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Evaluation of the genus *Hypnea* phytochemical and pharmacological potential

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ARTICLE INFO

ABSTRACT

The red seaweed *Hypnea* J.V. Lamouroux is a cosmopolitan genus of the family Cystocloniaceae. It has been used in folk medicine, especially in eastern Asian countries. However, little literature highlighted the phytochemical and pharmaceutical values of its different species. In the past centuries, and until now, different *Hypnea* species have also been widely utilized as a main component in food recipes because they are rich in various bioactive compounds including polysaccharides, particularly 'κ-carrageenans', polyphenolics, vitamins, tannins, saponins, terpenoids, alkaloids, sterols, and minerals. Additionally, the aforementioned constituents have been shown to combat different diseases and complications due to their outstanding antioxidant, anti-inflammatory, antibacterial, anti-proliferative, gastroprotective, anticoagulant, enzyme inhibitor, and immunostimulatory potentials. Considering the aforementioned issues, this review aims to provide detailed information about the different phytochemical and pharmacological potentials of species of the genus *Hypnea*, as well as their mode of action.

1. Introduction

Algae, including seaweeds, are commonly regarded as "healthy foods" due to their low lipid content and high levels of polysaccharides and unsaturated fatty acids, as well as vitamins A, B_1, B_{12}, C, D, and E, riboflavin, niacin, pantothenic and folic acid, and minerals such as calcium, phosphorus, sodium, iodine, potassium, and trace elements [1–4]. Algae are important reservoirs for value-added natural cocnsitituents with a wide range of biological actions, including antioxidant, antibacterial, anticancer, and antiviral characteristics. Temperature sensitivity and the alkaline strength parameter, rather than time, determine these features [5].

The genus *Hypnea* J.V. Lamouroux comprises 63 taxonomically accepted species and infraspecies, that are part of the family Cystocloniaceae. Ecologically, it thrives in the intertidal and subtidal zones of tropical and warm temperate coastal regions. The genus *Hypnea* is

very important in food manufacturing due to its high contents of κ-carrageenan [6]. Taxonomically, the genus *Hypnea* has an erect or prostrate thallus that is cylindrical to flattened with a membranous to cartilaginous consistency. The thallus organization is uniaxial and pseudo-parenchymatous, with a main axis and apical cell growth and apex shape varying. Branching is primarily irregular, but dichotomous or lateral branching can also be found in some species. The pigmentation of thalli is variable. The length of the thallus usually varies depending on the species habitat. The thallus is attached to the substrate through discoid structures, stolons, or rhizoidal branches, depending on the species. In general, several complex sulfated polysaccharides, particularly carrageenans, are found members of the Rhodophyta. Carrageenan is a galactose-rich carbohydrate polymer that holds significant economic importance, and it is usually extracted from multiple species of marine red seaweeds, including *Hypnea* spp., called carrageenophytes [7]. It has been established that the association between molecular weight and

melting and gelling temperatures is positively significant, while the correlation with sulfate concentration was non-significant [8]. Additionally, it was found that the mild extraction conditions are important in producing the essential structural alterations, affirming the best yield and quality [9].

The polysaccharides that constitute carrageenans are comprised of alternating α-(1–3) and β-(1–4) linked D-galactosyl residues. The modification of the disaccharide repeating unit through the presence of ester sulphate groups and the inclusion of 3,6-anhydro galactose as a 4-linked residue lead to production of several types of carrageenans. Among these types, λ-, κ-, and ι-carrageenan are currently available for commercial uses. The properties of the major carrageenan types are typically influenced by the extent of their sulphation, and κ-carrageenan is of significant commercial significance because of its exceptional gel-forming properties and excellent gel-forming capabilities. κ-Carrageenan is a key commercial important sulfated polysaccharide. Because of their outstanding physical functional qualities, such as gelling, thickening, gelling, and stabilizing. κ -Carrageenans are frequently used in the food business [10]. Generally, carrageenans extracted from the genus *Hypnea* has been used in a wide range of non-food products, including but not limited to medicines, cosmetics, printing, and papers [11]. The genus *Hypnea* is a valuable source of phytochemicals that play a vital role in medicine, such as phenols, tannins, saponins, flavonoids, terpenoids, alkaloids, and sterols. Chemical compounds and polysaccharides obtained from *Hypnea* species exhibit promising anti-inflammatory, antioxidant, antibacterial, antiproliferative, gastro-protective, anticoagulant, enzyme inhibitor, and immunostimulatory properties. This review will include information on the phytochemical and pharmacological potential of members of the genus *Hypnea*, as well as, when appropriate, their mode of action (Fig. 1).

2. Materials and methods

A bibliographic inquiry was conducted through an examination of the available information on *Hypnea* species by consulting ethnobotanical literature and reputable global scientific databases including Marine lit, Pubmed, Scopus, EBSCO, and Google Scholar Database. The Marine Lit, World Register of Marine Species and AlgaeBase databases were utilized for the validation of scientific names.

3. Pharmacological potential of the genus *Hypnea*

3.1. Hypnea bryoides Børgesen 1943

Certain species of red seaweeds include the linear sulfated polysaccharide family known as carrageenans which can be isolated from their cell walls. When added to salt solutions in tiny concentrations, these natural polymers can generate viscous solutions or thermoreversible gels. As a result, they are frequently employed as texturing, thickening, suspending, or stabilizing agents in a wide range of industrial applications, including experimental medicine, pharmaceutics, food items, and cosmetics. Carrageenan, also known as phycocolloids, is a water-soluble sulfated galactan isolated from various marine red seaweed species of the Rhodophyta. The characterization of carrageenan from *H. bryoides* was conducted in Oman. Alkalinity and temperature exerted a significant influence on carrageenan yield, with the highest reported value being 26.74 ± 5.01 %. Elevated temperatures markedly decreased the molecular weights of the recovered carrageenan, ranging from $5.95 \pm 0.49 \times 10^5$ Da to $13.90 \pm 0.14 \times 10^5$ Da. Additionally, sulfate content was substantially reduced with increasing alkaline concentration, ranging from 7.62 ± 5.52 % to 17.02 ± 0.14 %. In gerernal, optimizing the extraction process of carrageenans from *H. bryoides* should be further deeply investigated [12].

3.2. Hypnea cervicornis J. Agardh 1851

HCA (*H. cervicornis* agglutinin) was isolated from the Brazilian *H. cervicornis*. The glycoprotein porcine stomach mucin, with a minimum inhibitory concentration of 19 g/mL, was the only inhibitor of the lectin haemagglutinating activities. The presence of simple sugars did not affect its haemagglutination. The matrix-assisted laser desorption/ionization MALDI-TOF-MS spectrometry molecular weights of native, reduced, and carbamidomethylated HCA were 9196.6 Da and 9988.2 Da, respectively, indicating that the protein's basic structure is cross-linked by seven disulfide links. This unusual structural characteristic, together with its N-terminal sequence and amino acid makeup, clearly shows that HCA belongs to a different protein family than the similar Japanese alga *Hypnea japonica* isolectins Hypnin A1 and Hypnin A2. HCA, on the other hand, has a significant degree of resemblance to agglutinin. The phenomenon of mechanical hypernociception in rats, induced by carrageenan, ovalbumin (as an antigen), and prostaglandin E2, was investigated in the context of the mechanisms underlying the action of HCA. The intravenous administration of lectin at various time

Fig. 1. *Hypnea musciformis* from the Egyptian coastal water of Hurghada city, the Red Sea.

points resulted in a reduction of hypernociception triggered by carrageenan and antigens. However, when lectin was combined with mucin, the suppressive impact was completely abolished, underscoring the significance of carbohydrate-binding sites. The correlation between the inhibition of inflammatory hypernociception by HCA and the decrease in neutrophil recruitment to the plantar tissue of rats was established, although this relationship was not observed with regards to the inhibition of pro-hypernociceptive cytokine production (TNF-α, IL-1β, and CINC-1). Furthermore, the HCA-mediated inhibition of PGE2-induced mechanical hypernociception was observed, which was further corroborated by the prevention of this effect upon injection of a nitric oxide synthase inhibitor [13,14].

