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Evaluation of brown macroalgae *Sargassum* as a source of active substances: a review of active substances

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ABSTRACT: *Sargassum* seaweeds are widely distributed across temperate and tropical seas globally, boasting abundant biomass, an affordable price, high aesthetic value, and being rich in a diverse range of active substances. To assess the viability of *Sargassum* seaweeds as a source of active substances, a search was conducted on the Web of Science, Google Scholar and CNKI for relevant active substances derived from it. Additionally, the isolated active substances were categorized based on the species of *Sargassum* seaweeds. Finally, through cluster analysis using Citespace, the research trends regarding the active substances from *Sargassum* seaweeds were identified. Between 2014 and 2025, research on the active substances sourced from *Sargassum* seaweeds predominantly centered around polysaccharides and polyphenols. Fatty acids came next in focus, trailed by terpenes and phytosterols. The *Sargassum* species under study were mainly concentrated on 95 species. Among them, it was found that 5.38% of *Sargassum* seaweed, which included *S. fusiforme*, *S. fulvellum*, *S. horneri*, *S. pallidum* and *S. wightii*, contained nine or more active substances. However, in over 42% of the studied *Sargassum* seaweeds, fewer than two types of active substances were detected. Since 2004, active substances from approximately 40 species of *Sargassum* seaweeds have been isolated, and over 470 types of active substances have been identified. Among them, terpenoids accounts for around 30%, followed by polyphenols and polysaccharides, while other substances such as alkaloids and heterocyclic substances can make up to 20%. The authors also constructed the Database of Bioactive Substances from *Sargassum* seaweeds for searching active substances isolated from *Sargassum* seaweeds. CiteSpace analysis shows a clear hotspot shift: separating and purifying non-carbohydrate bioactive substances is a fast-growing core direction. Previously, polysaccharides dominated due to easy extraction and mature activity research. However, with advanced separation technologies and exploration of "niche" substances, non-carbohydrates (terpenoids, alkaloids, etc.) now show great potential, promising to break research bottlenecks. This study offers theoretical and practical support for *Sargassum* application, guiding product innovation in pharmaceuticals, food, and cosmetics.

1. Introduction

Sargassum seaweeds represent a group of brown algae that are prevalently distributed along tropical and temperate coastlines across the globe. Over 1,000 species, varieties, and variants of this genus were identified on the Algaebase website [1], with more than 340 species having been definitively verified [1, 2]. For a long time,

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coastal inhabitants have utilized them as food [3], traditional medicine [4, 5], fertilizer[6] and animal feed [7]. Subsequently, there has been a spate of reports regarding products like *Sargassum*-enriched drinks [8] and cookies [9] enriched with *Sargassum* also appeared one after another. In reality, the majority of *Sargassum* seaweeds possess a coarse texture and a pungent fishy odor, rendering them unpalatable for direct consumption. The number of edible *Sargassum* species is relatively limited, principally consisting of *Sargassum confusum*, *S. fusiforme*, *S. hemiphyllum*, *S. kjellmanianum*, and *S. polycystum* [6]. A small fraction of *Sargassum* seaweeds serves as industrial raw materials for manufacturing products such as alginate [10], and mannitol [11]. However, a greater proportion of them are disregarded and left to decompose, not only squandering valuable resources but also contributing to environmental pollution [12, 13].

In recent years, the development of *Sargassum* seaweeds has garnered extensive attention in the fields of medicine, food, and industry [14]. *Sargassum* species are not only consumed as traditional edible seaweeds but are also incorporated into functional foods and nutritional supplements due to their high content of dietary fibers, vitamins, minerals, and bioactive compounds. For instance, polysaccharides derived from *Sargassum*, such as fucoidan and alginate, are widely used as natural thickeners, stabilizers, and emulsifiers, while also contributing health benefits including prebiotic effects and enhanced immune modulation. In the pharmaceutical sector, *Sargassum*-derived bioactive substances have shown great potential for drug development. Numerous studies have reported their anti-oxidant [15], anti-bacterial [16], anti-inflammatory [17], and anti-viral properties [18], making them promising candidates for therapeutic agents against chronic inflammation, microbial infections, and viral diseases. However, on the whole, the utilization of *Sargassum* seaweeds still remains at a stage of low-value applications, and a significant number of Sargassum species have yet to be thoroughly investigated. *Sargassum* seaweeds are characterized by rich biodiversity and abundant biomass, which renders them an ideal reservoir of active substances. There have been numerous reports on active substances derived from *Sargassum* seaweeds, encompassing polysaccharides [19], fatty acids [20], glycolipids [21], sterols [22], terpenes [23], and other substances [24, 25].

The development of active substances from *Sargassum* seaweeds represents the primary route for the high-value utilization of these *Sargassum* resources. As far as we are aware, at present, there is a dearth of a comprehensive summary regarding the research status and development trends of active substances present in *Sargassum* seaweeds. The aim of this review was to investigate the distribution, research standing, and future trends of active substances sourced from *Sargassum* seaweeds. Moreover, the isolated and purified active substances were categorized based on *Sargassum* species, with the intention of promptly accessing information about these active substances and further provide data support for promoting the utilization and development of *Sargassum* resources.

2. Results and discussion

2.1 The distribution and types of active substances from Sargassum seaweeds

The Web of Science, Goole scholar and CNKI databases were employed to search for relevant papers published on *Sargassum* seaweeds between 2014 and 2024. It was revealed that over the past decade, research

on the active substances derived from *Sargassum* seaweeds primarily centered around polysaccharides and polyphenols. This was followed by fatty acids (saturated fatty acid and polyunsaturated fatty acids), and then terpenes and sterols (Figure 1). Among the reported active substances, mycosporine-like amino acids (MAAs) and glycolipids from *Sargassum* seaweeds had received the least research attention. There were no more than 10 and 20 articles reported on them respectively. Currently, MAAs have only been detected in three species of seaweeds, namely *S. crassifolium* [26], *S. fusiforme* [27] and *S. stenophyllum* [28]. Only 15 species of seaweeds were found to contain glycolipids (Figure 1), such as *S. cristaefolium* [29], *S. filipendula* [30], *S. horneri* [20], *S. myriocystum* [31], *S. naozhouense* [32], *S. pallidum* [33], *S. platycarpum* [34], *S. vulgare* [35], and others. MAAs and glycolipids are active substances that have emerged in recent years, characterized by diverse structures and abundant activities, and hold promising application prospects in the fields of food [36, 37], medicine [38, 39], and cosmetics [40]. Additionally, it is crucial to note that aside from the eight types of active substances mentioned above, *Sargassum* seaweeds are also abundant in other types of active substances like alkaloids and heterocyclic compounds (Figure 1). These findings have demonstrated that *Sargassum* seaweeds constitute a highly prolific source of active substances. Their structural diversity and broad application potential, coupled with their current scarcity in the literature, position them as high-value targets for further exploration. We argue that a strategic shift in research efforts toward these neglected compounds is essential to fully unlock the biotechnological potential of *Sargassum* seaweeds.

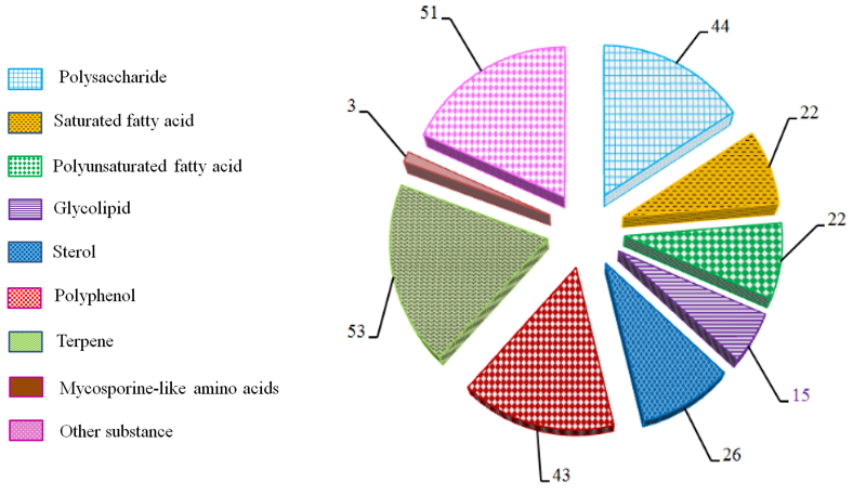


Figure 1 Classification of active substances from *Sargassum* seaweeds. The data are from Web of Science, Goole scholar, and CNKI databases published between 2014 and 2025. (The number next to the pie chart represents the number of *Sargassum* species that contain the corresponding substance.)

Furthermore, diverse types of active substances were categorized based on *Sargassum* species (Table 1). A total of 95 species of *Sargassum* seaweeds were identified as containing the aforementioned active substances (the same species of *Sargassum* from different origins was not double-counted), including *S. fusiforme*, *S. horneri*, *S. muticum*, *S. polycystum*, *S. thunbergii*, *S. wightii*, and other varieties. Based on the quantity of active substance types, 95 species of *Sargassum* seaweeds were grouped into three categories: Group I, where the number of active substance types was less than or equal to 2; Group II, with the number ranging from 3 to 5; and Group III, having 6 or more types. As shown in Figure 2, among these *Sargassum* seaweeds, over two-fifths (42.11%) of them have only been found to contain one or two active substances,

indicating that more types of active substances remain unproven. 17.89% of *Sargassum* seaweeds contained six or more types of active substances, specifically *S. fusiforme*, *S. fulvellum*, *S. horneri*, *S. pallidum* and *S. wightii*. According to incomplete statistics, there are more than 340 species of seaweeds globally [1]. Meanwhile, a greater number of *Sargassum* seaweed species containing active substances have yet to be identified [41, 42]. This implies that at least two-fifths of *Sargassum* seaweeds have not been thoroughly investigated up to this point.

