistulosa	Russia	Stipe	0.5	/	/	/	/	Usov et al. [74]
Alaria marginata.	Russia	Whole plant	/	0.9	47.5–80.6	10.2–28.3	/	Usoltseva et al. [75]
Alaria ochotensis	Russia	Sterile tissue	5.7	/	17.6 ± 1.8	/	/	Skriptsova et al. [42]
Alaria ochotensis	Russia	Fertile tissue	8.6	/	25.2 ± 2.8	/	/	Skriptsova et al. [42]
Alaria sp.	Russia	Frond	3.8	/	54.0	24	/	Vishchuk et al. [76]
Alaria sp.	Russia	Sporophyll	5.7	/	48.4	29	/	Vishchuk et al. [76]

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Table 1 (*continued*)

Species	Location	Part of thallus	Crude content (%DW)	Purified content (%DW)	Fucose content (mol %)	Sulfate content (%DW)	Molecular weight (kDa)	References
Costaria costata	China	Whole plant	5.0 ± 0.3	/	31–61	10.8 ± 1.1	/	Qu et al. [77]
Ecklonia cava	South Korea	Whole plant	1.8 ± 0.8	/	61.1 ± 1.6	20.1 ± 0.7	18–359	Lee et al. [78]
Ecklonia maxima	South Africa	Whole plant	4.26	/	20.79 ± 0.23	21.33 ± 0.12	150	Qu et al. [35]
Eisenia bicyclis	Korea	Whole plant	1.4	/	/	13.5	/	Ermakova et al. [79]
Ecklonia radiata	Australia	Whole plant	3.0–5.4	/	18.2–29.7	15.6–30.3	/	Lorbeer et al. [41]
Kjellmaniella crassifolia	Japan	Whole plant	4.3 ± 0.0	/	66.1	33.5	94–136	Liu et al. [80]
Kjellmaniella crassifolia	China	Whole plant	3.8	/	/	25.2	/	Song et al. [81]
Laminaria angustata	Japan	Frond	2.6	/	36.3	/	21–23	Kitamura et al. [82]
Laminaria bongardiana	Russia	Balde	2.9	/	20.0	23.2	/	Bilan et al. [83]
Laminaria claustonii	England	Stipe	1.8–3.4	/	/	/	/	Black [84]
Laminaria claustonii	England	Frond	2.4–4.5	/	/	/	/	Black [84]
Laminaria digitata	England	Frond	3.5	/	46–65	11–18	/	Mabeau et al. [48]
Laminaria digitata	France	Frond	5.5	/	/	/	/	MacArtain et al. [85]
Laminaria digitata	Denmark	Frond	3.4–11.2	/	/	/	/	Bruhn et al. [86]
Laminaria hyperborea	Norway	Bulk powder	/	/	98	54	7.3–469	Kopplin et al. [87]
Laminaria longipes	Japan	Whole plant	0.35	/	100	13.3	254.1–838.7	Usoltseva et al. [12]
Lessonia nigrescens	Chile	Whole plant	3.32	/	20.05 ± 0.24	16.51 ± 0.04	105	Qu et al. [35]
Lessonia trabeculata	Peru	Whole plant	4.15	/	16.39 ± 0.26	1.18 ± 0.02	162	Qu et al. [35]
Lessonia vadosa	Chile	Blade	4.7	/	/	37.7	3.2	Chandía and Matsuhiro [88]
Macrocystis pyrifera	Australia	Whole plant	7.59 ± 0.95	/	16.2 ± 0.3	18.6 ± 0.6	/	Lorbeer et al. [41]
Saccharina cichorioides	Russia	Whole plant	1.5–2.4	/	72–85	/	20–40	Zvyagintseva et al. [89]
Saccharina gurjanovae	Japan	Whole plant	/	/	64.3	28.2	810	Prokofjeva et al. [90]
Saccharina japonica	Japan	Frond	2.2–4.3	/	/	/	/	Honya et al. [91]
Saccharina japonica	Russia	Whole plant	0.5–1.2	/	50–54	/	/	Zvyagintseva et al. [89]
Saccharina japonica	Japan	Whole plant	1.7	/	/	/	/	Mizuno et al. [92]
Saccharina japonica	Russia	Sterile tissue	3.2	/	40.7 ± 3.9	/	/	Skriptsova et al. [42]
Saccharina japonica	Russia	Fertile tissue	6.3	/	24.9 ± 3.0	/	/	Skriptsova et al. [42]
Saccharina japonica	Russia	Frond	0.7	/	21	62	/	Vishchuk et al. [76]
Saccharina japonica	Russia	Sori	1.4	/	23	58	/	Vishchuk et al. [76]
Saccharina japonica	Russia	Whole plant	0.9–4.3	/	/	/	/	Skriptsova [62]
Saccharina japonica	Russia	Sori	2.6–3.4	/	/	/	/	Skriptsova [62]
Saccharina japonica	China	Whole plant	1.39	/	20.11 ± 0.38	14.16 ± 0.16	126	Qu et al. [35]
Saccharina japonica	China	Whole plant	3.3 ± 0.5	/	33.1	16.0 ± 3.6	/	Qu et al. [77]
Saccharina japonica	Russia	Whole plant	0.87–4.26	/	/	/	/	Skriptsova [62]
Saccharina latissima	England	Frond	2.1–2.7	/	/	/	/	Black [84]
Saccharina latissima	Russia	Frond	8.8	/	/	/	/	Obluchinskaya [93]
Saccharina latissima	Faroe Islands	Frond	3.8–4.2	/	62.8–63.9	19.0–22.6	/	Ehrig and Alban [94]
Saccharina latissima	Germany	Frond	1.8–2.3	/	45.2–45.9	14.4–15.5	/	Ehrig and Alban [94]
Saccharina latissima	Denmark	Frond	2.3–6.2	/	/	/	/	Bruhn et al. [86]
Saccharina longicruris	Canada	Whole plant	1.3 ± 0.8	/	/	14.2 ± 1.8E-5	576	Rioux et al. [37]
Saccharina longissima	Japan	Frond	2.6	/	/	/	21–23	Kitamura et al. [82]
Saccharina sculpera	China	Whole plant	6.1 ± 0.0	/	60	26.6 ± 0.7	/	Qu et al. [77]
Undaria pinnatifida	Japan	Rhizoid and stem	9.2–19.3	/	20.8–49.0	6.9–22.8	/	Sasaki et al. [95]
Undaria pinnatifida	Japan	Sporophyll without sori	3.2	/	/	/	/	Skriptsova et al. [96]
Undaria pinnatifida	Japan	Sporophyll with sori	16.0	9.82	52.4–58.5	14–29	30–80	Skriptsova et al. [96]
Undaria pinnatifida	Argentina	Sporophyll	13.3–20.7	/	45–55	13.0–26.3	/	Arijón et al. [97]
Undaria pinnatifida	Korea	Sporophyll	3.9	/	72.3	7.4	2185	Kim et al. [98]
Undaria pinnatifida	China	Whole plant	4.1 ± 0.2	/	52.0	12.5 ± 1.4	/	Qu et al. [77]
Undaria pinnitifida	New Zealand	Frond	3.0–13.0	2.8–4.8	4.3–16.4	22.1–28.0	/	Mak et al. [99]
Undaria pinnitifida	New Zealand	Sporophyll	25–70	5.1–13.3	8.6–15.0	14.4–34.6	/	Mak et al. [99]
Phaeophyceae/Scytothamnales								
Scytothamnus australis	New Zealand	Whole plant	8.5	/	91.7	/	/	Wozniak et al. [33]
Splachnidium rugosum	New Zealand	Whole plant	8–9	/	86.0–88.3	/	/	Wozniak et al. [33]
Bacillariophyceae/Naviculales								
Halamphora sp. AQ4	China	Whole plant	1.4–5.0	/	20.45–43.11	1.0–4.5	/	Lai et al. [100]