The morphology of *Hypnea* was studied, and its weight and photosynthetic activity were assessed before renewal to document the growing state. *Hypnea* was collected every 5 days, for a total of four times (including the original value). After the culture was completed, the pigment contents were measured. By varying salinity (25, 30, 35, 40, 45, and 50 ‰) and temperature (15, 20, 25, and 30 °C), researchers observed the growth rates and changes of several photosynthetic pigments in *H. cervicornis*. The results of cultural circumstances are that

changes in salinity and temperature have a major impact on *H. cervicornis* growth. Growth rates increase initially, then drop, as temperature rises, but growth rates decrease as salinity rises. The ideal salinity and temperature for growth are 25 ‰ and 25 °C, respectively. The effects of salinity and temperature on photosynthetic pigments in *H. cervicornis* are considerable or highly significant [15].

3.3. Hypnea charoides J.V. Lamouroux 1813

The red macroalga *H. charoides*, commonly known as ibaranori, is commonly found thriving along the coast of the Japanese islands, particularly in Okinawa prefecture where it is favored as a food source. Despite being recognized as a health-promoting food, the specific mechanism underlying its beneficial effects remains unclear. The presence of carrageenans in the red seaweeds may contribute to its hypocholesterolemic and anticoagulant properties in humans. Therefore, the polysaccharides found in the macroalgae, specifically κ-carrageenan, might exhibit a promising potential as dietary supplements that support overall health [16]. At 25 °C, the Na-salt of κ-carrageenan solution extracted from *H. charoides* exhibited Newtonian behavior at
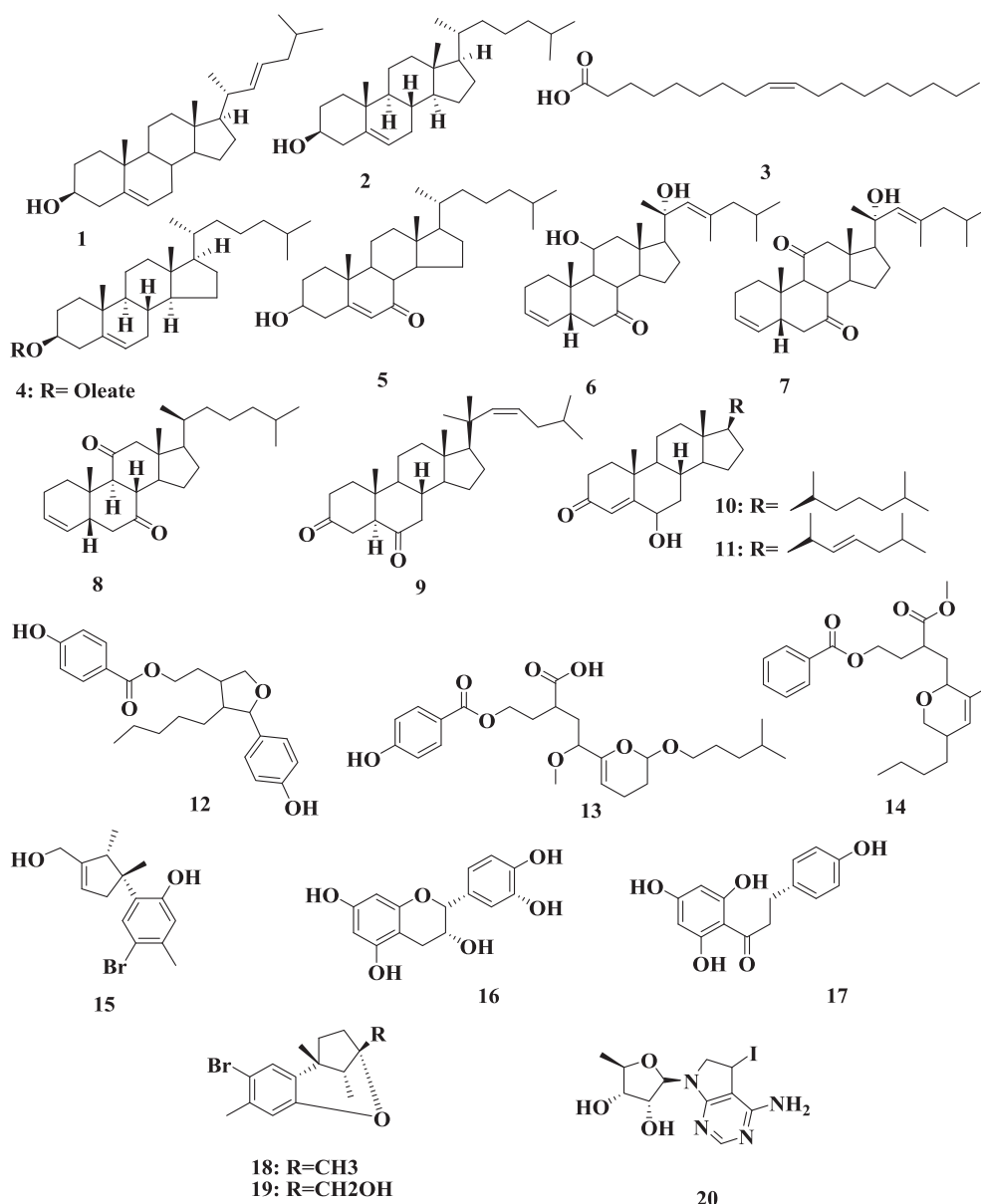

Fig. 2. Chemical structures of compounds 1–20.

concentrations less than 1.0 %, but the K-salt exhibited plastic behavior even at 0.3 %. At varied concentrations of the K-salt of κ-carrageenan, the transition temperature at which dynamic viscoelasticity declined fast was discovered to be 15 °C or 20 °C. Gelation occurred at low temperature (0 °C) for the K-salt of κ-carrageenan at concentrations greater than 0.5 %, but not for the Na-salt, even at a concentration of 2.0 %. When 0.1 % KCl was added to a 0.2 % solution of K-salt of κ-carrageenan, very significant dynamic viscoelasticity was found. The gel formation of the κ-carrageenan isolated from Ibaranori might be attributed to intra- and intermolecular K^+-bridges within and between molecules [17].

3.4. Hypnea flagelliformis Greville ex J. Agardh 1851

The chemical structures of the compounds present in the different *Hypnea* species are represented in Fig. 2. 22-Dehydrocholesterol (**1**), cholesterol (**2**), oleic acid (**3**), cholesterol oleate (**5**), and (22*E*)-cholesta-5,22-dien-3β-ol-7-one (**5**) were detected in ethyl acetate extract of *H. flagelliformis* collected from Persian Gulf [18,19].