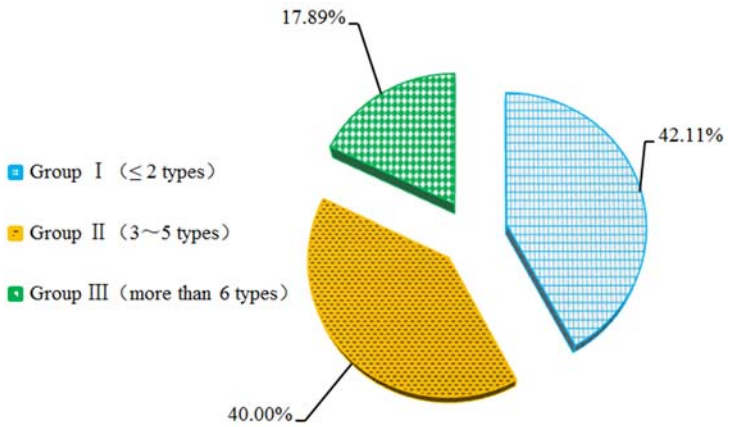
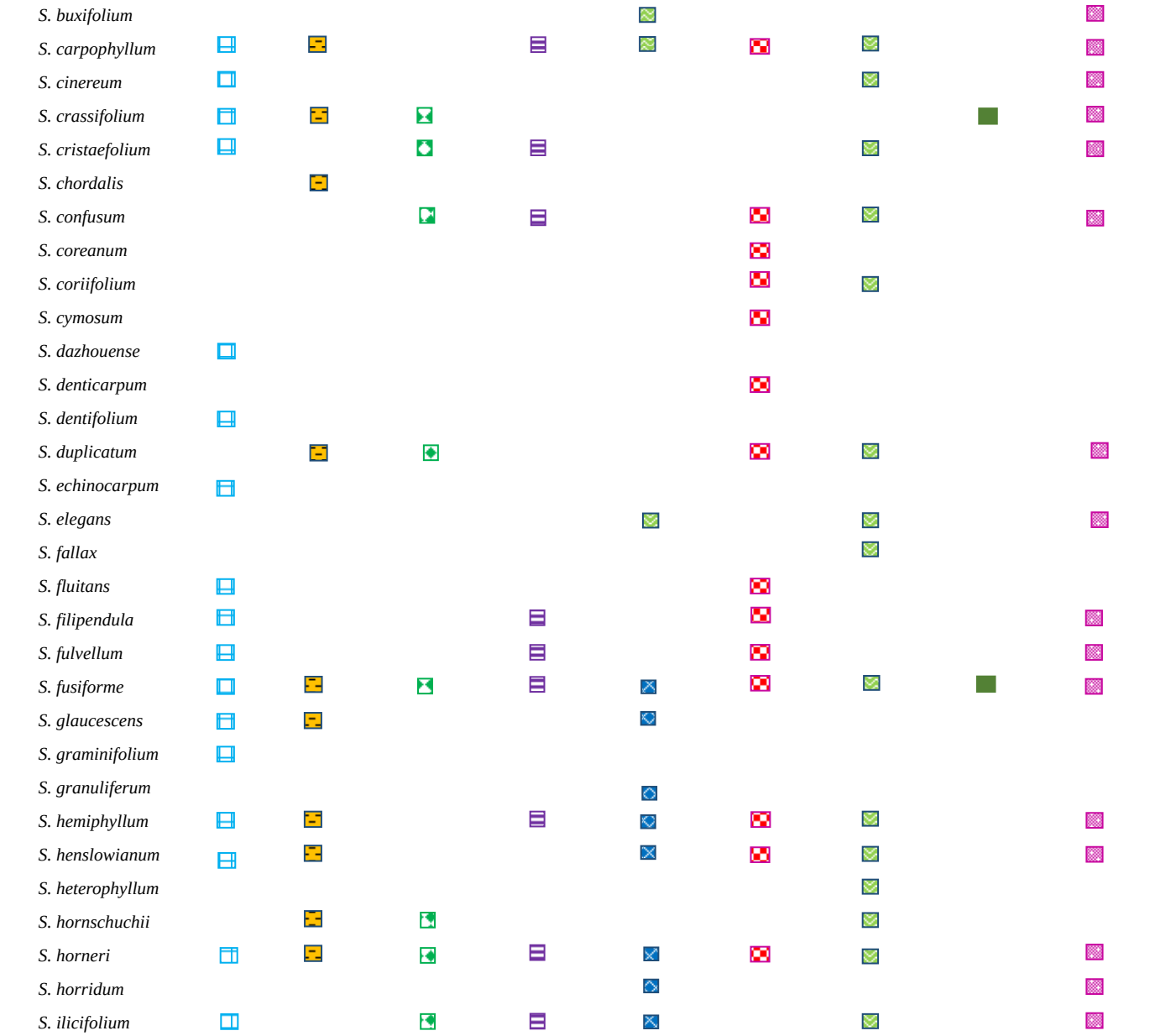


Figure 2 The percentage of different groups (according to the amount of the type of active substance) of active substance contained in 95 species of *Sargassum* seaweeds. The data are from Web of Science, Goole scholar, and CNKI databases published between 2014 and 2025. (The number next to the pie chart represents the percentage of *Sargassum* containing the corresponding number of active substances in the total number of *Sargassum* seaweeds.)

This classification underscores a significant research gap and uneven exploration across different *Sargassum* species. The fact that such a large proportion (42.11%) of species have been linked to only one or two types of active substances strongly suggests that the current scientific understanding of their phytochemical composition is far from complete. This is not necessarily an indicator of low biochemical potential but rather a reflection of limited investigative effort. We posit that the highly studied species in Group III, such as S. fusiforme and S. horneri, should serve as models for future phytochemical profiling of under-explored species. The substantial number of uninvestigated *Sargassum* species, coupled with the incomplete mapping of those already identified, represents a vast and largely untapped resource for the discovery of novel bioactive compounds. A more systematic and comprehensive screening approach is urgently needed to fully evaluate the chemotaxonomic and biotechnological potential of this genus.

Table 1 The types and distribution of active substances from *Sargassum* seaweeds

Species	Active substances								
	P	SF	PF	GL	ST	PP	TE	MA	OT
	S								
S. acinarium			■						
S. angustifolium	■				■	■	■		■
S. aquifolium	■				■	■			■
S. asperifolium		■			■		■		■
S. autumnale	■						■		
S. binderi	■	■	■		■	■			■
S. boveanum					■		■		■


S. buxifolium
S. carpophyllum
S. cinereum
S. crassifolium
S. cristaefolium
S. chordalis
S. confusum
S. coreanum
S. coriifolium
S. cymosum
S. dazhouense
S. denticarpum
S. dentifolium
S. duplicatum
S. echinocarpum
S. elegans
S. fallax
S. fluitans
S. filipendula
S. fulvellum
S. fusiforme
S. glaucescens
S. graminifolium
S. granuliferum
S. hemiphyllum
S. henslowianum
S. heterophyllum
S. hornschuchii
S. horneri
S. horridum
S. ilicifolium

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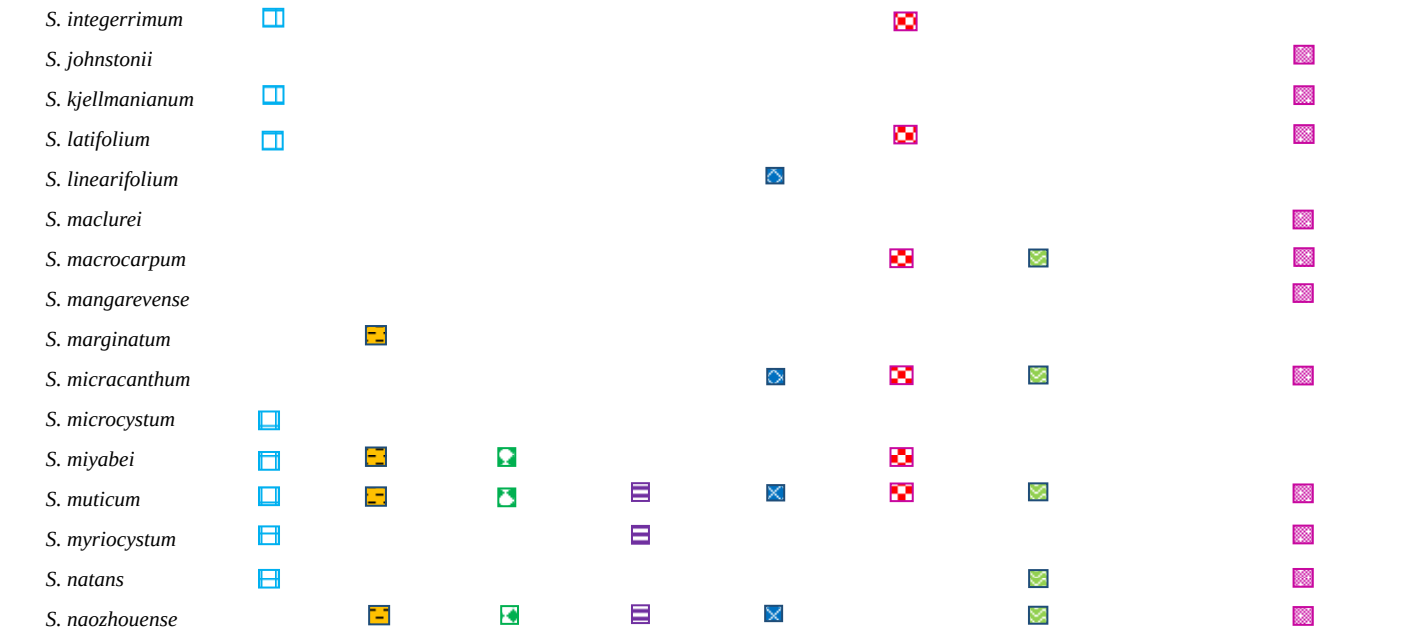
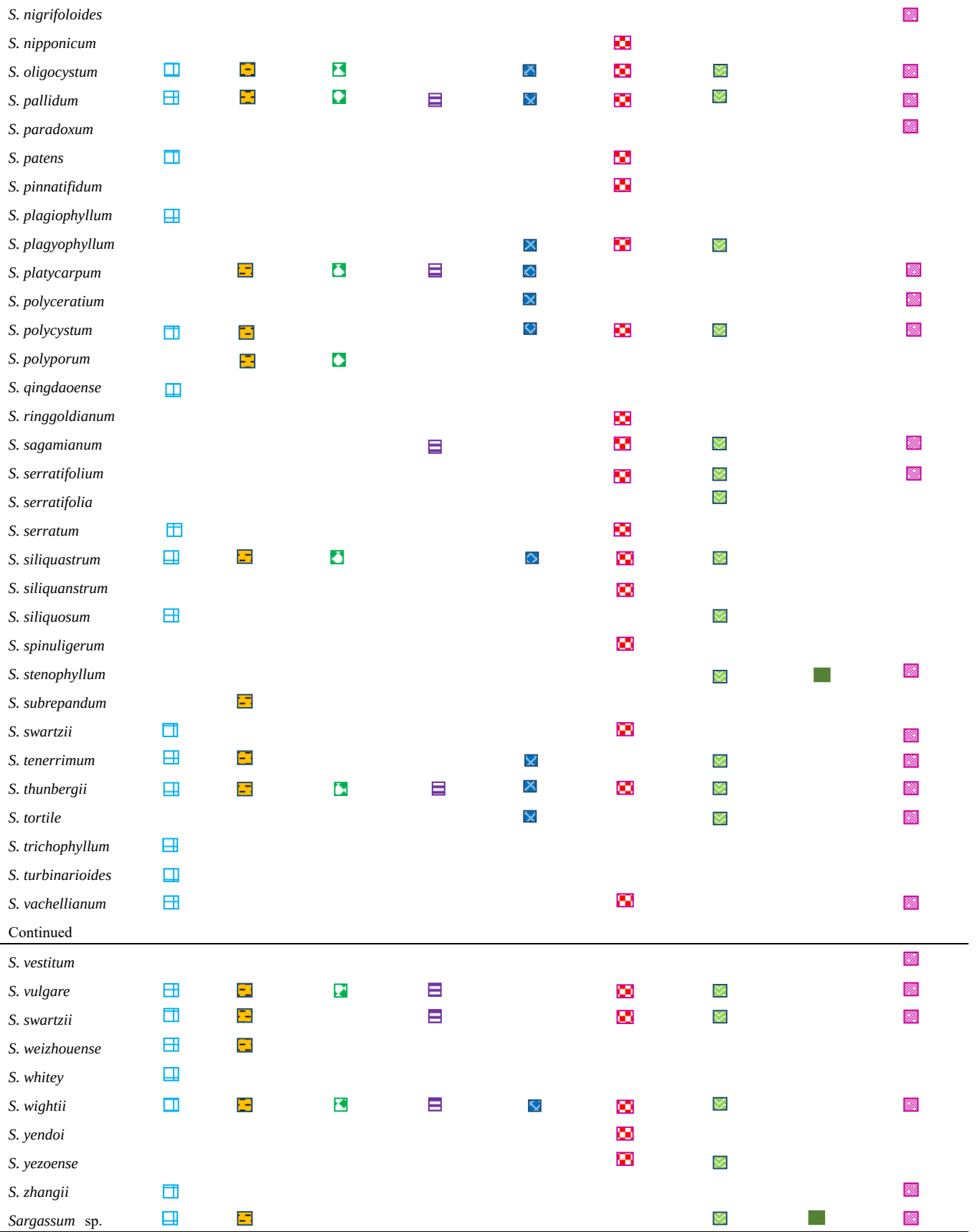

S. integerrimum
S. johnstonii
S. kjellmanianum
S. latifolium
S. linearifolium
S. maclurei
S. macrocarpum
S. mangarevense
S. marginatum
S. micracanthum
S. microcystum
S. miyabei
S. muticum
S. myriocystum
S. natans
S. naozhouense



Note: PS, SF, PF, GL, ST, PP, TE, MA, and OT represent polysaccharide, saturated fatty acid, polyunsaturated fatty acid, glycolipid, sterol, polyphenol, terpene, mycosporine-like amino acids, and other active substance, respectively. The data are from Web of Science, Goole scholar, and CNKI databases published between 2014 and 2025.