summer compared to spring [77]. Fucose is one of the main sulfated sugars in fucoidans and thus it is understandable that sulfate content and fucose proportion show a similar trend with season. The factors that drive seasonal variations in fucoidan composition remains unclear. Life history stage is deemed to have influences on fucoidan composition. For instance, fucoidans most brown algae (*Alaria ochotensis*, *Sargassum pallidum*, *Fucus vesiculosus* and *Laminaria japonica*) show increased levels of fucose content but decreased levels of galactose during their reproductive phase compared to sterile phase [42,91,101]. However, fucoidan from *U. pinnatifida* during the period of sporogenesis shows a significant increase in galactose proportion with unchanged fucose content [96]. Due to the close relationship between environmental changes and physiological history of the algae, it is difficult to identify possible factors that regulate compositional structure of fucoidan. The seasonal variation of fucoidan composition may be driven by the combination of environmental factors (e.g., temperature, light) and algal life history stage. The average MW of fucoidan also varies with season. For instance, the highest molecular weight of 2024 kDa for *Fucus serratus* fucoidan occurs in February while the lowest molecular weight of 1336 kDa occurs in March [36]. The changes of fucoidan MW with season are related to fucoidan composition mentioned above. It is worth noting that the extraction and purification conditions can also influence structural composition and MW of fucoidan [102].

4. Fucoidan biosynthesis pathway

Histochemical and autoradiographic techniques have proven that synthesis of fucoidan chains takes place in the Golgi-rich perinuclear area, specifically in Golgi-derived vesicles [103,104]. Synthesized sulfated polysaccharides in vesicles are transferred to the cell membrane and released through reverse pinocytosis in *Pelvetia* that can synthesize sulfated material in all cell types [103,104]. In *Laminaria* spp. fucoidan synthesis is confined to specialized secretory cells that discharge fucoidans to the surface of the thallus through mucilage canals [103,104].