Ethyl acetate extract of *H. flagelliformis* was shown to have a substantial cytotoxic impact against *Artemia salina*, as demonstrated by lethal concentration 50 (LC$_{50}$) values of 4 g/mL. Furthermore, aqueous methanol (50 %) extract of *H. flagelliformis* was shown to be effective. The Broth-dilution technique revealed that the algae methanol and aqueous methanol extracts had no antifungal or antibacterial activity against *S. aureus*, *E. coli*, *C. albicans*, and antifungal activity against *Aspergillus niger*. Only the ethyl acetate extracts showed antibacterial action against *S. aureus*, with a Minimum Inhibitory Concentration (MIC) of 2 g/mL [20].

Ethyl acetate extract of *H. flagelliformis* obtained from Tamil Nadu, India, has cytotoxicity targeting HeLa cell lines, which are known to be of human cervical cancer origin. The anticancer effects of ethyl acetate extract were demonstrated, with a half maximal inhibitory concentration (IC$_{50}$) value of 138.321 g/mL [21].

N-Allyl-*N*, *N*-dimethylamine, 4-methyl-2-heptanone, 2-hexyn-1-ol, 1-tridecene, 4-methyl-2-mercaptopyridine1-oxide, N-Isopropyl-3-phenylpropanamide, tridecanal, N-allyl-*N*, *N*-dimethyl amine, 1-nonadecene, diphenylamine, 1-hexadecane, dodecanal, 1-hexadecene, 6,10dimethyl-2-undecanone, 10-undecenoic acid, 9-(3-oxooctanoyloxy)-methyl ester, n-hexadecanoic acid, tetradecyl trichloroacetic acid, 1,4-eicosadiene and n-tetracosanol-1 were detected in GC–MS of the ethyl acetate extract of *H. flagelliformis* collected from Tamil Nadu, India [22].

3.5. Hypnea japonica Tanaka 1941

22-Dehydrocholesterol (**1**) was detected in the hexene extract of Japanese *H. japonica* [23]. The peptides hypnin A, hypnin B, hypnin C, and hypnin D were extracted from an aqueous ethanol extract of *H. japonica*. The most abundant peptide, hypnin A, was a monomeric peptide with a molecular weight of 4200, an isoelectric point of 4.3, and a high serine and glycine content. The amino acids at its N- and C-termini have been identified as tyrosine and serine, respectively. Hypnins B and C were thought to be dimeric or trimeric versions of hypnin A or a similar peptide, Hypnin D was significantly different from the others. Other than human and mouse FM3A tumor cells, hypnin A was capable of agglutinating animal erythrocytes. Its hemagglutinating action was completely suppressed by glycoproteins having complex N-glycosidic sugar chains [16].

The nutritional value of protein concentrates extracted from *H. charoides* and *H. japonica* was assessed in developing rats. There were no significant variations in net protein ratio or biological value across any diet groups. Although the values of true protein digestibility (ranging from 90.5 to 90.6 %), nitrogen balance (ranging from 108 to 113 mg/rat.day), net protein utilization (ranging from 80.1 to 81.3 %), and utilizable protein (ranging from 80.1 to 81.3 %) were significantly

lower than those of the casein control, they were comparable to those of other common plant protein concentrates. Furthermore, the growth performance of rats fed the two protein concentrate diets was adequate, and neither protein concentrate had a detrimental influence on growth [23].

Despite their tiny size (9 KDa), the *H. japonica* isolectins belong to a new lectin family. The carbohydrate-binding characteristics of three isolectins (hypnin A1, A2, and A3) were discovered, as well as the amino acid sequence of hypnin A3. Using frontal affinity chromatography with approximately 100 pyridyl-aminated oligosaccharides, the isolectins, which had no affinity for monosaccharides, selectively bound to the core (1–6) fucosylated N-glycans while ignoring the other oligosaccharides investigated, including (1–2), (1–3), and (1–4). Surface plasmon resonance investigations on an immobilized glycoprotein with and without core (1–6) fucose confirmed the binding selectivity of hypnin A3 with fucosylated N-glycans [24].

3.6. Hypnea musciformis (Wulfen) J.V. Lamouroux 1813

23-methyl-5 ∼ −cholesta-l,22-diene-11,20-dihydroxy-7-one (**6**), 5β-cholest-l-en-20-hydroxy-7,11-dione (**7**), and 5β-Cholest-3-en-7,11-dione (**8**) isolated from the hexane extract of Indian *H. musciformis* [25]. 5β-Cholest-3-ene-7,11-dione (**8**) is a diketo steroid isolated from the hexane extract of Indian *H. musciformis* [26].

20-Hydroxy-5α-cholest-22-ene-3,6-dione (**9**), 6α-hydroxy-cholest-4-ene-3-one (**10**), and 6α-hydroxy-cholest-4,22-diene-3-one (**11**) were detected in dichloromethane/methanol extract from the *H. musciformis* collected from Morocco. The dichloromethane/methanol extract and compound (**11**) exhibited porcine pancreas elastase (PPE) inhibition [27].

5β -cholest-1-ene-20-hydroxy-7,11-dione (**7**) isolated from the hexane extract of Indian *H. musciformis* [28]. 2-(tetrahydro-5-(4-hydroxyphenyl)-4-pentylfuran-3-yl)-ethyl-4-hydroxy benzoate (**12**), 2–2-[(4-hydroxy benzoyl)-oxy]-ethyl-4-methoxy-4-2-[(4-methyl pentyl)oxy]-3,4-dihydro-2H-6-pyranylbutanoic acid (**13**) and 3-((5-butyl-3-methyl-5,6-dihydro-2H-pyran-2-yl)-methyl)-4-methoxy-4-oxobutyl benzoate (**14**) are substituted aryl meroterpenoids, isolated from ethyl acetate fraction of *H. musciformis*. 2-(tetrahydro-5-(4-hydroxyphenyl)-4-pentylfuran-3-yl)-ethyl-4-hydroxy benzoate (**12**) displayed comparable inhibitory effects on 2,20-diphenylpicrylhydrazyl radical and Fe^{2+} ion chelation, with IC$_{50}$ values of 25.05 μM and 350.7 μM, respectively, to those of the commercial antioxidant gallic acid (IC$_{50}$ 32.3 μM and 646. μM, respectively). This was followed by (**10**) (IC$_{50}$ 231.2 μM and 667.9 μM, respectively) and (**13**) (IC$_{50}$ 322.4 μM and 5115.3 μM, respectively) [29].