2.2 The research status and trend of active substances from Sargassum seaweeds

Having outlined the global research landscape and identified under-explored compounds, we now turn to a detailed examination of the well-established active substances that have been the focus of international research. Foreign studies on the active substances in *Sargassum* seaweeds has been relatively in-depth, chiefly concentrating on the extraction, isolation, identification, and/or activity investigations of substances such as polysaccharides, primarily fucoidan; polyphenols, mainly phlorotannins; and terpene, predominantly meroterpenoids.

2.2.1 Fucoidans in Sargassum and their bio-activities

Among numerous well-established substances, fucoidan—a sulfated polysaccharide—has been extensively investigated for its diverse biological properties. The *in vitro* anti-oxidant capacity, anti-cancer activity, ability to stimulate immune responses, and capacity to modulate the activity of immune cells for reducing inflammation of fucoidan isolated from diverse *Sargassum* seaweeds, including *S. ilicifolium* [43], *S. echinocarpum* [44], *S. thunbergii* [45], *S. ilicifolium* [43], *S. fusiforme* [46], have been validated. These fucoidans have demonstrated a broad spectrum of *in vitro* biological activities, including anti-fungal, anti-oxidant, anti-diabetic, and anti-inflammatory properties. As summarized in Figure 3, the multifaceted bioactivities of *Sargassum*-derived fucoidans exhibit significant mechanistic overlaps, particularly in their anti-inflammatory, antioxidant, anti-diabetic, and immunomodulatory effects.

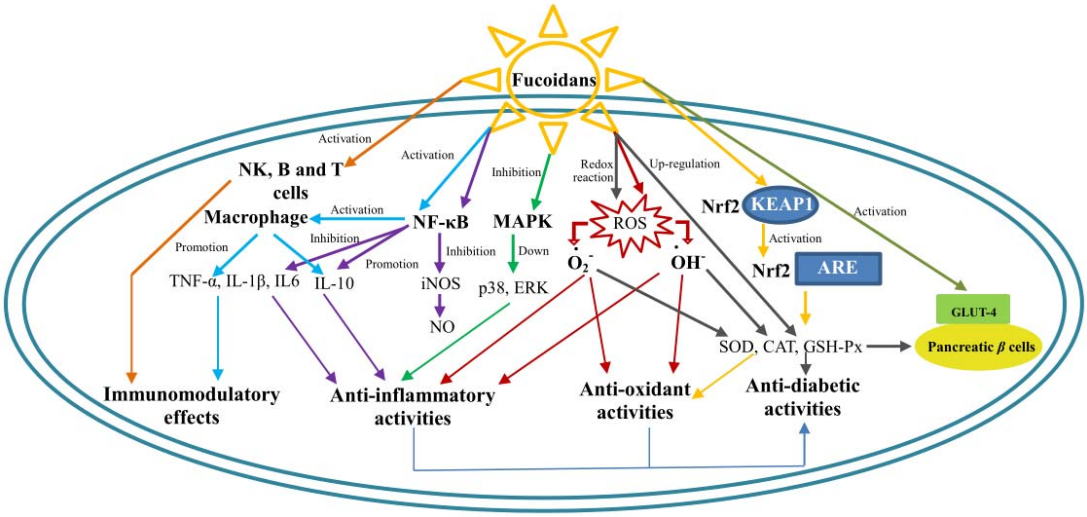


Figure 3 The action sites of activities of fucoidans from *Sargassum* seaweeds

Firstly, the close interconnection between oxidative stress and inflammation underpins the overlapping anti-inflammatory and antioxidant mechanisms. Inflammatory responses are frequently accompanied by increased oxidative stress. Through its potent free radical scavenging ability, *Sargassum* polysaccharide alleviates inflammation by reducing overall oxidative stress levels. For example, fucoidan from *S. fusiforme* enhances the activity of key intracellular antioxidant enzymes such as superoxide dismutase (SOD) and catalase (CAT), thereby strengthening the cellular antioxidant defense system [13, 47]. Low molecular weight fucoidan from *Sargassum confusum* was shown to possess significant anti-inflammatory and antioxidant activities in a HaCaT keratinocyte model. Specifically, in tumor necrosis factor-α/interferon-γ (TNF-α/IFN-γ) stimulated HaCaT cells, fucoidan alleviated oxidative stress by activating the nuclear factor erythroid

2-related factor 2/heme oxygenase-1 (Nrf2/HO-1) signaling pathway, thereby effectively scavenging intracellular reactive oxygen species (ROS). Concurrently, fucoidan inhibited the activation of the mitogen-activated protein kinase (MAPK) and nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) signaling pathways. This inhibition led to the downregulation of key epithelial-derived innate cytokines (Interleukin-25 (IL-25), IL-33, and thymic stromal lymphopoietin (TSLP)), ultimately resulting in reduced production of various inflammatory cytokines (IL-1β, IL-6, TNF-α) and chemokines. Importantly, the cytoprotective effects of SCF were substantially diminished upon inhibition of HO-1 by zinc protoporphyrin (ZnPP), confirming that its action is largely dependent on the Nrf2/HO-1 pathway. In summary, fucoidan confers protection against inflammatory and oxidative damage by coordinately modulating the NF-κB, MAPK, and Nrf2/HO-1 signaling pathways. Notably, this antioxidant mechanism is analogous to that of hesperetin, which ameliorates non-alcoholic fatty liver disease (NAFLD). In both oleic acid-induced HepG2 cells and a high-fat diet-induced rat NAFLD model, hesperetin was shown to activate the upstream phosphatidylinositol 3-kinase/ protein kinase B (PI3K/AKT)-Nrf2 signaling pathway [48]. This activation boosted the expression of a suite of antioxidant enzymes (including SOD, glutathione peroxidase (GPx), and HO-1), effectively mitigating hepatic oxidative stress. Crucially, this antioxidative effect was demonstrated to be the prerequisite for its anti-inflammatory action, as the suppression of NF-κB activation and the subsequent reduction in pro-inflammatory cytokines (TNF-α, IL-6) were abolished when the Nrf2 pathway or its downstream antioxidants (SOD/GPx) were inhibited. These findings collectively underscore a common and pivotal mechanism: the coordinated modulation of the Nrf2-antioxidant and NF-κB-inflammatory axes serves as a fundamental strategy for bioactive compounds to exert cytoprotective effects. This not only reinforces the reliability of targeting oxidative stress as a therapeutic approach but also suggests that *Sargassum* fucoidans could be developed as multi-target agents for managing chronic metabolic diseases where inflammation and oxidative stress are intertwined, such as NAFLD and type II diabetes.

Secondly, the anti-inflammatory effects of fucoidan are closely linked to immunomodulation. Borazjani et al. revealed a clear inverse correlation between the molecular weight and bioactivity of fucoidan from *S. angustifolium*. Specifically, the fraction with the lowest molecular weight exerted the most potent proliferative effect on RAW264.7 cells and induced the highest nitric oxide (NO) production at a concentration of 50 μg/mL [49]. Similarly, purified fucoidans demonstrated significant antioxidant, anti-wrinking, and skin-whitening potential. Their anti-inflammatory mechanism was elucidated in lipopolysaccharide (LPS)-stimulated RAW264.7 macrophages, where both compounds dose-dependently and concertedly inhibited the production of NO, prostaglandin E2 (PGE2), and pro-inflammatory cytokines (TNF-α, IL-1β, IL-6), and downregulated the protein expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2), without compromising cell viability [50]. This inhibition of NF-κB activation mirrors the anti-inflammatory mechanism observed with hesperetin in NAFLD models [48]. The consistent suppression of NF-κB across different *Sargassum* species and compound classes indicates that this is a central anti-inflammatory mechanism worthy of prioritization in future studies.

Thirdly, significant mechanistic overlap also exists between the antioxidant and anti-diabetic activities of fucoidan. Substantial evidence indicates that elevated oxidative stress significantly promotes insulin resistance and pancreatic β-cell dysfunction, a key feature of type 2 diabetes [51]. In exploring this pathology, a study on eudesmin revealed its effect on insulin resistance in 3T3-L1 adipocytes and HepG2 cells. Subsequent transcriptomic analysis identified FER1L6 as the most significantly altered gene in insulin-resistant HepG2 cells. Notably, knockdown of FER1L6 markedly enhanced glucose transporter type 4 (GLUT4) expression and ameliorated insulin resistance, highlighting its therapeutic potential. The antioxidant capacity of fucoidan from *S. fusiforme* mitigates oxidative damage to pancreatic islet cells [52]. Concurrently, its immunoregulatory activity can ameliorate the chronic inflammatory state associated with diabetes by modulating immune function [52]. This dual action is critical, as chronic inflammation and oxidative stress are established core mechanisms in the pathogenesis of diabetes and its complications. The dual targeting of oxidative stress and inflammation positions fucoidan as a promising multi-functional agent for diabetes management. For instance, Jia et al. elucidated the multi-targeted anti-diabetic mechanisms of *Hizikia fusiforme* polysaccharide (HFP) in type II diabetic rats. HFP ameliorated core diabetic phenotypes, including hyperglycemia, insulin resistance, and dyslipidemia, through a concerted action on both host metabolism and gut microbiota. At the molecular level, HFP activated the insulin receptor substrate (IRS)/ phosphatidylinositol 3-kinase (PI3K)/AKT/GLUT signaling pathway to enhance glycogen synthesis in the liver and skeletal muscle, while simultaneously suppressing gluconeogenesis by downregulating early growth response 1 (Egr-1) and phosphoenolpyruvate carboxykinase (PEPCK). Additionally, HFP remodeled the gut microbiota, which was strongly correlated with metabolic improvements. A complementary *in vitro* assay further revealed that HFP inhibits starch hydrolysis, contributing to postprandial blood glucose stabilization. However, most evidence remains preclinical. We strongly advocate for more structured research to validate these effects in more animal models of diabetes that better mimic human pathophysiology, and ultimately in clinical trials, to translate these compelling mechanistic overlaps into tangible therapeutic applications.

Additionally, the role of fucoidan in mitigating oxidative stress-related cellular damage extends beyond diabetes. *Panax notoginseng* saponins (PNS) activated the cAMP/PKA signaling pathway, which in turn suppressed nicotinamide adenine dinucleotide phosphate oxidase 2 (NOX2)-mediated oxidative stress, thereby inhibiting platelet apoptosis [53]. This mechanism was consistently observed in hyperlipidemic mice, where a 12-week PNS supplementation alleviated platelet mitochondrial dysfunction and apoptosis. The critical roles of the cAMP/PKA pathway and subsequent NOX2 suppression were definitively confirmed using specific pharmacological inhibitors, which abolished the protective effects of PNS. Fucoidan may protect various cell types through analogous mechanisms. Taken together, these findings indicate that fucoidan may act as a versatile regulator of redox homeostasis, which warrants deeper investigation into its molecular targets and dose-dependent effects. In our view, future studies should not only focus on validating these protective roles in diverse disease models but also explore the possibility of integrating fucoidan into multi-target therapeutic strategies for metabolic syndrome and related complications.