Bioinformatics studies reveal the genes encode for enzymes that involved in fucoidan biosynthesis and lay the foundation for identifying fucoidan biosynthesis pathways. Michel et al. [105] first reported the fucoidan biosynthesis pathway in *Ectocarpus siliculosus*, and proposed the de novo pathway catalyzed by GDP-mannose 4,6-dehydratase (GM46D) and GDP-fucose synthetase (GFS) (Fig. 3). Functional genomics analysis reveals the same biosynthesis pathway of fucoidans in *Saccharina* [106]. Michel et al. [105] also first proposed another biosynthesis pathway of fucoidans in *Ectocarpus siliculosus*. This is an alternative salvage pathway can yield GDP-fucose directly from l-fucose (Fig. 3). In mammalian cells, free cytosolic l-fucose is first phosphorylated by l-fucokinase (FK). GDP-fucose pyrophosphorylase (GFPP) then catalyzes the reversible condensation of fucose-1-phosphate with GTP to form GDP-fucose. In *Ectocarpus siliculosus,* the conversion of l-fucose to GDP-fucose is catalyzed by a single bifunctional enzyme with similarity to both human FK and GFPP. This salvage pathway was also identified in the genomes of *Cladosiphon okamuranus* and *Nemacystus decipiens* [109,110].

5. Fucoidan production in marine algae

5.1. Fucoidan content in various marine algae

To date, most reports on fucoidans are related to brown macroalgae, with very few involving diatoms (Table 1). For brown macroalgae, 102 species in six orders were documented, with most species from Fucales (49) and Laminariales (30). In these two orders, *Sargassum* and *Saccharina* are the most studied genera, respectively (Table 1). There are a large range for crude fucoidan content (Table 1). The highest content of 70 % has been reported in *Undaria pinnatifida* of Laminariales while the smallest is 0.25 % in *Padina boryana* of Dictyotales (Table 1). Laminariales has the largest range of crude fucoidan content (0.35–70 %) although the species number reported is lower than that in Fucales. Ectocarpales has a similar content range (1.6–18.25 %) to Fucales (0.32–18 %) despite only six species in Ectocarpales being reported. It is worth noting that big ranges within or beyond order is caused not only by species differences but also different parts of thallus. For instance, the largest content of 70 % was found in *Undaria pinnatifida* sporophyll while the smallest content of 0.5 % was reported in the whole plant of *Padina boryana*. After reviewing the published data, we find that sporophyll usually has much higher fucoidan content compared to other parts of thallus. The crude fucoidan content in *Undaria pinnitifida*

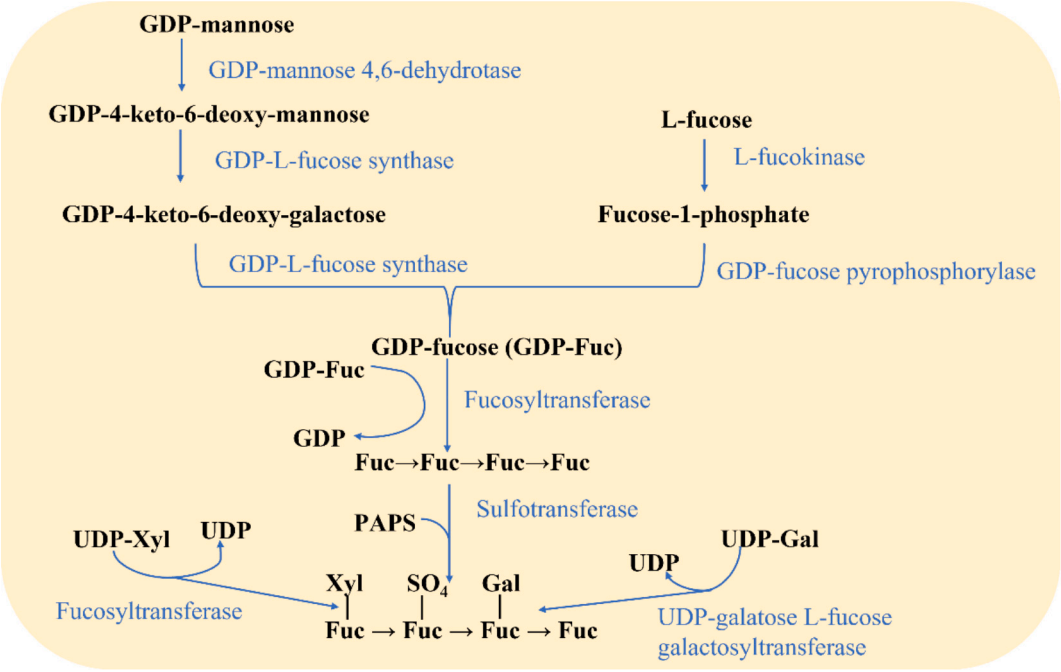

Fig. 3. Two biosynthesis pathways of fucoidans in brown seaweeds. PAPS, adenosine 3'-phosphate5'-phosphosulfate. The pathways refer to the following literature [104,106–108]. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

sporophyll in New Zealand can be as high as 25–70 % that is related to maturation degree of sporophyll while it varies from 3 to 13 % for frond [99]. Furthermore, sporophyll with sori (a cluster of sporangia) has higher crude fucoidan content compared to those without sori (Table 1). For instance, the crude fucoidan content of *Undaria pinnatifida* sporophyll with sori in Japan was 16 % while it was only 3.21 % for sporophyll without sori [96]. It has been suggested that fucoidans, due to their hydroscopic nature, can reduce desiccation and aid the release of reproductive cells [103]. In addition, fucoidans in the extracellular matrix can supply instant swelling for the conceptacle enabling simultaneous discharge of swarmers [111].