(−)-Epicatechin (**15**) and phloretin (**16**) isolated from the supercritical fluid extraction of a dried *H. musciformis* collected from the Colombian Caribbean, prevent oxidative damage in human low-density lipoproteins LDLs. The extracts garnered using low pressure (10–20 MPa) in tandem with 8 % ethanol yielded a 42 % increase in protection. Conversely, extracts obtained via high pressure (30 MPa) and 8 % ethanol resulted in a 62.5 % increase in protection [9]. Through aqueous extraction, sulphate polysaccharide (PLS) was obtained with a yield of 31.8 % from *H. musciformis* dry weight, with the total carbohydrate content accounting for 99 % of the sample. The sulphate content of the polysaccharide was 5.08 %, while the percentage of carbon was 25.98 %. Pretreatment with PLS in all doses exhibited inhibition of castor oil-induced diarrhea, with a reduction in the total amount of stool, diarrheal stools, and the severity of diarrhea. PLS (90 mg/Kg) proved effective in decreasing castor oil- and PGE2-induced enteropooling. Furthermore, PLS (90 mg/Kg) demonstrated an increase in Na^+/K^+-ATPase activity in the small intestine and decreased gastrointestinal transit, possibly through the activation of cholinergic receptors. The intestinal contents of animals pretreated with PLS (90 mg/kg) exhibited a decrease in cholera toxin-induced fluid secretion and Cl^- ion levels, possibly through the reduction of toxin—GM1 receptor binding. PLS confers anti-

diarrheal activity by increasing Na^+/K^+-ATPase activity, inhibiting gastrointestinal motility, and blocking the toxin—GM1 receptor binding [30].

The PLS was tested for anti-inflammatory activities in Swiss mice by producing paw edema and peritonitis using inflammatory agents such as carrageenan and dextran. To assess the efficiency of the PLS, samples of paw tissue and peritoneal fluid were collected and tested for myeloperoxidase (MPO) activity, NO_3/NO_2 levels, and interleukin-1 (IL-1). Both carrageenan-induced and dextran-induced edema were significantly reduced in mice pre-treated with PLS at a dosage of 10 mg/kg. In a peritonitis model, it also suppressed total and differential peritoneal leucocyte counts. PLS amazing effects were finally erased when combined with L-arginine therapy, however, the NO synthase blocker (aminoguanidine) showed hints of recovery. PLS was also discovered to reduce the inflammatory response by modulating neutrophil migration which appeared to be dependent on the NO pathway[31].

A sulfated-polysaccharide fraction isolated from *H. musciformis* was shown to have gastroprotective properties and modes of action. After 30 min, mice were given sulfated-polysaccharide fraction (3, 10, 30, and 90 mg/kg, p.o.) followed by 50 % ethanol (0.5 mL/25 g, p.o.). Other groups of mice were given N(ω)-nitro-L-arginine methyl ester (L-NAME) (10 mg/kg i.p.), aminoguanidine (100 mg/kg i.p.), or glibenclamide (10 mg/kg i.p.). Gastric injury was caused after delivering a sulfated-polysaccharide fraction (30 mg/kg, p.o.) to the aminoguanidine group after 30 min and to the other groups after an 1 h. A dose-dependent gastroprotective effect of sulfated-polysaccharide fraction against ethanol-induced stomach damage was observed. However, L-NAME or glibenclamide therapy restored this effect. The gastroprotective activity of the sulfated-polysaccharide fraction was unaffected by the administration of aminoguanidine [32].

The antioxidant, neuroprotective, antibacterial, and anticancer properties of κ-carrageenan are derived from *H. musciformis* (Hm-SP). Hm-SP was found to have significant antibacterial and antifungal properties against *S. aureus* and *C. albicans*, respectively. In human breast cancer (MCF-7) and human neuroblastoma (SH-SY5Y) cell lines, Hm-SP had no cytotoxicity. However, the addition of Hm-SP greatly inhibited the ability of these cancer cells to proliferate. Furthermore, Hm-SP protected SH-SY5Y cells against 6-hydroxydopamine-induced neurotoxicity via modulating mitochondrial transmembrane potential and lowering Caspase 3 activity. Furthermore, Hm-SP exhibited minimal antioxidant potential and did not cause any substantial cytotoxicity or changes in cell proliferation in the Balb/c 3 T3 murine fibroblast cell-line [33].

Feeding the fish κ-carrageenan extract from *H. musciformis* improved nonspecific immune measures and boosted survival and growth. Immune stimulants are a potential alternative to antibiotics and contribute in disease prevention in aquaculture. The weight growth of κ-carrageenan in a fish model was tracked throughout a 15-day feeding study. The immunostimulant was assessed by monitoring the relative expression of transferrin, interleukin 1 (IL-1), and growth hormone (GH) in the spleen following daily injection for 24 h and 15 days. The poisonous activity of Kc was examined in brine shrimp (*Artemia salina*) nauplii, however no significant toxic effects were identified at any dosage investigated. The administration of κ-carrageenan resulted in a favorable trend in growth rate and fish survival values [34].

In vitro, antioxidant activity and cell viability of sulfated galactans produced from *H. musciformis* were assessed. Galactose and sulfate were the major components, with minor protein contamination. A sulfate ester S = O link, a 3,6-anhydrogalactose C—O bond, nonsulfated -*D*-galactose, and a C-O-SO_4 bond in galactose C4 were shown to be responsible for the polydisperse profile of these sulfated galactans (F1.0). In a lipid peroxidation assay, sulfated galactan F1.0 revealed excellent antioxidant activity, with F1.0 at 8 mg/mL promoting 57.92 % peroxidation inhibition and hydroxyl radical scavenging activity [35].

H. musciformis provided the protein fraction ($F_{40/70}$) recovered by ammonium sulfate precipitation, which was found to be high in lectin.

This fraction was tested for beta-1,3-glucanase and chitinase activity, as well as antifungal activity against the human pathogen yeasts *C. albicans* and *C. guilliermondii*. β-1,3-glucanase and chitinase enzymes were found in the $F_{40/70}$ fraction, with a specific activity of 1880.7 and 276.43 Units/mg protein, respectively. The $F_{40/70}$ fraction successfully inhibited the growth of *C. guilliermondii* at doses of 45, 100, and 450 g protein/ml while only having a minor inhibitory impact on *C. albicans* at all concentrations examined. The inhibitory impact was demonstrated to be fungistatic, as was the presence of the glycoprotein fetuin. [36]. The fraction ($F_{40/70}$) was reported to have antifungal activities against *T. rubrum* and *C. lindemunthianum*, inhibiting spore germination completely at doses of 500, 1000, and 2000 g/mL. At a dose of 2000 g/mL, there was a tendency to suppress the growth of *C. musae* and *F. oxysporum*, but the findings were statistically insignificant. At the measured dosages, the fraction did not affect the fungus *E solani* and *A. niger*. The presence of the glycoprotein fetuin, which is identified by the agglutinin in the fraction, negated the antifungal effect against *C. lindemunthianum* and *T. rubrum*. The protein fraction contains agglutinin, the mechanism of action on spore germination is thought to include it. [37].

HCA and HML are lectins isolated from *H. cervicornis* and *H. musciformis*, respectively. HML binds to GalNAc/Gal that has been replaced with a neutral sugar through 1–3, 1–4, or 1–2 links in *O*-linked mucin-type glycans and Fuc(α1–6) GlcNAc of *N*-linked glycoproteins [38].

H. musciformis methanol extracts were tested on rabbits and mice. In rabbits, *H musciformis* significantly reduced blood total cholesterol, triglyceride, and low-density lipoprotein cholesterol levels. It reduced the occurrence of many cardiovascular diseases by lowering cholesterol and total lipids. Despite *H. musciformis* methanolic extract injection elevated glucose levels, this may have been a transitory rise due to the action of glucagon or the *H. musciformis* extract contains several amino acids that may be converted into glucose. The *H. musciformis* extract treatment also significantly boosted dopamine levels. The possible action of the *H. musciformis* methanol extract on dopamine and other brain biogenic amines suggests that *H. musciformis* extract is psychotropic and anxiolytic. A rise in dopamine levels may also be advantageous [39].