2.2.2 Phlorotannins in Sargassum and their bio-activities

Phlorotannins, as the principal polyphenols in marine macroalgae, have also attracted significant research interest. Phlorotannins extracted from *S. ilicifolium* [54], *S. linifoliumas* [55], *S. carpophyllum* [56], *S. macrocarpum* [57] and *S. vulgare* [58], showed *in vitro* anti-fungal, anti-oxidant, anti-diabetic, anti-inflammatory activities, as well as other biological activities. The mechanism of anti-inflammatory, anti-oxidant, anti-bacterial, and anti-tumor effects of phlorotannins from *Sargassum* seaweeds were mentioned in Figure 4.

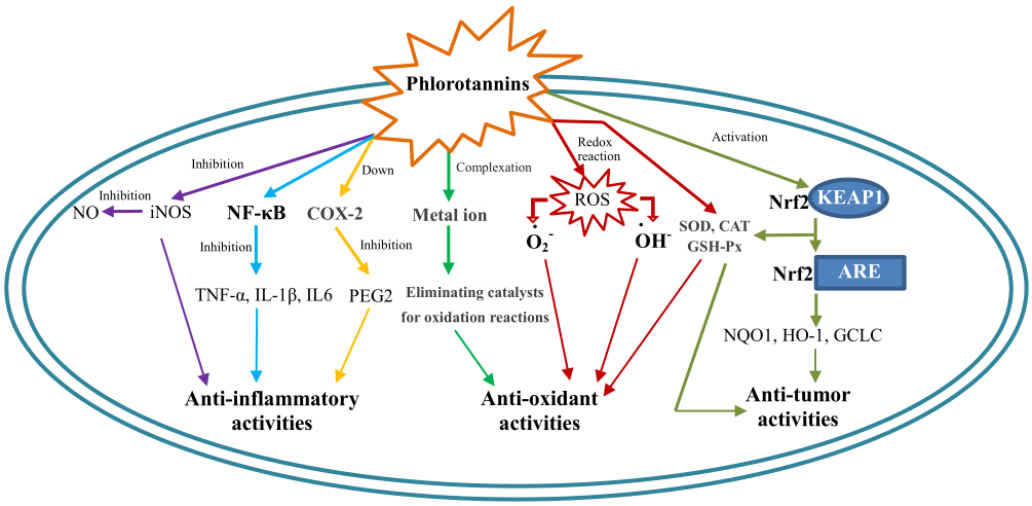


Figure 4 The action sites of activities of phlorotannins from *Sargassum* seaweeds

Phlorotannins derived from exert an anti-inflammatory effect by inhibiting the activity of NF-κB and reducing the production of inflammatory factors such as TNF-α, IL-1β, and IL-6. Phlorotannins from *Sargassum muticum* exhibited anti-proliferative effects against lung (A549) and colon (HCT-116) carcinoma cells. In addition, they suppressed ROS production in human neutrophils and inhibited PGE2 production via COX-2 in human whole blood [59]. In addition, phlorotannins can significantly inhibit the production of NO in RAW 264.7 macrophages [58, 60], showing excellent anti-inflammatory potential. PGE2 contributes to inflammation by inducing vasodilation, pain, and fever, whereas NO enhances vascular permeability and exacerbates the inflammatory response. These two mediators act synergistically to initiate and sustain inflammatory processes. This synergistic mode of action enhances their therapeutic appeal for treating complex inflammatory disorders. However, most current evidence is derived from *in vitro* models. Thus, we emphasize the necessity for future research to validate these effects in relevant animal models of inflammation and to further elucidate the structure-activity relationships among phlorotannins from different *Sargassum* species. Such studies would be critical for optimizing their application as natural anti-inflammatory agents in functional foods or pharmaceuticals.

In addition, phlorotannins of *Sargassum* contain multiple phenolic hydroxyl groups, which can directly react with free radicals. Phlorotannins of *S. linifoliumas* and *S. fusiforme* can also activate the antioxidant enzyme system, such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px), protecting cells from oxidative stress [24, 55]. When cells are stimulated by polyphenols of *S. muticum*, Nrf2

dissociates from Keap1, transfers from the cytoplasm into the nucleus, and binds to ARE. Subsequently, the activated Nrf2-ARE complex initiates the transcriptional upregulation of key antioxidant [55] and cytoprotective genes, including HO-1, NQO1, and GCLC in the downstream signaling pathway [61]. This coordinated enhancement of cellular antioxidant defenses not only mitigates oxidative damage but also contributes to the suppression of tumor cell proliferation and survival, demonstrating the multi-faceted anti-cancer potential of *S. muticum* polyphenols. The activation of the Keap1-Nrf2-ARE pathway underscores the potent antioxidant and anti-cancer capabilities of *Sargassum* phlorotannins. However, their specific efficacy and bioavailability require further investigation to fully harness their therapeutic potential.

Furthermore, an investigation using a diabetic rat model revealed that algal polyphenols ameliorate diabetic conditions through multi-faceted mechanisms. They enhanced insulin secretion from pancreatic β-cells, potentially via inhibition of α-glucosidase and α-amylase, consequently improving serum insulin levels [55]. Moreover, treatment reduced urea, cholesterol, triglycerides, and hepatic malondialdehyde (MDA), indicating renal and hepatic protection. The activation of AMP-activated protein kinase (AMPK), which enhances insulin sensitivity, was identified as a key underlying mechanism for these metabolic improvements. Phlorotannin significantly inhibited adipogenesis by concomitantly downregulating key adipogenic transcription factors, including peroxisome proliferator-activated receptor γ (PPARγ), CCAAT/enhancer-binding protein α (C/EBPα), sterol regulatory element-binding protein 1 (SREBP1), and fatty acid-binding protein 4 (FABP4), in a dose-dependent manner [62]. This effect was mechanistically linked to the activation of AMPK, confirming that dieckol suppresses adipogenesis primarily through the AMPK signaling pathway.

2.2.3 Meroterpenoids in Sargassum and their bio-activities

Another important class of bioactive compounds, meroterpenoids, has also been extensively investigated for its therapeutic potential. Derived from various *Sargassum* species, including *S. macrocarpum* [63, 64], *S. yezoense* [65], *S. serratifolium* [66], and *S. siliquastrum* [67], they exhibit a broad spectrum of biological activities. These include inhibitory effects against amyloid β aggregation, anti-inflammatory properties, antioxidant capacity, BACE1 inhibition, anti-inflammatory effect on RAW 264.7 macrophages, inhibitory effect on M1 polarization of mouse bone marrow-derived macrophages, and cytotoxicity against human cancer cells. Additionally, species such as *S. asperifolium* [68], *S. oligocystum* [69] and *S. wightii* [70] are recognized as rich sources of bioactive steroids. As illustrated in Figure 5, the phenolic hydroxyl groups in *Sargassum* meroterpenoids contribute to their free radical-scavenging ability by directly reacting with reactive oxygen species [64]. Furthermore, these compounds enhance cellular antioxidant defense systems by modulating the activity of key enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px) [71].

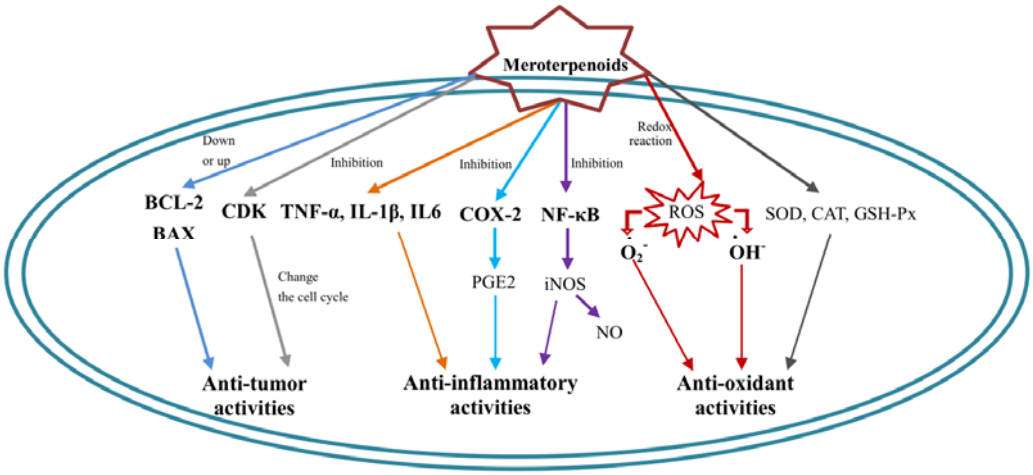


Figure 5 The action sites of activities of meroterpenoids from *Sargassum* seaweeds

The anti-inflammatory activity of meroterpenoids is mediated through multiple pathways. In both LPS-stimulated macrophages and a mouse model, they inhibit the synthesis and release of pro-inflammatory mediators, including prostaglandin E2 (PGE2), interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) [72, 73]. This was achieved through preventing IκB-α degradation, thereby inhibiting the nuclear translocation of NF-κB and the subsequent production of key pro-inflammatory mediators, including iNOS, COX-2, NO, PGE2, and cytokines [74]. Moreover, meroterpenoids can disrupt inflammatory signaling pathways, notably the nuclear factor-κB (NF-κB) pathway, thereby blocking the transmission of inflammatory signals and alleviating the overall inflammatory response. In a V79-4 Chinese hamster lung fibroblast model, Indole-6-carboxaldehyde (I6CA) derived from *S. thunbergii* was confirmed to activate the Nrf2 signaling pathway, thereby upregulating HO-1 to scavenge ROS and inhibit H_2O_2-induced cytotoxicity. I6CA also conferred anti-apoptotic effects by enhancing the B-cell lymphoma 2/ Bcl-2-associated X protein (Bcl-2/Bax) ratio, preserving mitochondrial membrane integrity, and preventing cytochrome c release [75]. The multi-target anti-inflammatory action of *Sargassum* meroterpenoids, spanning from enzyme inhibition to transcriptional regulation, underscores their therapeutic potential for treating complex inflammatory diseases. Future research should focus on elucidating structure-activity relationships to optimize their efficacy and exploring their synergistic effects with conventional anti-inflammatory agents.

In terms of anticancer activity, *Sargassum* meroterpenoids promote apoptosis in HeLa cell lines through upregulation of pro-apoptotic proteins like Bax and caspase-3, and downregulation of anti-apoptotic proteins such as Bcl-2 [76]. They also induce cell cycle arrest by inhibiting cyclin-dependent kinases (CDKs) or altering the expression levels of cyclins, thereby preventing DNA replication and cell division. It is important to note that these mechanisms of action are not independent of each other. Instead, they may work in synergy and influence each other, jointly exerting the biological activities of *Sargassum* meroterpenoids. However, the specific modes of action may vary depending on factors such as differences in the chemical structures of meroterpenoids, cell types and the action environment. The multi-mechanistic anticancer actions of *Sargassum* meroterpenoids, particularly their dual induction of apoptosis and cell cycle arrest, highlight their potential as promising chemotherapeutic or chemo-preventive agents.

2.2.4 Other active compounds in Sargassum and their bio-activities

In addition to the active substances mentioned above, various other active substances have been isolated from *Sargassum*, for example, fucoxanthin [77], fatty acids [78], and other substances [79]. *Sargassum* is regarded as the source of new and value-added bioproducts [80], demonstrating broad application prospects in fields like medicine, health products and cosmetics. Despite our knowledge, *S. confusum*, *S. fluitans*, *S. natans*, *S. horneri*, *S. muticum* and *S. serratifolium* have been extensively studied abroad. In the future, more research efforts will be centered on other varieties of *Sargassum* seaweeds. Some countries have added *Sargassum* to their new food lists. For example, Korea has included six types of *Sargassum* seaweeds-*S. confusum*, *S. horneri*, *S. sagamianum*, *S. serratifolium*, *S. siliquastrum* and *S. thunbergii*-in its new food list. In the fields of new drug development and food applications, screening active substances from *Sargassum* seaweeds, studying their pharmacological properties, and precisely analyzing their active mechanisms will remain major research topics in the future.

