

Red Seaweeds as Resource of Bioactive Compounds and Therapeutic Potential: a Review on Anticancer Agents

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Abstract

The use of natural compounds derived from macroalgae constitute an alternating strategy in the creation of anticancer medications. Seaweed refers to macroalgae. Red seaweeds are rich in bioactive compounds, including alkaloids, carotenoids, mycosporine-like amino acids, phycobiliproteins, polyphenols, polysaccharides (carrageenan, porphyran), and lipids. Some of these bioactive compounds have demonstrated a unique chemical framework. The bioactive compounds have been investigated as an anticancer potential *in vitro* studies. Among these compounds content, polyphenols are the most promising as an anticancer, due to their abundance in the red seaweeds. This review provides bioactive compounds from red seaweeds and their natural sources. The review involves papers published from 2010 to 2025. The study might be used as a reference in development of red seaweed extracts in the future which include preclinical and clinical investigations, standardizations and formulations, molecular mechanisms as anticancer and toxicity studies.

Keywords: Anticancer, bioactive compound, macroalgae, pharmacological activity, seaweed

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Introduction

Seaweeds are important elements of traditional medicine and nutrition. Seaweed contains primary and secondary metabolites that may be helpful in the treatment of particular disorders. Seaweeds have many properties which can be developed in various fields or industries, including dietary supplements, pharmaceuticals, functional food, cosmetics, and other industrial applications [1]. Red seaweeds constitute a source of raw materials for extracting polysaccharides, which are an industrial product such as agar and carrageenan. These polysaccharides comprise the most abundant components of red seaweeds, which are not degraded by mammalian enzymes. Therefore, red seaweeds are a plant rich in fiber materials [2]. Polysaccharides are major constituents of red seaweeds. The polysaccharide content in red seaweeds is 70 % of the dried weight [3]. Red seaweeds are also rich in protein, lipids, vitamins, minerals, and essential bioactive secondary metabolites, which can be used to maintain human health [4]. Seaweeds, including red seaweeds, have been utilized as traditional medicine for generations, such as for anticancer [5].

Cancer remains a serious concern in many countries in the world, as one of the major causes of death. Cancer is still incurable, especially when it is late-stage or metastatic, even with major improvements in cancer treatments [6]. By 2022, it has been outlined by the International Agency for Research on Cancer that nearly 9.7 million cancer-related deaths and more than twenty million new cancer cases were recorded worldwide, along with non-melanoma skin cancers [7]. In detail, lung cancer has also become the most often diagnosed cancer (over 2.5 million new cases). Following lung cancer, breast cancer in women ranked second, accounting for 11.6% of diagnoses. The next leading causes of cancer deaths include colorectal, prostate, and stomach cancer, contributing 9.6%, 7.3%, and 4.9% of diagnoses, respectively. With a predicted 1.8 million mortalities, lung cancer was not only the most common cause of diagnosis but also the leading cause of cancer-related deaths (18.7% of all cancer-related deaths). Further, colorectal (9.3%), liver

(7.8%), breast (6.9%), and stomach cancer (6.8%) were the next most common causes of cancer-related fatalities, after lung cancer. These figures highlight the requirement for continued investigations, increased awareness, and the development of efficient therapeutic approaches. All of which are pivotal in the battle against these deadly illnesses [7].

Despite considering that red seaweeds are frequently utilized for a number of therapeutic purposes, writings on the chemical structures of these plants are poorly documented in the references. This review aims to provide information regarding the current bioactive compounds of red seaweeds as anticancer agents and their natural sources, including alkaloids, carotenoids, mycosporine-like amino acids, phycobiliproteins, polyphenols, carrageenan, porphyran, and lipid. These bioactive compounds were summarized from several species of red seaweeds, including *Ahnfeltiopsis flabelliformis*, *Caloglossa leprieurii*, *Chondria armata*, *Colpomenia sinuosa*, *Eucheuma muricatum*, *Hypnea concornis*, *Laurencia* sp., *Lophocladia* sp. *Mastocarpus pacificus*, *Porphyridium purpureum*, *Porphyra* sp., *Portieria hornemannii*, *Pyropia yezoensis*, *Odonthalia corymbifera*, *Rhodomela confervoides*, *Symphycladia latiuscula*,. The review includes articles published between 2010 and 2025.

Methods

The reviewed articles published between 2010 and 2025 were retrieved from the online databases which included Google Scholar, PubMed, Science Direct, Springer Link and Wiley Online. In the selection of literature search, main keywords included alkaloid or carotenoid or MAAs or phycobiliproteins or polyphenol or polysaccharides or carrageenan or porphyran or lipids + content of red seaweed. Besides, other keywords used were anticancer + activity of red seaweed. The review includes articles published between 2010 and 2025 that were based on the criteria of inclusion and exclusion. The criteria for chosen articles' inclusion were (1) all papers published between 2010 and 2025, (2) studies regarding the chemical scaffolds of the bioactive compounds, natural sources and anticancer properties of red seaweeds. The exclusion criteria were (1) all criteria as mentioned in the inclusion standards, however, related to brown and green seaweed, (2) those written in any language other than English.