The aqueous extract of *H. musciformis* was used in the biosynthesis of Ag/AgCl-NPs. In vitro testing of Ag/AgCl-NPs yielded IC_{50} values of 40.45, 24.08, and 36.95 g/mL for the suppression of Ehrlich ascites carcinoma (EAC), colorectal cancer (HCT-116), and breast cancer (MCF-7) cell lines, respectively. The considerable increase in ATG-5 gene expression in MCF-7 cells suggests that autophagy cell death may occur in addition to apoptosis. Caspase-3 protein production in EAC cells verified the onset of apoptosis. In vivo, study of Ag/AgCl-NPs on mice revealed inhibition of 22.83 % and 51 %, respectively [40].

The hot plate test, the acetic acid-induced writhing test, and the formic acid-induced test were used on Swiss albino mice to assess the potential analgesic qualities of *H. musciformis* ethanol extracts, with each test delivered at a 500 mg/kg dosage. An ethanol extract from carrageenan-induced paw edema was used as an anti-inflammatory option in an experiment. Mices given an intraperitoneal injection of carrageenan displayed a time-dependent increase in paw edema. Diclofenac is used as a reference standard in investigations on the analgesic and anti-inflammatory properties of drugs. Formic acid-induced paw discomfort is a well-researched in vivo model of pain that can be utilized for analgesic research. It is crucial to do both phases of the formic acid test because different analgesics may have distinct effects in the early and late stages. The *H. musciformis* extract exhibits an anti-nociceptive effect that may be connected to its peripheral action. It shows this effect by inhibiting the nociceptive response in both the early and late phases of the formic acid test, outperforming the reference drug receiving group (diclofenac). During the hot plate test, findings revealed the presence of supraspinal nociception and central antinociception being concurrently operative. *H. musciformis* has potent anti-inflammatory and pain-relieving properties in animal models (percent

inhibition identified at 28.22 % on the acetic acid technique, 42.3 % on the hot plate method, and 48.7 % on the cold plate method) [41].

The study conducted Mendes et al. [42] assessed the ability of four natural and cultivated *H. musciformis* specimens to prevent the replication of acyclovir-resistant herpes simplex virus types 1 (HSV-1) and 2 (HSV-2) strains. The major goal was to see if the culture methods had any effect on the antiviral activity. The crude extract of *H. musciformis* exhibited 90 % inhibition against HSV-1 at the maximum non-toxic concentrations; however seaweed extracts, subjected to phytohormone treatments displayed over 99 % inhibition at the same maximum non-toxic concentrations. The seaweed extract treated with gibberellic acid showcased a selectivity index more than ten times greater than that of the crude extract (298.5 vs. 16.8, respectively). A higher selectivity index was similarly evident in seaweeds treated with 6-benzylaminopurine, although this was not the scenario with indoleacetic acid (36.69 and 13.88, respectively). In terms of HSV-2, at the maximum non-toxic concentrations, the crude *H. musciformis* extract reduced viral replication by 90 %, whereas the hormones-treated seaweed extracts inhibited over 98 % of viral replication [42].

3.7. Hypnea pannosa J. Agardh 1847

10-bromo-7, 12-dihydroxy-$\Delta^{3\ 4}$-laurene (17), filiformin (18), and filiforminol (19), halogenated terpenes, were detected in chloroform extract of *H. pannosa,* collected from Pakistan [43].

The proximate composition and amino acid profile of *H. pannosa* and *H. musciformis* were detected. The two most abundant components present in these seaweeds were the total protein (16.31 ± 0.72 % DW for *H. pannosa* and 18.64 ± 1.12 % for *H. musciformis*) and dietary fiber (40.59 ± 0.95 % DW for *H. pannosa* and 37.92 ± 1.44 % for *H. musciformis*). The content of crude lipid, carbohydrates, and ash were 1.56 ± 0.22 %, 22.89 ± 1.26 %, and 18.65 ± 0.54 % for *H. pannosa* and 1.27 ± 0.41 %, 20.60 ± 1.68 %, and 21.57 ± 1.04 % for *H. musciformis*, respectively. Both *H. pannosa* and *H. musciformis* contained all the essential amino acids, accounting for 52.27 % and 53.89 % of the total amino acids, respectively. The limiting amino acids for *H. pannosa* (53.3, 14.6, and 25.8 mg/g protein; respectively) and *H. musciformis* (45.6, 16.2, and 26.2 mg/g protein; respectively) were Lysine, methionine and tyrosine [44].

Pyruvate glucogalactan sulfate was obtained from *H. pannosa*, cultivated in Okinawa, Japan. The yield of the polysaccharide was 17.2 %, and it exhibited total carbohydrates, pyruvic acid, sulfuric acid, and ash contents of 55.2 %, 3.8 %, 35.2 %, and 24.3 %, respectively. Liquid and thin-layer chromatography identified 3,6-Anhydro-α-*D*-galactose, β-*D*-galactose, α-*D*-galactose, and *D*-glucose. The ^{1}H and ^{13}C NMR spectra assigned 1,3-linked β-*D*-galactose, 1,4-linked anhydro-α-*D*-galactose, 1,4-linked α-*D*-galactose, 1,4-linked β-*D*-glucose, and pyruvic acid (carboxyl acetal, methyl proton, and methyl carbon). Terminal *D*-galactose 0.1 mol), 1,4-linked *D*-glucose (1.0 mol), and 1,2,3,4,6-linked *D*-galactose (3.7 mol) were revealed from methylation analysis for native polysaccharide, and terminal *D*-galactose, 1,4-linked *D*-galactose (1.9 mol), 1,4-linked *D*-glucose (1.0 mol), 1,3-linked *D*-galactose (1.7 mol), and 1,3,4,6-linked *D*-galactose (0.3 mol) which substituted with pyruvate group at 4 and 6 positions for desulfated polysaccharide [45].

The methanol extract of *H. pannosa* was detected for its antifungal properties. The screening demonstrated favorable results against *Trichophyton longifusus* while indicating a lower level of activity against *Candida glabrata* and *Microsporum canis*. In contrast, the extract was determined to be ineffective against *Fusarium solani* [46].

The ethanol and methanol extracts were found to possess remarkable antioxidant activity. The ethanol extract of *H. pannosa* was found to exhibit significant activity for 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid (ABTS) and 2,2-Diphenyl-1-picrylhydrazyl (DPPH) free radicals (118.56 % and 124.30 %, respectively) [47].

The phytochemical composition, total phenolic and flavonoid contents, and antioxidant activity of *H. pannosa* from Bangladesh coastal water were assessed using various in vitro assays [48]. Screening of phytochemicals revealed that *H. pannosa* contained diverse types of bioactive compounds, including terpenoids, saponins, phlobatannins, phenolics, and flavonoids. Methanol extract of *H. pannosa* showed the highest activity, followed by ethanol and water extracts. The presence of diverse chemical compositions with antioxidant activity [48].