2.3 Current research status of active substances from Sargassum seaweeds in China

Building upon the global context, it is crucial to examine the research efforts in China, given its status as a major repository of Sargassum biodiversity. China is one of the world's major producers of *Sargassum* seaweeds, with 131 *Sargassum* species distributed in the Yellow Sea, East China Sea, and South China Sea [80]. Among these, approximately 120 *Sargassum* species inhabit the South China Sea, including 64 species endemic to China [2]. Common *Sargassum* species in China include *S. fusiforme* (*Hizikia fusiformis*), *S. graminifolium*, and *S. feldmannii*, which are characterized by high biodiversity and substantial biomass. Particularly in sea areas such as the Xisha Islands and Nansha Islands, most *Sargassum* resources grow naturally along coastlines, providing a convenient resource foundation for relevant research and applications [81].

Currently, research on *Sargassum* in China is developing vigorously. Researchers have conducted comprehensive investigations into the classification [82], distribution [83], growth characteristics [84], and habitat patterns [85] of *Sargassum*, carried out in-depth analyses of the physical and chemical properties of substances such as polysaccharides and terpenoids, and explored its potential activities in antioxidant [86], antibacterial [87], and anti-tumor [88] effects [89]. However, compared with Japan and South Korea, Chinese research still lags in terms of systematicness and depth, with relatively limited application directions. At present, only a small portion of *Sargassum* is used as feed [90] or pharmaceutical raw materials [91] after simple processing, resulting in low resource added value.

Traditional medicinal *Sargassum* species such as *S. fusiforme*, *S. pallidum*, *S. horneri*, and *S. thunbergii* have become aquaculture varieties in recent years due to growing market demand [92-94]. According to the *2023 China Fishery Statistical Yearbook*, the annual output of *S. fusiforme* in China reached 33,372 tons. However, the frequent large-scale "golden tides" (massive *Sargassum* blooms) in the southern Yellow Sea and northern East China Sea [95, 96] have also posed the challenge of converting "ecological hazards into

resources". How to achieve a win-win situation for ecological protection and economic development remains a key issue to be addressed urgently.

A search of literature on *Sargassum* published in the CNKI database from 2014 to 2024 shows that domestic research mainly focuses on the extraction, isolation, and activity analysis of polysaccharides [97] and polyphenols [98], as well as the cultivation, nutritional composition, and related fields of *Sargassum*. In contrast, there is very little research on other active substances such as sterols [99], polypeptides [100], and mycosporine-like amino acids [27]. Although researchers have paid attention to components with application prospects in food and medicine, such as polysaccharides and fucoxanthin [106] [88, 101-105], the overall research still shows a bias of "prioritizing common components while neglecting less-studied active substances". Compared with overseas research, domestic studies are more concentrated on five *Sargassum* species, including *S. confusum* and *S. fusiforme* (see Figure 6), and activity research mostly focuses on anti-tumor, antioxidant, and antibacterial properties, with insufficient exploration of other potential activities. It is worth noting, however, that there are still a large number of underutilized active substances in *Sargassum*, which hold great potential in the discovery of new bioactive substances and are expected to be developed into high-value products such as specific-effect drugs and natural preservatives in the future.

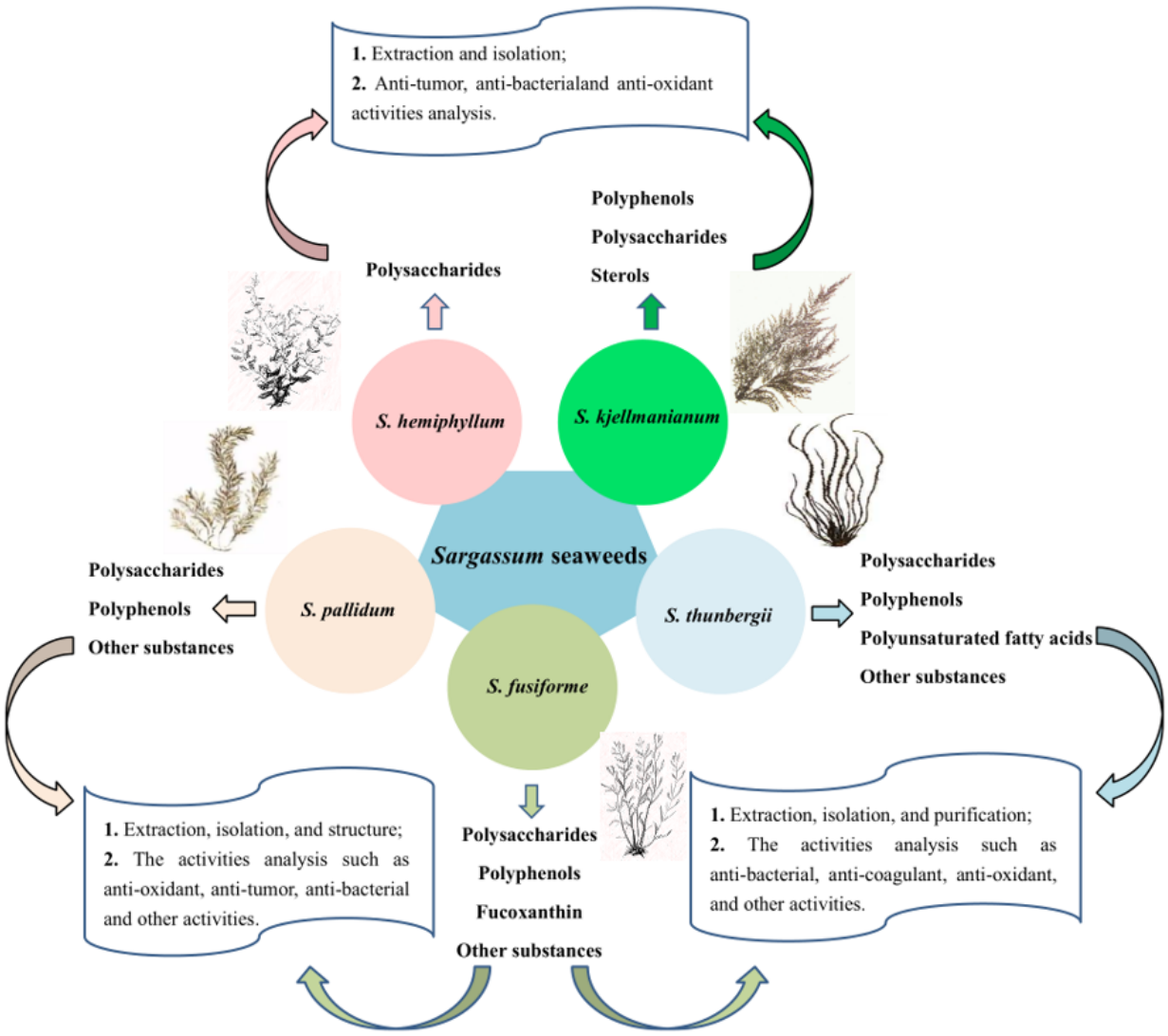


Figure 6 The active substances from the five common *Sargassum* seaweeds in China

Research on *Sargassum* in China already has a solid foundation in terms of resources and basic research, but there is still significant room for improvement in systematicness, coverage of active substances, and resource utilization efficiency. If future efforts can focus on the aforementioned directions, it will not only fully tap the active potential of *Sargassum* and promote its high-value application in fields such as medicine and food but also achieve the coordinated development of ecology and economy through the resource conversion of"golden tides", making *Sargassum* an important growth driver in the development of China's marine biological resources.

2.4 Isolated and identified substances from Sargassum seaweeds

Moving beyond the general bioactivity profiles, a deeper understanding of *Sargassum*'s potential requires a detailed examination of the specific compounds that have been isolated and structurally characterized. Since the late 80s, the development of marine biological drugs and other marine biotechnologies has been a hot topic and focal point globally. The isolation and purification of active substances from *Sargassum* seaweeds hold crucial enlightenment and reference value for elucidating the material basis of *Sargassum* seaweeds efficacy and developing new compounds. To date, a variety of substances have been isolated and purified from *Sargassum* seaweeds. For instance, over 20 substances, including homogeneous polysaccharides [81], α-linolenic acid [82], saringosterol [83], fucosterol [82], have been isolated from *S. fusiforme*. However, there has been a lack of a comprehensive summary of the active substances isolated and purified from *Sargassum* seaweeds so far. Therefore, in this review, the substances isolated from seaweeds were summarized by searching the papers published in the Web of Science, Google Scholar, and CNKI databases from 1980 to 2024. Currently, the research on the isolation and identification of bioactive substances from *Sargassum* has formed a pattern characterized by "initial scale formation and prominent focus". Active substances from over 58 species of *Sargassum* seaweeds have been isolated and purified, and more than 480 kinds of active substances have been identified (Figure 7, active substances of the same species obtained from different species of *Sargassum* seaweeds were not calculated cumulatively). Among these, terpenoids were the most abundant, accounting for over 30%. Polyphenols ranked second, with a proportion close to 17%. Other substances such as alkaloids and heterocyclic substances accounted for approximately 20%. There have been few studies on the isolation and purification of fatty acids and glycolipids, and no reports on the isolation and purification of MAAs from *Sargassum* seaweeds have been found yet. The dominance of terpenoids and polyphenols suggests these are prioritized in current studies, yet the untapped potential of other classes warrants further exploration. Future work should aim to expand the isolation efforts to under-investigated species and compound types, which may reveal novel bioactive molecules with unique applications.

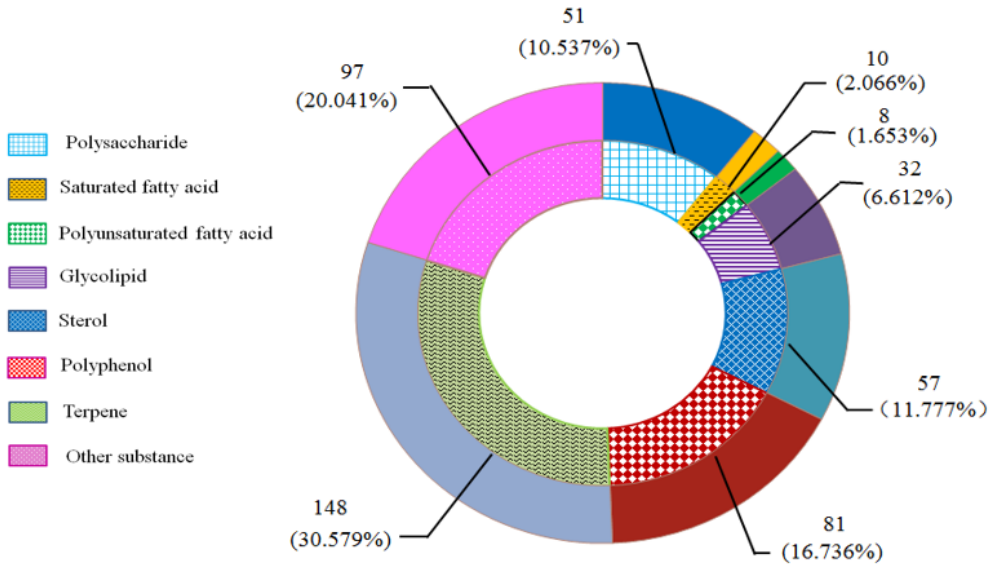


Figure 7 The types of active substances isolated and identified from *Sargassum* seaweeds. The data are from Web of Science, Goole scholar, and CNKI databases published between 1980 and 2024. (The number and the percentage in brackets next to the pie chart represent respectively the number of *Sargassum* seaweeds containing the corresponding active substances and their percentage of the total number of *Sargassum* seaweeds.)