The fucoidan content in whole plant ranges from 0.25 % to 16 % (Table 1), with the lowest value in *Saccharina japonica* and the highest value in *Undaria pinnatifida* and both from Laminariales (Table 1). Therefore, the range of fucoidan is much smaller when the same position of thallus is compared. In addition to different parts of thallus, the same species in different locations also show different fucoidan contents. For instance, *Saccharina japonica* frond collected in Japan had a fucoidan content of 2.2–4.3 % while it was only 0.7 % for that collected in Russia [76,91].

In addition to brown macroalgae, recent studies demonstrate that diatoms can also synthesize fucoidans. For instance, Vidal-Melgosa et al. [2] traced the existence of fucoidans in both dissolved and particulate organic matter during a series of diatom blooms in the North Sea. Further experiments showed that the diatoms of *Chaetoceros socialis* and *Thalassiosira weissflogii* and *Nitzschia frustulum* could produce and excrete fucoidans into seawater [2,10]. However, very few studies quantified fucoidan content and excrete rate in diatoms. Until now, only one study reported that the crude fucoidan content in *Halamphora* sp. AQ4 ranged from 1.4 % to 5.0 % (Table 1).

It is worth noting that extraction methods can significantly affect the crude fucoidan content of seaweeds [102]. Different solvents, including water, acids and $CaCl_2$ are used under different conditions (e.g., temperature, time, and pH) to extract crude fucoidan from seaweeds. Therefore, it should be cautious to compared crude fucoidan contents using different extraction methods. In contrast, almost all studies used anion-exchange chromatography to purify high-quality fucoidan from crude fucoidan. Therefore, it is more feasible to compare purified fucoidan content among species. The purified fucoidan content varies from 0.1 % to 13.3 %, with the minimum found in *Alaria angusta* and the maximum in *Undaria pinnatifida*, both belonging to the Laminariales order (Table 1). Compared to Laminariales, Fucales exhibits a more restricted range of purified fucoidan content (0.38–8.67 %) although there are more species (49) being documented. The content variation for Dictyotales is even limited, ranging from 1.9 % to 4.4 %, which may be attributed to the fewer species (14) reported. For the orders of Desmarestiales, Scytothamnales and Naviculales, there is an absence of data regarding purified fucoidan content is available, indicating a need for further investigation in future research.

5.2. Environmental factors affecting fucoidan content in marine algae

5.2.1. Light

The biosynthesis of fucoidans in algae is regulated by environmental factors, among which, light may be the most important one. For instance, *Fucus vesiculosus* accumulated more fucoidan under light conditions compared with dark conditions. In addition, excretion rates of fucoidan carbon by *F. vesiculosus* under light conditions amounted to 19.9 ± 5.08 mg C kg^{-1} DW h^{-1} based on enzyme hydrolysis and 39.2 ± 10.37 mg C kg^{-1} DW h^{-1} based on acid hydrolysis, while under dark conditions, *F. vesiculosus* excreted 11.5 ± 3.46 and 28.3 ± 7.10 mg C kg^{-1} DW h^{-1} based on enzyme and acid hydrolysis, respectively [7]. The higher fucoidan content and excretion rate under light conditions should be related to photosynthesis that drives the biosynthesis of fucoidan. Field investigation also shows a positive and significant relation between solar irradiance (50–700 μmol photons m^{-2} s^{-1}) and fucoidan content in *S. latissima,* and *L. digitata*. However, this relation was not found for the natural population of L. *digitata* at Hanstholm [86], and the reasons remain unknown. The effect of light on fucoidan content may be related to seasonal variation. The high light intensity and dose in summer may simulate the biosynthesis of fucoidan [62].

5.2.2. Nutrient

In addition to light, nutrient is another essential environmental factor that can affect fucoidan content in algae. Bruhn et al. [86] conducted both field investigation and lab experiments to explore the relationship between fucoidan content of seaweeds and environmental factors. The field investigation shows that crude fucoidan content of seaweeds decreased with the increase of tissue nitrogen content (1.5–5 %) in L. *digitata*, indicating that environmental nitrogen increase would reduce fucoidan content. However, lab experiment showed that fucoidan content of L. *digitata* increased with tissue nitrogen content when it increased from 0.6 to 1.35 %. The field results were regulated by the combination of multiple environmental factors, which may contribute to the inconsistent with lab results. The combination of field and lab studies suggests a two-phase response of fucoidan synthesis to tissue nitrogen content. When tissue nitrogen content is <1.5 %, fucoidan content increased with tissue nitrogen content, indicating the synthesis of fucoidan, probably some enzymes, need nitrogen component. However, when tissue nitrogen content is >1.5 %, it can stimulate the synthesis of other compounds, e.g., storage carbohydrates (laminarin and mannitol) rather than fucoidan [86]. In terms of phosphate, a positive relation was found for *Stephanocystis crassipes* while a negative relation was found for *Sargassum pallidum* from a filed investigation when phosphate concentration varied from 0.021 to 1.19 μM L^{-1} [62]. The specific reasons for the differential responses remain unknown. Laboratory experiments are needed to examine the separate effects of phosphate.