The crude ethanol extract of *H. pannosa* underwent toxicity assessment at a dose of 150 mg/kg, which revealed no indication of toxicological manifestations, side effects, behavioral alterations, or mortality in the test rats. This suggests that the extract can be well-tolerated and safe at this specific dose. Nevertheless, when administered at doses of 250 and 500 mg/kg, the same extract yielded toxic side effects. Rats displayed decreased spontaneous motor activity, paralytic effects, loss of sensation, and experienced death within 30 min of drug administration. The results demonstrate the notable analgesic effect of *H. pannosa* extract. The tail-flick latency times at 90, 120, and 150 min were found to be highly significant at a dose of 150 mg/kg, indicating a significant increase in reaction time for the tail flick method with DMSO and pathedine served as controls. The extract of *H. pannosa* possesses analgesic properties, which may be attributed to the involvement of central mechanisms. Following the administration of extract, the frequency of locomotion, rearing, and immobility duration within the open field environment were all modified. The decrement in spontaneous motor activity suggested the extract central depressant action. The application of crude *H. pannosa* extract engendered a reduction in locomotor activity. The precise mechanics of this depression remain unclear at present, yet one may surmise that *H. pannosa* ethanol extract could exert a CNS depressant effect by impeding cortex function. The antiemetic properties of the ethanol extract of *H. pannosa* exhibited greater inhibition of emesis at a dosage of 200 mg/kg in comparison with chlorpromazine served as control. The *H. pannosa* extract demonstrated a 40.38 % inhibition compared to chlorpromazine's 32.99 % inhibition. The mode of action remains unknown. Oral copper sulphate induces emesis by peripheral action and the peripheral 5-HT4 plays a vital role in this action, the *H. pannosa* extract was efficacious in preventing its effect, suggesting that the extract has a peripheral antiemetic activity [49].

3.8. Hypnea pseudomusciformis Nauer, Cassano & M.C. Oliveira 2015

The long-term viability of the seaweed *H.pseudomusciformis* culture and its usage as a human food source. From a prototype farming project in Traíri, Northeastern Brazil, the environmental indicators revealed very effective utilization of energy, nitrogen, and phosphorus, which increased algal biomass by 383 %, 894 %, and 1860 %, respectively, throughout the culture. Furthermore, *H. pseudomusciformis* culture absorbs carbon and does not contaminate the environment [50]. By employing animal models to study orofacial pain, the analgesic properties of sulphated polysaccharides from *H. pseudomusciformis* were evaluated. Various substances such as formalin, capsaicin, cinnamondehyde, acidified saline, glutamate (in cutaneous models), and hypertonic saline (in corneal models) were demonstrated to induce immediate pain responses. Pre-treatment with sulphated polysaccharides significantly reduced nociceptive behaviors associated with acute pain. Ruthenium red and ketamine were effective in reducing antinociception, rather than inhibiting it. Glibenclamide and L-NAME enhanced the effects of sulphated polysaccharides. Heating, naloxone, and methylene blue had no impact on the analgesic properties of sulphated polysaccharides. Furthermore, sulphated polysaccharides exhibited no indications of antioxidant activity or cytotoxic effects. Our findings support the role of sulphated polysaccharides as a suppressor of orofacial pain in acute conditions, potentially through modulation of glutamatergic, nitrergic, TRPs, and K + ATP pathways, underscoring its therapeutic significance [51].

3.9. Hypnea valentiae (Turner) Montagne 1841

The total phenolic content (70.08 ± 0.34 %) was determined within the polyphenol compound of the methanol extract of *H. valentiae*. The phytochemicals present in *H. valentiae* were identified to be flavonoids, saponins, tannins, phenolics, alkaloids, and steroids. The antimicrobial activity of the polyphenol compounds was evaluated against *E. coli* (12 mm), *K. oxytoca* (Zone of Inhibition=17 mm), *S. aureus* (14 mm), *P. aeruginosa* (11 mm), *B. subtilis* (15 mm), *Serratia* sp. (13 mm), *Salmonella* sp. (16 mm), *E. amylovora* (10 mm), *L. monocytogenes* (12 mm) *Xanthomonas* sp. (11 mm), *E. carotovora* (18 mm), *Alkaligens* sp. (15 mm), *R. stolonifer* (16 mm), *A. japonicus* (13 mm), and *A. nidulans* (18 mm). Additionally, the free radical scavenging activity of the polyphenol compound was assessed using various parameters such as total antioxidant capacity (78.12 ± 0.22 %), reducing power (75.09 ± 0.39 %), hydrogen peroxide scavenging activity (73.18 ± 0.32 %), DPPH (61.41 ± 0.27 %), ABTS (56.84 ± 0.41 %,) hydroxyl-scavenging assay (60.09 ± 0.37 %), superoxide anion radical scavenging (59.75 ± 0.17 %), and nitric oxide scavenging (68.25 ± 0.31 %) [52].

The halogenated tubercidin analog, namely 5-deoxy-5-iodotubercidin **(20)**, which has been derived from the brown alga *H. valentiae*, demonstrated an inhibitory effect on adenosine kinase. Compound **(20)** has been reported to possess potent adenosine kinase inhibitory properties. Furthermore, this compound has been subjected to testing for its potential application in the treatment of cancer and brain diseases [53,54].

The biological synthesis of gold nanoparticles (AuNPs) was obtained from the aqueous extract of *H. valentiae*. The DPPH test (84.5 ± 1.45 %), hydrogen peroxide assay (70.6 ± 0.8 %), and ferric-reducing ability of plasma (FRAP) assay (90.54 ± 2.3 %) were conducted to evaluate the biosynthesized Hv-AuNPs potential to scavenge free radicals. The anti-cancer effects of Hv-AuNPs were tested on lung cancer (A549) cells through the epithelial-mesenchymal transition (EMT) signaling pathway. The Hv-AuNPs demonstrated strong cytotoxic activity against lung cancer cells (IC_{50} = 23.68 μg/mL), and the nanoparticles effectively controlled cell migration and colony formation at 50 μg/mL. The reverse transcription polymerase chain reaction gene expression analysis confirmed that the Hv-AuNPs potentially downregulated the Vimentin expression at 50 μg/mL and exhibited high anti-cancer activity [55].

The antibacterial, antioxidant, and anticoagulant properties of κ-carrageenan were detected. Furthermore, *H. valentiae* is used to create the larvicidal efficacy of methanol extract against *Aedes aegypti* larvae at varied doses. The antibacterial zones of inhibition at various doses are compared to the increased activity against bacterial infections at 40 mg/mL. κ- Carrageenan is effective in all antioxidant activities, with overall antioxidant activity of 70.1 0.61 % of radical at a concentration of 250 g/mL. DPPH scavenging is effective in the suppression of (65.74 0.58 %) radical at a concentration of 160 g/mL, while hydroxyl scavenging (65.72 0.60 %) activity is seen at a concentration of 125 g/mL. κ-Carrageenan fraction anticoagulant actions (Activated partial thromboplastin time (aPTT) and prothrombin time (PT)) are investigated. Activated partial thromboplastin time activity is highest in *H. valentiae* and heparin sulphate (106.50) [56].