To gain a better understanding of the active substances isolated from each species of *Sargassum* seaweeds, we categorized these substances according to the species of *Sargassum* seaweeds. As shown in Figure 8 and Table 2, 47 active substances have been isolated from *S. horneri*. Additionally, over 35 active these substances according to the species of *Sargassum* seaweeds. Substances have been isolated from *S. macracarpum*, *S. siliquastrum* and *S. spinuligerum*, while 20 or more active substances have been obtained from *S. carpophyllum*, *S. fusiforme*, *S. muticum*, *S. naozhouense*, *S. polycystum*, *S. thunbergii* and *S. wightii*. In comparison to other *Sargassum* seaweeds, these eleven *Sargassum* species have been the subject of in-depth research, and more than 300 active substances have been derived from them, including a series of novel polysaccharides [84], glycolipids [35], sterol [85], polyphenol [58], terpenes [21, 57], and other substances [86, 87]. However, among the aforementioned *Sargassum* seaweeds, the isolation of active substances from a larger number of *Sargassum* seaweeds species has not been extensively studied. This implies that there are potentially many more active substances that could be obtained from *Sargassum* seaweeds. The fact that over 300 compounds have been derived from just eleven species suggests that the genus as a whole represents a much larger and virtually untapped reservoir of chemical diversity. Currently, the "hot-cold differentiation" research model is essentially a form of "extensive utilization" of *Sargassum* species resources, which is inconsistent with the goal of "efficient development of marine resources". Further research must deliberately expand its scope to include neglected and endemic *Sargassum* species, which could not only yield new structural classes of bioactive molecules but also provide insights into the ecological and evolutionary aspects of chemical diversity within this genus.

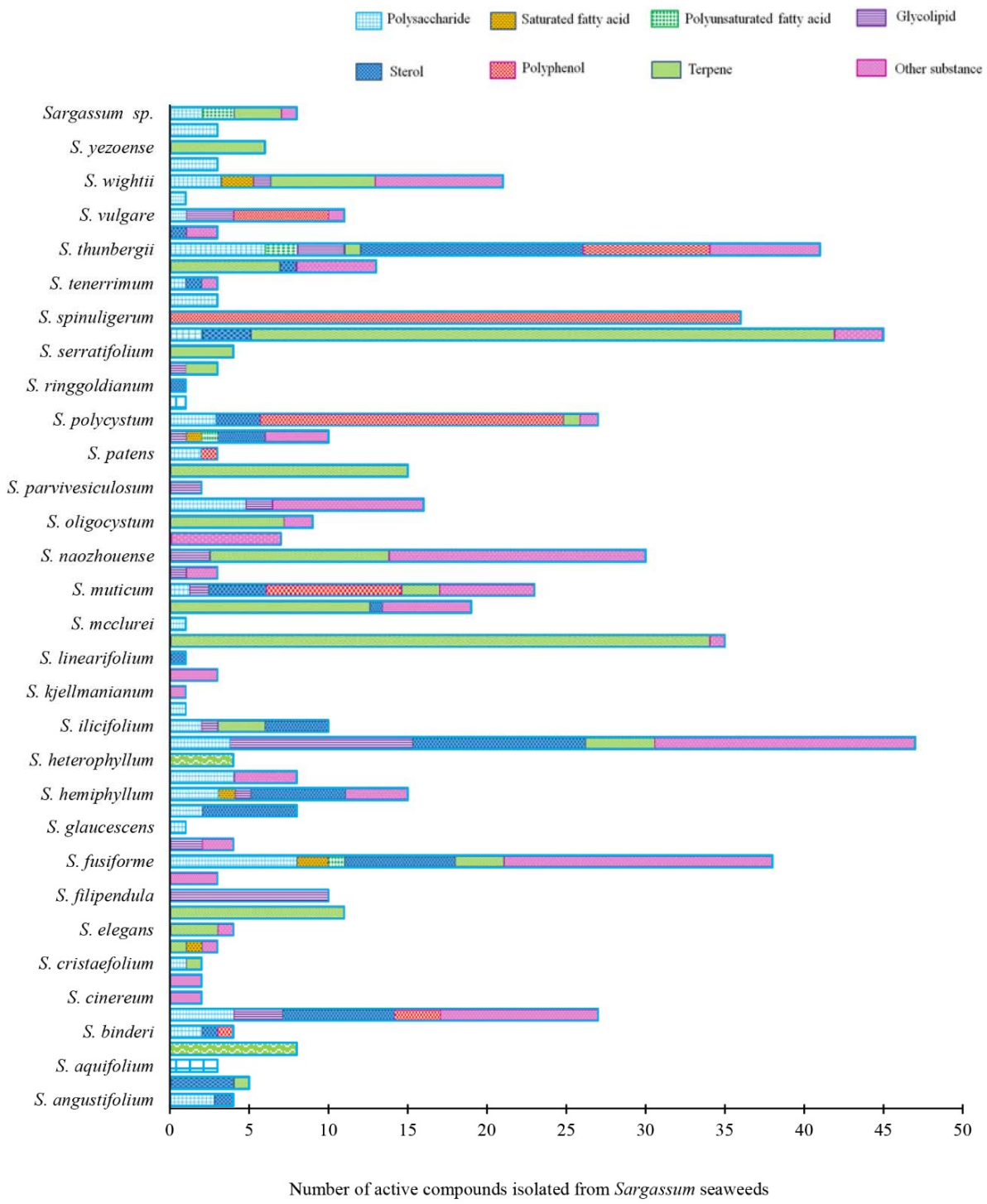


Figure 8 The distribution of active substances isolated and identified from *Sargassum* seaweeds. The data are from Web of Science, Goole scholar, and CNKI databases published between 1980 and 2025.

Table 2 Active substance(s) isolated from each species of *Sargassum* seaweeds

No.	*Sargassum* species	Substance(s)	Ref.
1	*S. angustifolium*	Two polysaccharides	[88]
2	*S. asperifolium*	Four phytosterols and two terpene	[68]
3	*S. aquifolium*	Three polysaccharides	[89]
4	*S. autumnale*	Eight terpenes	[90]
5	*S. binderi*	One phytosterol and one polysaccharide	[91, 92]
6	*S. carpophyllum*	Four polysaccharides, three glycolipids, seven phytosterols, three polyphenols and ten other compounds	[56, 93-96]
7	*S. fallax*	Three terpenes	[97]

8	*S. filipendula*	Ten glycolipids	[30]
9	*S. fluitans*	Three other compounds	[92]
10	*S. fusiforme*	Seven polysaccharides, two saturated fatty acids, one polyunsaturated fatty acid, four phytosterols, three terpenes and twelve other compounds	[81, 83-85, 98-102]
11	*S. fulvellum*	Two glycolipids and two other compounds	[103-105]
12	*S. granuliferum*	Two polysaccharides and six phytosterols	[106]
13	*S. hemiphyllum*	One saturated fatty acid, one glycolipids, six phytosterols and four other compounds	[107-111]
14	*S. henslowianum*	One polysaccharide and four other compounds	[112-114]
15	*S. heterophyllum*	Four terpenes	[115]
16	*S. horneri*	Three polysaccharides, eleven glycolipids, ten phytosterols, four terpenes and fourteen other compounds	[83, 116-125]
17	*S. ilicifolium*	One terpene and one polysaccharide	[126, 127]
18	*S. kjellmanianum*	One other compound	[128]
19	*S. lacerifolium*	Three other compounds	[129]
20	*S. linearifolium*	One phytosterol	[130]
21	*S. macracarpum*	Thirty four terpenes	[64, 103, 131, 132]
22	*S. mcclurei*	One polysaccharide	[133]
23	*S. micracanthum*	Eleven terpenes and six other compounds	[134-140]
24	*S. muticum*	One polysaccharide, four polyunsaturated fatty acids, one glycolipid, three phytosterols, four polyphenols, one terpene, one flavonoid and two other compounds	[59, 126, 141-145]
25	*S. myriocystum*	One glycolipid and two other compounds	[31, 146]
26	*S. naozhouense*	Six glycolipids, eight terpenes, sixteen other compounds	[21, 32, 147, 148]
27	*S. nigrifoloides*	Six polyphenols and one polyunsaturated fatty acid	[149]
28	*S. oligocystum*	Three polysaccharides	[150]
29	*S. pallidum*	Two polysaccharides, one glycolipid and ten other compounds	[151-153]
30	*S. parvivesiculosum*	Two glycolipids	[154]
31	*S. paradoxum*	Fifteen terpenes	[155]
32	*S. platycarpum*	One glycolipid, one saturated fatty acid, one polyunsaturated fatty acid, three phytosterols and four other compounds	[34, 156, 157]
33	*S. polycystum*	One polysaccharide, three phytosterols, nineteen polyphenols, one terpene and one other compound	[158-162]
34	*S. serratifolium*	Four terpenes	[163-165]
35	*S. siliquastrum*	Therty two terpenes and one other compound	[166-171]
36	*S. siliquastrum*	Thirty six polyphenols	[172-174]
37	*S. tenerrimum*	One polysaccharide	[175]
38	*S. tortile*	Six terpenes, one phytosterol and one other compound	[176]
39	*S. thunbergii*	Five polysaccharides, two saturated fatty acids, two glycolipids, nine phytosterols, eight polyphenols and four other compounds	[90, 177-183]
40	*S. vulgare*	Three glycolipids, six phytosterols and one other compound	[35, 58]
41	*S. whitey*	One polysaccharide	[184]
42	*S. wightii*	Two polysaccharides, two saturated fatty acids, one glycolipids, five terpenes, two flavonoids, and eight other compounds	[86, 87, 185-190]
43	*S. weizhouense*	One polysaccharide	[191, 192]
44	*S. yezoense*	Five terpenes	[193, 194]
45	*S. zhangii*	Three polysaccharides	[195]
46	*S. vachellianum*	One other compound	[196]

Note: The data are from Web of Science, Goole scholar, and CNKI databases published between 1980 and 2024.

Furthermore, most of the substances currently isolated and identified remain at the "bioactivity detection" stage [35, 57, 110, 112, 113]. In the future, efforts should be made to carry out targeted development in line with the needs of the pharmaceutical, food, and cosmetics industries, enabling bioactive substances from *Sargassum* to move from the "laboratory" to "industrialization" and truly realize their economic and social values.

2.5 Database of bioactive substances from Sargassum seaweeds

To transform the accumulated knowledge on *Sargassum* phytochemistry into an accessible and searchable format, we have constructed the database of bioactive substances from *Sargassum*. This tool allows for the rapid retrieval of compounds by species and bioactivity. The aforementioned reports indicate that nearly a hundred substances have been detected in *S. fusiforme* [24, 197]. A series of substances, including polysaccharides, phlorotannins, terpenes, sterols, fatty acids and other substances were isolated and identified from *S. fusiforme*, with the structural formulas of some of them presented in Figure 9. For instance, a newly discovered polysaccharide [84], multiple phlorotannins [152], dehydrololiolide [150], fucosterol [82], α-linolenic acid [82] and dibutyl phthalate [102] have been isolated and characterized. To facilitate rapid access to information regarding the bioactive substances isolated from various types of *Sargassum* seaweeds, the authors of this paper have developed the Database of Bioactive Substances from *Sargassum* seaweeds (http:// http://webvpn.jou.edu.cn:58888/, to gain entry to this database, users must obtain the specific account details provided by the authors.). To the best of our knowledge, this represents the first database, both domestically and internationally, that enables searching for bioactive substances isolated from specific *Sargassum* seaweed species along with their corresponding activities. The data within it are drawn from over 220 literature references. The development of this database fills a significant gap in the organization and accessibility of phytochemical data related to *Sargassum*, providing a valuable tool for accelerating future research and applications.