5.2.3. Temperature

Temperature can also affect fucoidan content in algae. There was a positive relation between temperature and content of fucoidan in *S. japonica* and *Stephanocystis crassipes* when temperate changed from −1 to 23 °C [62]. It is well known that fucoidan has antioxidant activities [112] and thus the higher fucoidan contents at higher temperatures may play a protective role in eliminating reactive oxygen species induced by thermal stress. On the other hand, the relation between temperature and content of fucoidan for *Sargassum pallidum* was not significant [62]. It is worth noting that the results above are based on filed investigation. In addition to temperature, other environmental factors may also affect fucoidan content simultaneously. To understand the separate effects of temperature, lab-controlled experiments are needed in future.

5.2.4. Salinity

In addition to light, nutrient and temperature, salinity can also affect algal fucoidan content in algae. Field investigation conducted by Bruhn et al. [86] shows that crude fucoidan content of seaweeds increased with salinity (15–25 ‰ for *S. latissima*, 30–35 ‰ for L. *digitata*). However, lab experiment showed that lower salinity (10 ‰ and 20 ‰) stimulated fucoidan content of *S. latissimi* compared to the normal salinity (30 ‰). The field results were also determined by other environmental factors simultaneously apart from salinity, which may explain their inconsistence with laboratory results. The salinity experiment indicates that lower salinity can induce fucoidan synthesis. This should be related to fucoidan function in regulating osmotic pressure. Cells can synthesize more fucoidan for strengthening the cell wall by cross-linking matrix cellulose microfibrils in response to osmotic stress [113].

5.2.5. Seasonal effects

A lot of studies investigated seasonal effects on algal fucoidan content. *Fucus serratus*, *F. vesiculosus* and *Ascophyllum nodosum* harvested off

the coast of Aberystwyth (UK) had the highest fucoidan content in autumn and the lowest in spring [36]. Similarly, fucoidan content in the brown alga *Undaria pinnatifida* collected in Peter the Great Bay (Japan Sea, Russia) increased markedly from April to July (from 3.2 to 16.0 % dry weight) [96]. The seasonal variation of fucoidan content in *U. pinnatifida* is determined by plant matures because sporogenesis in *U. pinnatifida* in Peter the Great Bay begins at the end of May, and reaches the maximum extent in July fucoidan [89]. In addition, *Undaria pinnatifida* sporophylls with sori has fivefold higher fucoidan content than those without sori [96]. Fucoidan content in *L. japonica* collected from Hokkaido Bay (Japan) tended to gradually increase from April to September, and reached the maximum in October when plant had the highest sporogenesis [91]. The crude fucoidan yield of *S. sculpera* cultivated in Sanggou Bay (China) increased from 2.9 % in March to 6.1 % dry wt in July as the plant matured [77]. On the other hand, Mature sporophytes of *U. pinnatifida* collected each month between November 2015 (late spring) and March 2016 (late summer) from Golfo Nuevo (Argentina) did not show significant seasonal variations [97]. Therefore, seasonal effects on algal fucoidan content could be driven by plant mature but may be also regulated by environmental factors, e.g., temperature, light and nutrient.

6. Ecological functions of Fucoidan

6.1. Degradation of fucoidan

It has been reported that microbial degradation of fucoidans is slower than that of other polysaccharides. For instance, laminarin, a dissolved energy storage polysaccharide, is referentially targeted by bacteria of different classes and it merely needs several hours to completely degrade laminarin with three enzymes [114–116]. In contrast, fucoidans can only be degraded by specialized bacteria that require dozens and even hundreds of different enzymes to work together [2,3]), suggesting that fucoidans are more recalcitrant among algal polysaccharides. Although a few bacteria belonging to the Bacteroidetes, Gammaproteobacteria or Planctomycetes–Verrucomicrobia–Chlamydiae can partially hydrolyze fucoidan, the most degradation rate they can achieve is 60 % [117]. Sichert et al. [3] found that even with >100 hydrolytic enzymes, *Lentimonas* sp. could not completely degrade fucoidan, indicating the recalcitrance and slow turnover of fucoidans in the ocean. To date, fucoidan is recalcitrant and cannot be fully enzymatically degraded by any microbial isolates. The strong recalcitrance of fucoidan is related to its complex, branched and highly sulfated structure. Fucoidan degradation pathways involve a combination of different fucoidanases, such as carbohydrate esterases, sulfatases and glycoside hydrolases. The first step for fucoidan degradation is that dismantling enzymes such as sulfatases and carbohydrate esterases act while the heavily decorated structure of fucoidans protects glycosidic linkages from enzymatic hydrolysis [118,119]. In addition, characterized *endo*-enzymes from glycoside hydrolase family 107 are highly substrate specific and can only cleave specific fucoidan backbones to produce sulfated fucose oligosaccharides [120,121]. All these steps indicate the difficulty of degrading fucoidan.