3. Critical analysis of the Pharmacological Potential and Economic Significance of *Hypnea* species

Taxonomically, the genus *Hypnea* comprises 63 accepted species names, 12 accepted varieties, and 1 accepted forma; In synonymy, there are 33 species names in the database of Algaebase at present [57]. Over the last decade, there has been a significant rise in the number of studies published on the metabolites identified in the *Hypnea* genus (Fig. 3). In this review, and based on the authentic published literature, we addressed the phytochemical and pharmaceutical of eight different species of the genus *Hypnea*. In the past centuries, different *Hypnea* species have also been widely used as a main ingredient in food recipes where they have a nutraceutical value and essential bioactive compounds including polysaccharides, particularly 'κ-carrageenans', polyphenolics, vitamins, tannins, saponins, terpenoids, alkaloids, sterols, and minerals. Species of the genus *Hypnea* also have been widely exploited to combat different diseases and complications due to their prominent antioxidant, anti-inflammatory, antibacterial, antiproliferative, gastroprotective, anticoagulant, enzyme inhibitor, and immunostimulatory potentials. Night species have been discovered as having considerable differences in their phytochemical and pharmacological activity, accounting for around 15 % of the *Hypnea* genus. Certain species in this genus have been thought to be a good source of food [58]. Analysis of the data provided on the phytoconstituents suggests notable deficiencies in our understanding of their involvement in the reported biological effects and health consequences of *Hypnea*, as well as the functions carried out by individual metabolites.

The phytochemical and pharmacological diversity of *Hypnea* and its metabolites was investigated. Its phytochemical composition and clinical uses vary significantly. Halogenated terpenes, meroterpenes, sterols, fatty acids, sulfated polysaccharides, and numerous nutrients are among the major phytochemical groups (Fig. 4). The genus *Hypnea* has been recognized as a valuable source of innovative natural compounds for therapeutic uses. Its antioxidant properties have been widely described (Fig. 4, Table 1–2).

Antimicrobial, antiproliferative, antioxidant, anti-inflammatory, gastroprotective, enzyme inhibition, and wound healing actions are among the pharmacological activities of the genus *Hypnea*. *H. musciformis* was the species that had undergone the most investigation. The phytochemical and pharmacological diversity of the genus *Hypnea* and its metabolites were considered. There is a significant variation in its phytochemical composition and clinical applications.
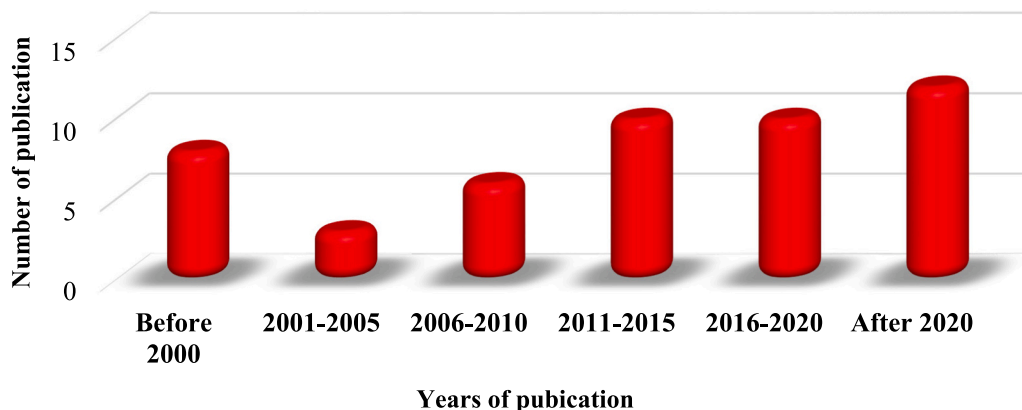

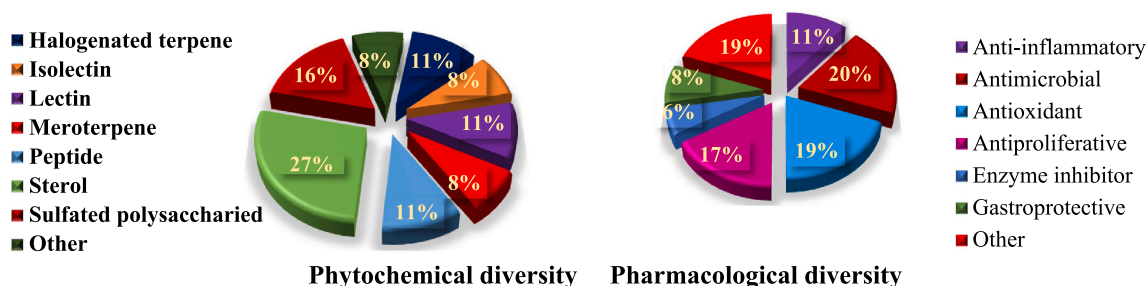**Fig. 3.** Publications about the genus *Hypnea*.

Fig. 4. Phytochemical and pharmacological diversity of genus *Hypnea*.

Table 1
Biological assays related to the therapeutic potential of *Hypnea* compounds.

No.	Compound name	Class		Activity	Reference
1	22-Dehydrocholesterol	Sterol	*H. flagelliformis*	–	[21]
2	Cholesterol	Sterol	*H. flagelliformis*	–	[21]
3	Oleic acid	Fatty acid	*H. flagelliformis*	–	[21]
4	Cholesterol oleate	Sterol	*H. flagelliformis*	–	[21]
5	(22*E*)-Cholesta-5,22-dien-3β-ol-7-one	Sterol	*H. flagelliformis*	–	[21]
6	23-Methyl-5 ~ −cholesta-l,22-diene-11,20-dihydroxy-7-one	Sterol	*H. musciformis*	–	[26]
7	5β-Cholest-l-en-20-hydroxy-7,11-dione	Sterol	*H. musciformis*	–	[26]
8	5β-Cholest-3-en-7,11-dione	Sterol	*H. musciformis*	–	[26]
9	20-Hydroxy-5α-cholest-22-ene-3,6-dione	Sterol	*H. musciformis*	–	[27]
10	6α-Hydroxy-cholest-4-ene-3-one	Sterol	*H. musciformis*	Antioxidant	[27]
11	6α-Hydroxy-cholest-4,22-diene-3-one	Sterol	*H. musciformis*	Porcine pancreas elastase inhibitor	[27]
12	2-(Tetrahydro-5-(4-hydroxyphenyl)-4-pentylfuran-3-yl)-ethyl-4-hydroxy benzoate	Meroterpenoid	*H. musciformis*	Antioxidant	[29]
13	2–2-[(4-Hydroxy benzoyl)-oxy]-ethyl-4-methoxy-4-2-[(4-methyl pentyl)oxy]-3,4-dihydro-2H-6-pyranylbutanoic acid	Meroterpenoid	*H. musciformis*	Antioxidant	[29]
14	3-((5-Butyl-3-methyl-5,6-dihydro-2H-pyran-2-yl)-methyl)-4-methoxy-4-oxobutyl benzoate	Meroterpenoid	*H. musciformis*	–	[29]
15	Epicatechin		*H. musciformis*	Antioxidant	[9].
16	Phloretin		*H. musciformis*	Antioxidant	[9].
17	10-Bromo-7, 12-dihydroxy-Δ3 4-laurene	Halogenated terpene	*H. pannosa*	–	[43]
18	Filiformin	Halogenated terpene	*H. pannosa*	–	[43]
19	Filiforminol	Halogenated terpene	*H. pannosa*	–	[43]
20	5-Deoxy-5-iodotubercidin	Halogenated tubercidin	*H. pannosa*	Adenosine kinase inhibitory Antiprofilative	([53]; [54])