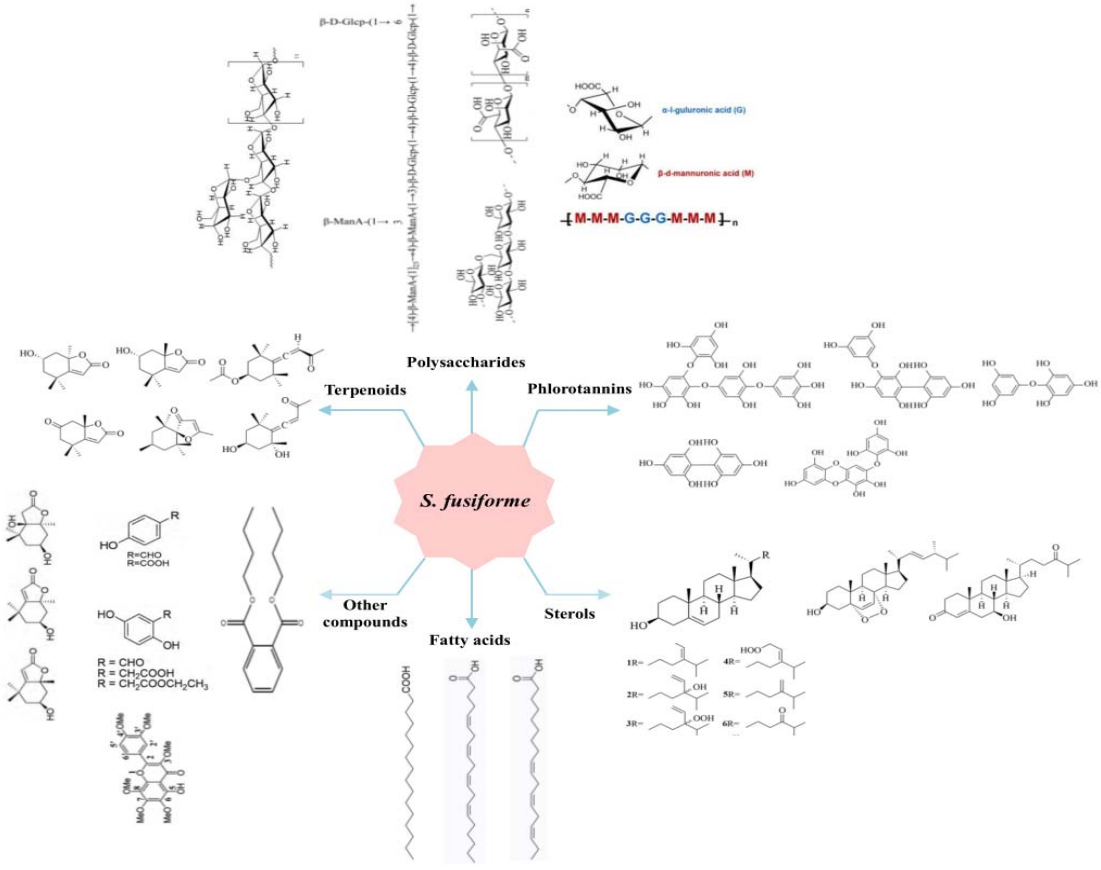
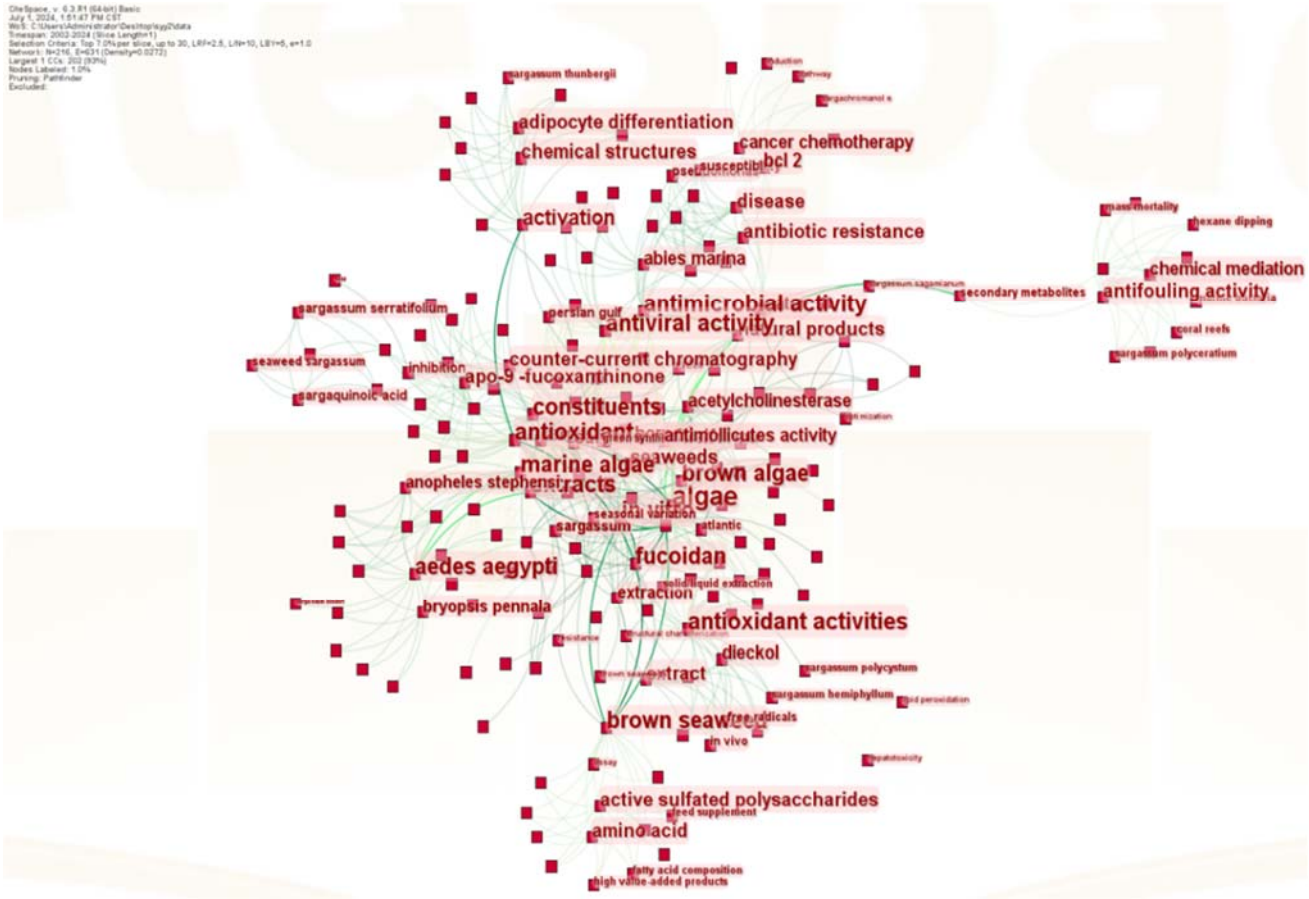
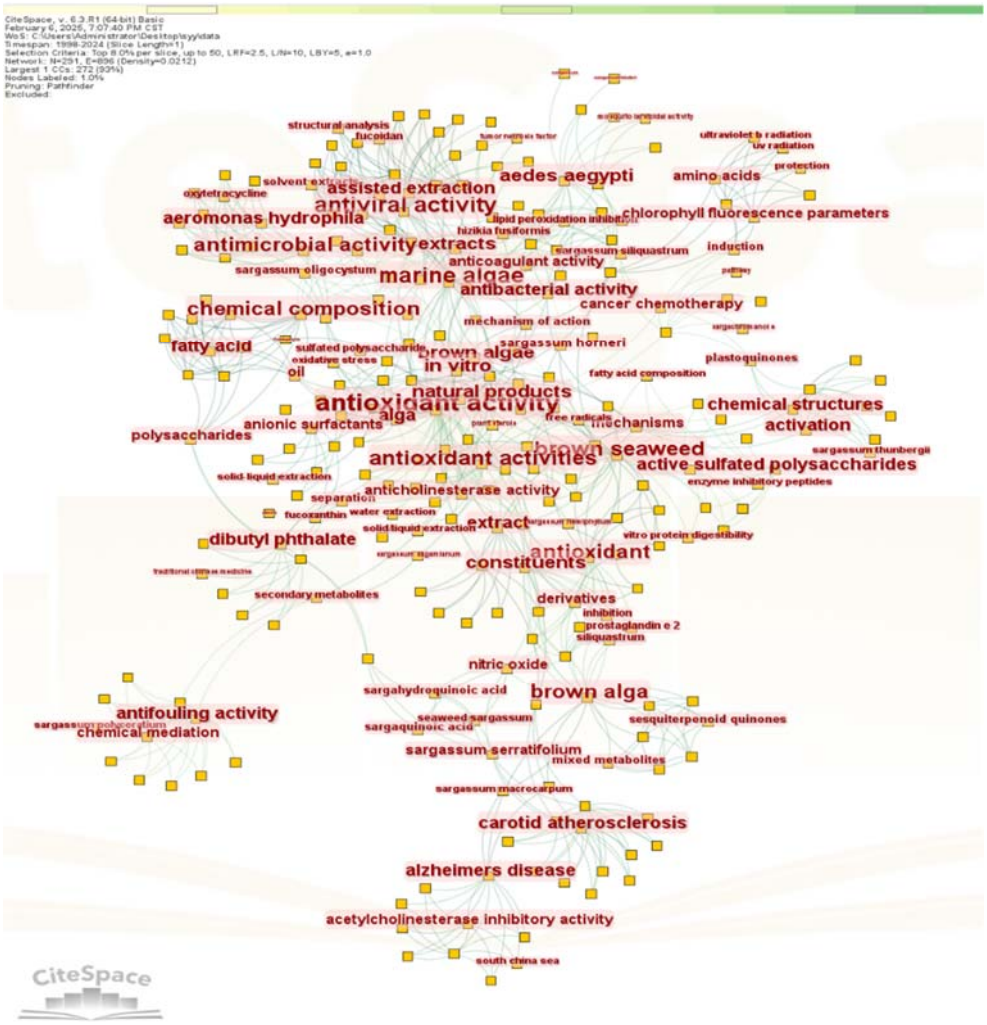


Figure 9 The structure of several active substaneces in *S. fusiforme*

Furthermore, by employing Citespace software, we conducted an analysis of relevant studies concerning *Sargassum* seaweeds spanning from 2020 to the present. At present, the research on *Sargassum* seaweeds mainly focuses on various physiological activities such as antioxidant properties, among which the researches on fucoidan are particularly prominent. Meanwhile, the researches on the composition analysis, extraction process and extracts of *Sargassum* seaweeds are also relatively concentrated. However, in the field of separation and purification of active substances, a concentrated research direction has not yet been formed (Figure 10A). A further analysis of the current research status of active substances from *Sargassum* seaweeds reveals that the current research mainly revolves around various physiological activities such as antioxidant properties. The structure, activity and action mechanism of polysaccharides, especially fucoidan, are the key areas of concern. In terms of extraction process, chemical composition and structure analysis, relatively clear research directions have also been formed. The isolation and purification of non-carbohydrate bioactive substances in *Sargassum* seaweeds, such as fatty acids, terpenoids (such as sargaquinoic acid, sargahydroquinoic acid, and so on), sterols and other bioactive substances, have shown a trend of becoming a research hotspot (Figure 10B).