In addition to intrinsic structure, the inhibition of fucoidans on microbes also contributes to their recalcitrance. For instance, the sulfated polysaccharide from the brown macroalga *Sargassum swartzii* shows antibacterial effects on human bacterial pathogens including *Escherichia coli*, *Salmonella typhi* and *Vibrio cholera* [122,123]. Sterilized fucoidans from *Laminaria japonica* significantly reduced the growth of *Escherichia coli* and *Bacillus cereus* [124]. There are two possible mechanisms of fucoidan's antibacterial effects. One mechanism is that fucoidans can bind with bacteria and destroy their cell membranes, which causes the leakage of intracellular substances (e.g., cytosol, proteins, and nucleic acids), and eventually cause the death of cells [125]. The second mechanism is related to the negatively charged property of sulfated polysaccharides that can trap nutrients (e.g., cationic minerals) in the culture medium, by which the bioavailability of the nutrients would reduce and thus inhibit growth of bacteria [126]. The antibacterial activity of fucoidan is related to many factors, such as the sugar type, category of glycosidic bond, the degree of branching, chain conformation, molecular weight, and sulfate content [127]. Among them, molecular weight and sulfate content are particularly important. Studies have shown that fucoidans with low molecular weight (5–50 kDa) and high sulfate content (over 20 %) have higher bioactivities [127,128].

6.2. Fucoidan's role in carbon sequestration

Basically, fucoidans can sequester carbon in two forms, dissolved organic carbon (DOC) and particle organic carbon (POC). Fucoidans are originally hydrosoluble and exist in seawater in the form of DOC after being excreted by algae [129]. Due to their recalcitrance to bacterial degradation, fucoidans can exist in seawater for >5000 years as refractory DOC [130,131]. In fact, the majority of observable DOC in the ocean has an estimated lifetime of 16,000 years [129,132]. Brown algae can excrete 18 to 62 % of their net carbon fixation into seawater, while fucoidans can account for 44 to 50 % of all exuded dissolved organic carbon [9,133]. The net primary production for wild macroalgae is estimated to be 1826 Tg C yr^{-1} [134]. Therefore, brown macroalgae can excrete about 155 Tg fucoidan-carbon yr^{-1}, which suggest that 93 Tg C yr^{-1} can be sequestered if 40 % of net primary production is released as DOC, 40 % of them are fucoidans, and 40 % of fucoidans are degraded by bacteria. The sequestered carbon by algal fucoidans is about 10 % of carbon sequestered by phytoplankton through biological carbon pump [134]. If fucoidans excreted by diatom are counted in, there will be more carbon sequestered by excreted fucoidans. There is no available information on excretion rates of fucoidan by diatoms and thus we do not know how much contribution can be made by diatoms yet, which should be done in future. Anyhow, the excreted fucoidan can make a solid contribution to carbon sequestration by the ocean, presenting a way by which brown algae and diatom can be used to capture and sequester CO_2, without a significant removal of nutrients from the ocean ecosystem. The carbon pool of DOC in the ocean (~660 Gt) is bigger than the sum of Earth's marine and terrestrial biota carbon, and is also close to the carbon in atmosphere [135]. Therefore, the changes of DOC can affect carbon pool in atmosphere and climate change significantly.

In addition to as DOC, fucoidans can form POC. It has been reported that fucoidans excreted by the centric diatom species *Thalassiosira weissflogii* and *Chaetoceros socialis* can form aggregates, leading to the transition from DOM to POM. These aggregates promote the formation of particles and thus carbon export from euphotic layer to deep oceans [10]. Vidal-Melgosa et al. [2] also found that the increasing concentration of excreted fucoidan led to aggregation of diatoms into particles, due to their stickiness during a series of diatom blooms in the North Sea. The adhesive fucoidan could increasingly draw down diatom cells through self-aggregation, contributing to carbon sequestration in the ocean. Additionally, partial fucoidans are kept inside cells as the important component of cell walls [3]. Recent study found that fucoidans content in *Halamphora* sp. AQ4 could reach 5 %. Supposing that fucoidan and carbon contents of diatoms are 3 % and 50 %, respectively, fucoidans production by diatoms in the form of POC is 1, 111 Tg $year^{-1}$. They can sink to seabed with diatom debris. In fact, fucoidans have been found to persist for centuries in sediments. Therefore, carbon in fucoidan can be stored for a long term [7].