Major phytochemical classes include halogenated terpenes, meroterpene, sterols, fatty acids, sulfated polysaccharides, and several nutrients (Fig. 3). The genus *Hypnea* has been identified as a valuable source for the development of novel natural products for clinical applications. Its antioxidant activities have been reported frequently (Fig. 4, Tables 1–2). The pharmacological activities of the genus *Hypnea* include antimicrobial, antiproliferative, antioxidant, anti-inflammatory, gastroprotective, enzyme inhibition, and wound healing activities. Additional research must be conducted to explore the bioactive metabolites obtained from *Hypnea*, with a focus on structure-activity relationship studies, possible mechanisms of action for clinical applications, and the synthesis of those phytochemicals in an economically viable manner. The level of sulphation influences the characteristics of the major κ- carrageenan kinds and is commercially relevant due to its remarkable gel-forming capabilities. κ- carrageenan is a significant economically important sulfated polysaccharide due to its outstanding gel-forming characteristics. κ- carrageenans are commonly employed in the food industry due to their remarkable physical functional properties such as gelling, thickening, gelling, and stabilizing. Carrageenan extracted from the genus *Hypnea* has been utilized in a variety of non-food goods such as medications, cosmetics, printing, and paper. Simultaneously, we are recording the underexplored regions that remain untapped within the realm of marine biodiversity, focusing specifically on bioactive compounds.

4. Conclusions

The genus *Hypnea* (family Cystocloniaceae) is a rich source of essential phytochemicals including phenols, tannins, saponins, flavonoids, terpenoids, alkaloids, and sterols. Several bioactive compounds and polysaccharides derived from *Hypnea* species have been found to have potent anti-inflammatory, antioxidant, antibacterial, antiproliferative, gastroprotective, anticoagulant, enzyme inhibitor, and immunostimulatory effects that are quite promising. Despite the widespread traditional utilization of red seaweeds, specifically *Hypnea*, across the globe, the understanding of its phytopharmacological capabilities remains inadequately limited. Investigation of the bioactive metabolites derived from *Hypnea* species should be combined with more in-depth structure-activity relationship studies, and with the elucidation of their possible mechanisms of action.

Abbreviations

^{13}C NMR   Carbon-13 nuclear magnetic resonance
^{1}H NMR   Proton nuclear magnetic resonance
5-HT4   Serotonin type 4receptor
A549   Lung cancer cell line
ABTS   2,2′-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid
Ag/AgCl-NPs   Biogenic silver and silver chloride nanoparticles

Table 2

Biological assays related to the therapeutic potential of *Hypnea* extracts.

No.	Species	Extract	Activity	Reference
1	*H. flagelliformis*	Ethyl acetate	Antiparasetic Antimicrobial Antiprofilative	[21]
2	*H. flagelliformis*	Aqueous methanol	Antiparasetic Antimicrobial Antiprofilative	[21]
3	*H. japonica*	Aqueous ethanol	Antiprofilative	[16]
4	*H. musciformis*	Ethanol	Antioxidant	[9]
5	*H. musciformis*	Aqueous PLS	Antidiarrhea	[30]
6	*H. musciformis*	Aqueous PLS	Anti inflammatory	[31]
7	*H. musciformis*	Aqueous PLS	Gastroprotective	[32]
8	*H. musciformis*	Aqueous PLS	Antioxidant Neuroprotective Antibacterial Antiprofilative	[33]
9	*H. musciformis*	Aqueous PLS	Immunostimulant	[34]
10	*H. musciformis*	Aqueous PLS	Antioxidant	[36]
11	*H. musciformis*	Aqueous PLS	Antifungal	[37]
12	*H. musciformis*	Aqueous PLS	Hemagglutination inhibition	[38]
13	*H. musciformis*	Methanol	Antihyperlipidemic Psychotropic Anxiolytic	[39]
14	*H. musciformis*	Ag/AgCl-NPs	Antiprofilative	[40]
15	*H. musciformis*	Ethanol	Analgesic Anti-inflammatory	[41]
16	*H. musciformis*		Antiviral	[42]
17	*H. pannosa*	Methanol	Antifungal	[47]
18	*H. pannosa*	Ethanol Methanol	Antioxidant	[47]
19	*H. pannosa*	Methanol Ethanol Aqueous	Antioxidant Antiemetic	[49]
20	*H. valentiae*	Methanol	antioxidant antimicrobial	[52]
21	*H. valentiae*	Gold nanoparticles	antioxidant Antiprofilative	[55]
22	*H. valentiae*	Methanol	Antibacterial Antioxidant Anticoagulant larvicidal	[56]

aPTT   Activated partial thromboplastin time
ATG-5   Autophagy related 5
AuNPs   Gold nanoparticles
Balb/c 3 T3   Murine fibroblast cell-line
CNS   Central nervous system
Da   Dalton
DPPH   2,2-Diphenyl-1-picrylhydrazyl
DW   Dry weight
EAC   Ehrlich ascites carcinoma cell line
EMT   Epithelial-mesenchymal transition
F1.0   Sulfated galactans F1.0
FM3A   Malignant neoplasms of the mouse mammary gland cell line
FRAP   Ferric-reducing ability of plasma
GalNAc/Gal   Disaccharide tumor marker of colon carcinogenesis
GC–MS   Gas chromatography–mass spectrometry
GH   Growth hormone
GlcNAc   N-Acetylglucosamine
GM1   Monosialotetrahexosylganglioside
HCA   *H. cervicornis* lectin
HCT-116   Colorectal cancer cell line
HeLa   Cervical cancer cell line

HML   *H. musciformis* lectin
Hm-SP   *H. musciformis* sulphate polysaccharide
HSV   Herpes simplex virus
i.p.   Intraperitoneal
IC_{50} Half maximal inhibitory concentration
IL-1   Interleukin 1
Kc   κ-Carrageenan
LC_{50} Lethal concentration 50
LDLs   Low-density lipoproteins
L-NAME   L-arginine methyl ester
MALDI-TOF   Matrix-Assisted Laser Desorption/Ionization Time of Flight
MCF-7   Human breast cancer cell line
MIC   Minimum Inhibitory Concentration
MPa   MegaPascal
MPO   Myeloperoxidase
Na+/K + -ATPase   Sodium/potassium adenosine-triphosphatase
p.o.   Per ora or 'by mouth
PLS   Sulphate polysaccharide
PPE   Porcine pancreas elastase
PT   Prothrombin time
SH-SY5Y   Human neuroblastoma cell line

Consent for publication

Authors read and approved the manuscript for the publication in Algal Research.

CRediT authorship contribution statement

Hani Saber: Writing – original draft, Conceptualization. **Mohammed I. Rushdi:** Writing – original draft, Validation, Supervision, Methodology, Conceptualization. **Abdullah A. Saber:** Writing – original draft, Software, Methodology, Conceptualization. **Usama R. Abdelmohsen:** Validation, Methodology, Investigation, Formal analysis. **Leonel Pereira:** Writing – review & editing, Conceptualization.

Declaration of competing interest

The authors declare that they do not maintain any financial or personal relationships with other people or organizations that could unduly influence this work.

Data availability

Data will be made available on request.

Acknowledgments

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