A. Cluster analysis diagram of *Sargassum* seaweeds



B. Cluster analysis diagram of active substances from *Sargassum* seaweeds

Figure 10 Cluster viewes of *Sargassum* seaweeds (A) and their active substances (B) studies. Data extracted from related studies collected in Web of Science. (A. Date have been collected between 2020 and 2025; B. Date have been collected between 1994 and 2025)

Beyond the established applications in pharmaceuticals, food, and cosmetics, the active substances from *Sargassum* seaweeds also hold considerable promise in emerging fields. In biotechnology, sulfated polysaccharides and polyphenols can serve as functional additives for microbial fermentation, enzyme stabilization, and metabolic engineering, thereby expanding their utility as bioactive modulators. From an environmental perspective, fucoidans and other complex polysaccharides exhibit strong metal-chelating and adsorption capacities, suggesting potential use in bioremediation of heavy metals and organic pollutants, as well as in carbon sequestration strategies to mitigate climate change. Furthermore, structurally diverse compounds such as terpenoids and polyphenols may be developed into sustainable biomaterials, including biodegradable films, coatings, and eco-friendly packaging. These possibilities underscore the broader interdisciplinary relevance of *Sargassum*-derived compounds and highlight the value of the constructed database as a resource to guide future innovation across biotechnology and environmental sciences.

Notably, the industrial translation of non-carbohydrate bioactive substances like terpenoids and alkaloids faces significant challenges that warrant in-depth discussion. Their typical low abundance

within the complex algal matrix and structural similarity to numerous analogues pose substantial difficulties for efficient isolation and purification at scale. These hurdles often result in low yields and high costs, currently limiting their commercial viability. However, their exceptional bioactivities, such as the potent anti-cancer properties of specific meroterpenoids and the neuroprotective effects of alkaloids, present immense value for high-end pharmaceuticals and premium cosmetics. To bridge this gap, future efforts must prioritize the development of advanced, cost-effective separation techniques such as high-speed counter-current chromatography and sustainable extraction protocols, which are crucial for unlocking the full industrial potential of these promising compounds.

In the future, it is crucial to move beyond single-compound investigations and consider the potential synergistic effects among different classes of active substances, such as polysaccharides, polyphenols, and terpenoids. Such interactions may amplify biological activities, offering enhanced antioxidant, anti-inflammatory, or immunomodulatory effects compared to individual compounds. Moreover, exploring the combined applications of these bioactive substances—for instance, in multifunctional pharmaceuticals, functional foods, or integrated cosmetic formulations—could open new avenues for high-value utilization of *Sargassum* resources. In addition, the integration of machine learning algorithms with traditional analytical approaches holds great promise for predicting structure–activity relationships of *Sargassum*-derived bioactive substances. By leveraging computational models to uncover hidden correlations, researchers can accelerate the identification of compounds with potent bioactivities and guide the rational design of innovative applications. Together, these perspectives not only highlight promising interdisciplinary research opportunities but also provide guidance for future studies aiming to translate laboratory findings into practical applications.

2.6 Non-isolated compounds in Sargassum seaweeds

While the preceding section and the established database catalog compounds that have been isolated and characterized, a vast chemical landscape within *Sargassum* remains unexplored due to isolation challenges. This section focuses on these non-isolated compounds, which have been merely identified through analytical techniques. Currently, numerous bioactive substances have merely been identified in *Sargassum* seaweeds, but have not been successfully isolated. For example, within *S. fusiformes*, several active substances 17-pentatriacontene, heptacosane and other substances were merely detected and had yet to be isolated [197, 198]. Similarly, through high-resolution mass spectrometry (HRMS), 89 substances were identified in *S. horneri* [199], while 139 substances were detected in *S. fluitans* using high-resolution ultra-performance liquid chromatography tandem mass spectrometry (UPLC/MS-MS) analysis (Rey et al. 2024). In *S. cristaefolium*, 33 principal substances were discovered [200], and multiple substances were found in *S. binderi* [201], *S. duplicatum* [202], *S. fluitans* [203], *S. horneri* [199], *S. polycystum* [204], *S. tenerrimum* [79], and other *Sargassum* seaweeds [205]; however, none of them had been isolated and obtained (Table 3). The active substances serve as the

fundamental materials underpinning the diverse functions of *Sargassum* seaweeds. Isolating active substances from *Sargassum* seaweeds represents a crucial avenue for procuring novel functional components. Conducting in-depth research on these as-yet-unisolated bioactive substances not only contributes to uncovering the biosynthetic mechanisms of *Sargassum* seaweeds but also offers robust support for the development of new drugs, functional food additives, and high-efficiency natural cosmetic raw materials.

Table 3 Substances of *Sargassum* seaweeds that have been identified or preliminarily identified in the past 5 years but have not been isolated

Sargassum seaweeds	Substance(s)	Activities	Ref.
S. aquifolium	14 compounds were identified using LC-HRMS	Anti-oxidant and anti-melanoma activities	[208]
S. binderi	21 compounds identified using GC-MS	Nephroprotective activity	[89]
S. cristaefolium	33 major compounds identified using LCMS UHPLC-HR-ESI-MS	Melanin inhibition activity	[68]
S. cristaefolium	24 compounds were identified using LC-HRMS	Anti-oxidant and anti-melanoma activities	[208]
S. cristaefolium	7 compounds were identified using UHPLC-ESI-ORBITRAP-MS/MS	Anti-inflammatory and anti-oxidant activity	[209]
S. dentifolium	Phytol, saturated fatty acids and phenolic	Anti-oxidant, anti-cancer and anti-viral activity	[210]
S. elegans	Multiple bioactive compounds	Anti-oxidant potential, carbohydrate and lipid digestive enzyme inhibitory activity, and glucose uptake activities	[211]
S. fluitans	8 major compounds identified using LC/QTOF-MS	Anti-cancer activities	[203]
S. fusiforme	48 compounds tentatively identified using ESI-MS/MS	Tyrosinase inhibition activity	[197]
S. fusiforme	79 secondary compounds were tentatively identified	Anti-oxidant activity	[24]
S. ilicifolium	51 compounds were identified using GC-MS	Hepatoprotective activity	[212]
S. muticum	14 compounds were identified using UPLC-ESI-MS/MS	Anti-oxidant and enzyme inhibition activities	[213]
	43 tannins were tentatively identified by HPLC-MS	Anti-oxidant activities, and as a potential antibacterial, antidiabetic, antiproliferation, and neuroprotective agent	[214]
S. polycystum	Carbohydrate, protein and phenolic identified using GCMS and LCMS/MS	Anti-oxidant and anti-cancer activities	[204]
S. polycystum	Phenols, carboxylic acid and other compounds identified using FT-IR	Anti-oxidant activity	[23]
S. polycystum	17 compounds were identified using LC-HRMS	Anti-oxidant and anti-melanoma activities	[205]
S. polycystum	12 free phenolic compounds identified using UHPLC-MS	Anti-oxidant activity	[215]
Sargassum sp. in Playa del Carmen, Quintana Roo, Mexico	Multiple compounds were identified using UHPLC-MS/MS	Anti-proliferative activity	[216]
Sargassum squarrossum	Multiple compounds were identified using HR-LCMS	Anti-cancer activity	[217]
S. subrepandum	Many bioactive constituents, such as polyphenols, flavonoids, terpenoids, triterpenoids, etc.	Anti-oxidant activity	[218]

Advanced separation techniques, such as preparative HPLC, counter-current chromatography, and supercritical fluid extraction, are essential for isolating the non-isolated compounds in *Sargassum* seaweeds, enabling detailed structural and bioactivity studies. Complementarily, computational approaches—including molecular docking, chemoinformatics, and machine learning-based structure–activity predictions—can help prioritize candidate compounds with high functional potential. Investigating possible synergistic effects among multiple bioactive substances may further enhance their efficacy. Systematic isolation and evaluation of these yet-unisolated compounds will expand the chemical diversity of *Sargassum* seaweeds and support their rational application in pharmaceuticals, functional foods, and high-value cosmetic products.

Despite the promising potential of *Sargassum*-derived bioactive substances, several limitations warrant consideration. Similar to traditional Chinese medicines (TCM) [206], these compounds often exhibit complex chemical compositions, multiple bioactive constituents, and diverse molecular targets, which complicate systematic elucidation of their mechanisms of action. The inherent instability of certain compounds and the presence of trace secondary metabolites further challenge reproducibility and consistent bioactivity evaluation. Moreover, current databases and literature provide information on only a fraction of the total *Sargassum* resources, with limited data on efficacy, toxicity, and functional indications, hindering translation to practical applications. To overcome these limitations, the integration of high-resolution analytical techniques, comprehensive chemical and molecular databases, and computational approaches such as network pharmacology and big data analysis is essential. Such strategies can facilitate the identification of active components, map their potential targets, evaluate safety and efficacy, and ultimately support quality control and rational utilization, in line with modern "food–medicine homology" [207] principles.

3. Conclusions

Sargassum seaweeds constitute an essential category of economic seaweeds. They are characterized by abundant resources and a relatively low cost, and are replete with diverse bioactive substances, including polysaccharides, fatty acids, terpenoids, sterols and alkaloids. To date, in the domains of medicine, food, health products, and cosmetics, the application of bioactive substances derived from *Sargassum* seaweeds, which possess mechanisms of action such as anti-inflammation, anti-tumor, and immunomodulation, along with activities like anti-oxidant, moisturizing, and whitening, as well as functions including blood lipid and blood sugar reduction and anti-fatigue, has progressively garnered attention. Research focused on the extraction and isolation of the principal chemical constituents from *Sargassum* seaweeds can facilitate the rational utilization of the various bioactive components therein, enhance the high-value utilization of *Sargassum* seaweeds resources, and assist in obtaining novel potential functional components for deployment in fields like medicine, food, and cosmetics.

In this study, a comprehensive investigation was carried out on the origin, research status quo, and development trends of bioactive substances in *Sargassum* seaweeds, categorized by species. Through a meticulous analysis of the distribution patterns and types of these bioactive substances in *Sargassum* seaweeds, along with a thorough review of domestic and international research progress, this review systematically summarizes the main findings: (1) *Sargassum* seaweeds are rich in a wide spectrum of bioactive compounds, with polysaccharides being the most extensively studied, while non-carbohydrate compounds such as terpenoids and alkaloids are emerging as new research hotspots; (2) the established database of bioactive substances from *Sargassum* seaweeds serves as a valuable resource for future research, enabling efficient data retrieval and analysis; (3) research trends analyzed via CiteSpace indicate a clear shift from traditional polysaccharide-focused studies towards exploring diverse chemical classes and their multi-functional applications.

This paper reveals the existing gaps in the research on *Sargassum*-derived bioactive substances and outlines future research directions, which include developing efficient and green extraction techniques for underutilized bioactive compounds, deepening the understanding of the structure–activity relationships of non-carbohydrate compounds, and expanding their applications beyond pharmaceuticals, food, and cosmetics into emerging fields such as biotechnology, environmental remediation, and sustainable biomaterials. Furthermore, it will be crucial to strengthen clinical and preclinical studies to validate the efficacy and safety of these compounds, while also enhancing standardized protocols for compound identification and quality control across different *Sargassum* species. This work thereby provides valuable insights for the development and utilization of *Sargassum* seaweed resources.

Moreover, while the present study systematically summarizes the diversity of bioactive substances from *Sargassum* seaweeds and establishes a dedicated database, its significance extends well beyond cataloging. The growing evidence of their multifunctionality suggests that *Sargassum*-derived compounds are not only valuable for pharmaceuticals, food, and cosmetics, but also highly promising in biotechnology, environmental remediation, and the development of sustainable biomaterials. By bridging traditional applications with emerging interdisciplinary opportunities, this work provides both a comprehensive reference and a forward-looking perspective, thereby positioning *Sargassum* as an underexplored yet strategic resource for future innovation.

Competing Interests

The authors declare no conflict of interest.

Data availability

The datasets used or analysed during the current study are available from the corresponding author on reasonable request.

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Experimental

Utilizing reports from the Web of Science, Google Scholar and CNKI, the reliable material sources of this systematic manuscript paper were obtained from the literatures published during recent ten and twenty years. Further, the cluster analysis of the research status of *Sargassum* has been analyzed using CiteSpace (w.6.3.R1).

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