Ocean afforestation is deemed as a potentially effective way to remove atmospheric CO_2 and alleviate climate change [136]. However, nutrient limitation is a big challenge for scaling up seaweed cultivation in open oceans. Fucoidans hardly contain any nitrogen or phosphorus, which is very important for algal growth [7,36]. Fucoidans biosynthesis thus requires light and CO_2, but does not use up the nitrogen or phosphorus reserves of algae. Therefore, brown algae can excrete fucoidan without any effects on their growth. This is particularly important for culturing seaweeds in open oceans. Here we propose a sustainable ocean

afforestation mode with brown macroalgae and there are four pathways for CO_2 sequestration (Fig. 4). The first pathway is that brown macroalgae excrete fucoidans into seawater to form refractory DOC after bacterial degradation. The second pathway is that the excreted fucoidans form POC via aggregation and POC sink to bottom of oceans. The third pathway is the export of thalli POC that is released during tissue fragmentation and breakage due to thallus decay, wave action and animal grazing [8]. The last pathway is to collect algal biomass for bioenergy, capture released CO_2 and store them in sub-seabed geological reservoirs, which can be termed Bioenergy with Carbon Capture and Storage (BECCS). To offset the cost of CO_2 capture and storage, part of the cultivated brown algae needs to be collected for food or biomedicines, which could make ocean afforestation economically feasible for carbon sequestration. Considering the property of fucoidans in anti-inflammatory and anti-tumour, biopharming may be a preferable field due to its high profit.

7. Fucoidan production in future oceans

Due to human activities, CO_2 is continuously emitted into atmosphere, leading to ocean warming and acidification. These two global variables are impacting algal growth and primary production [137]. Fucoidan production depends on two parameters, algal growth and fucoidan content in algae. In terms of brown seaweeds, temperature increase from 4 to 10 °C increased growth of *Desmarestia aculeata* but did not affect growth of *Alaria esculenta* or *Saccorhiza dermatodea*, and even reduced photosynthetic activity of *D. aculeata*, *A. esculenta* and *S. dermatodea* [138]. Therefore, the responses of brown algae to warming demonstrate obvious species differences. A positive relation between temperature and fucoidan content in *S. japonica* and *Stephanocystis crassipes* was found when temperate changed from −1 to 23 °C, while this relation was not significant for *Sargassum pallidum* [62]. This indicates that the response of fucoidan synthesis to warming may also have species differences. It is worth noting that the results above are based on field investigation. Laboratory experiments are needed to assess the separate effects of ocean warming on fucoidan content and production by algae.

In terms of ocean acidification, studies show that it commonly stimulates growth of brown macroalgae. For instance, ocean acidification (~1000 ppmv) increased relative growth rate of *Sargassum muticum* by 41 % after a 13-day culture [139]. High CO_2 level (1000 ppmv) also increased blade length, width, and weight of *Saccharina japonica* by 49.9 %, 40.3 % and 70.1 %, respectively [140]. The effects of CO_2 on fucoidan content have not been documented. Previous studies show that elevated CO_2 can usually enhance photosynthetic carbon fixation of seaweeds [141]. Therefore, fucoidan synthesis may be stimulated by elevated CO_2 as they are photosynthate. Studies show seaweeds can excrete DOC to maintain a stable C:N ratio in cells [142]. Fucoidans can be excreted as excessive carbon since they contain lots of carbon and seldom nitrogen. Combing the effects on growth and fucoidan synthesis, elevated CO_2 may enhance fucoidan production and excretion by algae, while relative studies need to be carried out to test this presumption.

In addition to ocean warming and acidification, nutrient is also an essential global variable that can affect fucoidan production. It is predicted that eutrophication may increase in coastal waters due to increased terrestrial input and mixing while nutrient levels in upper seawater of open ocean would decrease due to intensified stratification caused by warming [143,144]. Therefore, the trend of fucoidan production in response to nutrient changes in coastal areas and open oceans could be opposite. High nutrient levels commonly stimulate algal growth [145]. It has been also reported that high nitrogen and phosphorus availability can stimulate fucoidan content of some brown algae while does not affect or even reduce other algae's fucoidan content [62]. Therefore, species responses are different and more studies are required in future to have a more comprehensive understanding.

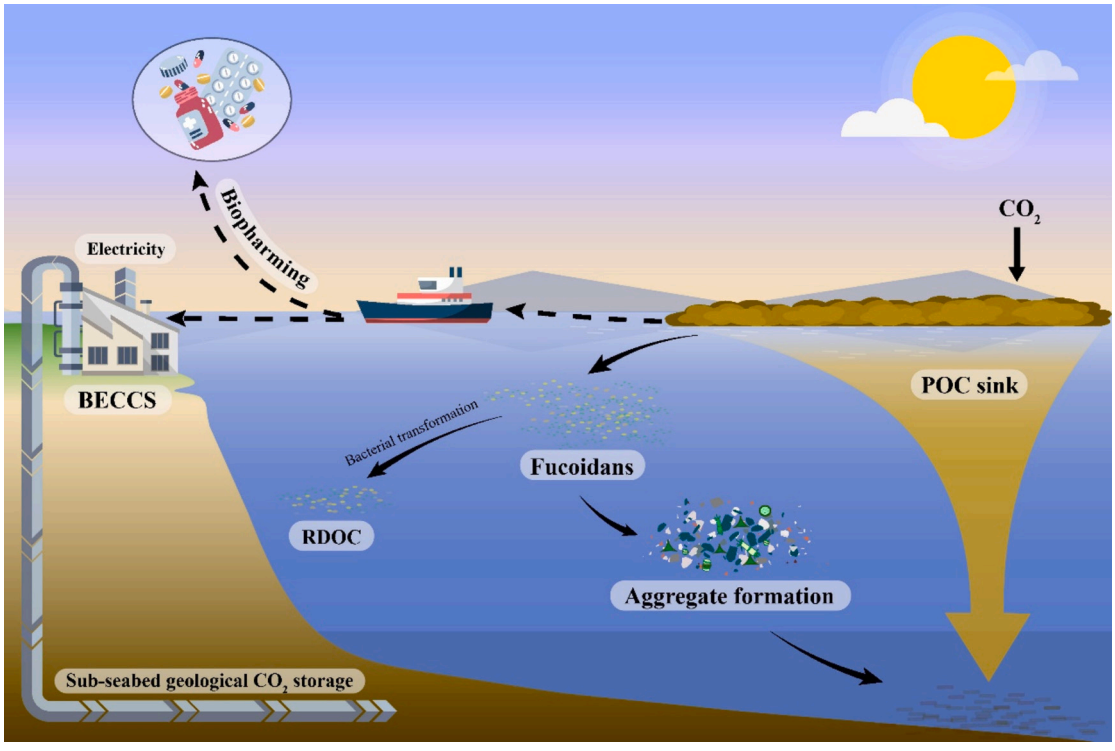

Fig. 4. A sustainable CO_2 sequestration mode of ocean afforestation using brown macroalgae. Four pathways of CO_2 sequestration combined with fucoidans application in biopharming are included in this mode. BECCS, Bioenergy with Carbon Capture and Storage; RDOC, refractory dissolved organic carbon; POC, particle organic carbon.

8. Conclusions and perspectives

In this study, the structure, biosynthesis pathway, distribution feature of fucoidans in marine algae are reviewed. Environmental factors that affect fucoidan production, including climate change variables, are analyzed. Ecological functions of fucoidans are discussed in depth. Furthermore, given the potential of fucoidans in carbon capture and storage, a sustainable CO_2 sequestration mode of ocean afforestation using brown macroalgae is proposed. While most studies focus on biological and biomedical application of fucoidans, this review article emphasizes the ecological functions of fucoidans after integrating the recent research progress. To further understand and explore fucoidans' ecological application, here are some recommendations for future studies.

(1) Fucoidans from other algae. Until now, most species that are reported to have fucoidans are from brown algae. Whether algae from other phyla can synthesize fucoidans remains to be explored. In addition, the information of fucoidan content in diatom remains very limited although diatoms are proved to be able to excrete fucoidans. To quantify fucoidan production by algae, the first thing needs to do is to clarify fucoidan source and their content in algae as much as possible.
(2) Quantify excretion rate of fucoidans by algae. To assess the contribution of fucoidans to DOC pool in the ocean, the excretion rate of fucoidans by algae must be known. However, we only know the excretion rate of fucoidans by *Fucus vesiculosus* for now. Therefore, more data on the excretion rate of fucoidans by other algae are in great need.
(3) The effects of environmental factors on fucoidan content. Environmental factors can significantly impact fucoidan synthesis and content in algae. However, most studies are based on field investigation, of which the results are based on the combined effects of multiple factors. To identify the separate effect of a single factor, lab experiments must be carried out. The effects of temperature and CO_2 on fucoidan synthesis particularly need to be investigated since the ocean gets warmer and CO_2 enriched.
(4) Overexpression of fucoidans by gene editing. Regardless of their application in biomedicine and carbon sequestration, a higher fucoidan production is expected. Culturing algae under an optimal environment is a way to produce more fucoidan. In addition to this, molecular techniques, e.g., gene editing can be used to build overexpression of fucoidan. Then higher fucoidan production can be achieved with less endeavor in regulating culture conditions.
(5) Interaction between algae and bacteria. The reasons why algae secret fucoidans remain unclear. It may be driven by constitutive production and regulation of intracellular stoichiometric ratio. In addition, bacteria may also induce fucoidan excretion and even affect their chemical composition [146,147]. This needs to be further studied. On the other hand, the excretion of fucoidan may also affect bacterial structure. It has been reported that fucoidans can change the bacterial community in paddy soil while their impacts on bacterial community on surface of algae or in seawater have not been studied [148]. This needs to be investigated in future since algae can excrete a large amount of fucoidans into seawater. Their antibacterial activity should impose impacts on structure of bacterial community and related biogeochemical processes.

CRediT authorship contribution statement

Wei Li: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Jichen Chen:** Writing – review & editing, Visualization, Methodology. **Yuan Feng:** Writing – review & editing, Visualization, Methodology. **Xu Li:** Writing – review & editing, Investigation, Data curation. **Guang Gao:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

Data will be made available on request.

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