Results and Discussion

Cancer diseases

Type of cancer

According to the National Cancer Institute (NCI), cancer refers to a condition where certain cells in the body grow and proliferate uncontrollably, leading to the formation of cancer and potentially spreading to nearby tissues and distant organs. Similarly, the World Health Organization (WHO) elaborates that cancer is a broad term that encompasses a diverse range of diseases capable of arising in close to any part of the body. Further, it was proposed that cancer is a disease marked by the unchecked growth of altered cells that undergo evolutionary changes through natural selection [8]. Later, the term cancer was recently defined as a multifaceted illness characterized by diverse cellular states and phenotypic variations [9]. As the symptoms and manifestations of cancer could vary widely from one individual to another, this reveals significant challenges for diagnosis and treatment.

Cancer encompasses a broad spectrum of types, generally categorized according to the specific type of tissue or cell from which they originate, and each category demonstrates unique characteristics, behaviors, and responses to treatment [10]. The primary categories of cancer include: (1) Carcinomas are the most prevalent, originating from epithelial tissues that line organs and body cavities. These include adenocarcinomas and squamous cell carcinomas, with common examples being lung, breast, and colorectal cancers; (2) Sarcomas are rarer and arise from connective tissues such as bone, muscle, and fat, including subtypes like osteosarcoma and liposarcoma; (3) Leukemias differ in that they do not form solid tumors but instead affect blood-forming tissues, leading to excessive abnormal white blood cells; (4) Lymphomas develop from the lymphatic system and are categorized into Hodgkin and non-Hodgkin lymphomas, often involving lymph nodes and sometimes other organs. Lastly, (5) melanomas stem from melanocytes, the skin's pigment-producing cells, and are particularly aggressive despite being a less common form of skin cancer [11]. Given the diverse nature of all these cancers, the development of cancer therapies and the implementation of personalized medicine, precisely customized diagnosis and treatment regimens, are critical for enhancing patient outcomes and quality of life. This method not only addresses the specific cancer type but also takes into account each patient's individual profile, resulting in a more effective healthcare environment.

Mechanism of anticancer

The advancement of cancer therapies marks a significant step forward in medicine, emphasizing the requirement to target the fundamental mechanisms that drive the growth and progression of tumor. Recently, several key approaches have been explored and investigated. One major approach is the induction of apoptosis, aiming to trigger and induce programmed cell death in malignant cells. Apoptosis is pivotal for controlling as well as regulating cell balance, and its

evasion could result in uncontrolled cell growth and diseases like cancer [12]. This strategy is pivotal as it selectively eliminates malignant cells while sparing healthy tissue, thus reducing the harmful side effects commonly associated with conventional treatments. Moreover, apoptosis-induced cell death causes minimal inflammation. Therefore, developing anticancer drugs that target this process has become a major area of interest [13]. In addition to the induction of apoptosis, cell proliferation inhibition targets the unregulated division of cancer cells that contributes to tumor development. By disrupting the signaling pathways responsible for excessive and aberrant cell proliferation, this therapy aims to reduce tumor size and restore the natural balance between cell growth and death [14].

Another advancement in cancer therapy is the use of anti-angiogenic treatments. This therapy targets the new blood vessel growth that provides tumors with the oxygen and nutrients they require to thrive [15]. Therefore, by disrupting the oxygen and nutrient supply of cancer cells, anti-angiogenic therapy has become a promising strategy for cancer therapeutic approaches [16]. To date, several anti-angiogenic agents have been discovered and developed, including monoclonal antibodies (Bevacizumab) and tyrosine kinase inhibitors (Sorafenib, Axitinib), etc. These anti-angiogenic agents could inhibit tumor growth by decreasing blood microvascular density [17]. Meanwhile, immunomodulation has been identified as an innovative approach in which treatments are intended to strengthen the body's immune system. Thus far, various immunotherapeutic strategies have been developed, including checkpoint inhibitors, monoclonal antibodies, therapeutic vaccines, and CAR-T cell therapy. These immunotherapies utilize the immune system to effectively target, recognize, and eradicate malignant cells [18].

Anticancer compounds from red seaweed

Alkaloids

Alkaloids in seaweed are classified into three groups, including: indole and halogenated indole alkaloids, phenylethylamine alkaloids and other alkaloids, such as 2,7-naphthyridine derivatives [19]. Indole and 2-phenylethylamine groups are the most common alkaloids in seaweeds. The indole group is the most alkaloid in red seaweed (Rhodophyta), while brominated and chlorinated alkaloids are dominant in green seaweed (Chlorophyta) [20]. Nevertheless, brominated indole alkaloids are also found in red algae, such as *Laurencia similis*. Polybrominated alkaloids from this algae include monoindole and bisindoles. Monoindole alkaloid consists of 1,3-dihydro-indole-2-one with 2-isopropylidene group and 3-benzyl group (**1**), 2-carboxylamino-benzoate and carbazole alkaloids [21]. The structure of bisindoles alkaloids consist of two indole groups i.e 3,3'-bis(2'-methylsulfinyl-2-methylthio-4,6,4',6'-tetrabromo)indole (**2**) [22]. Alkaloid of 2,7-naphthyridine (lophocladine B, **3**, Figure 1) derivatives are also found in some red algae [20].

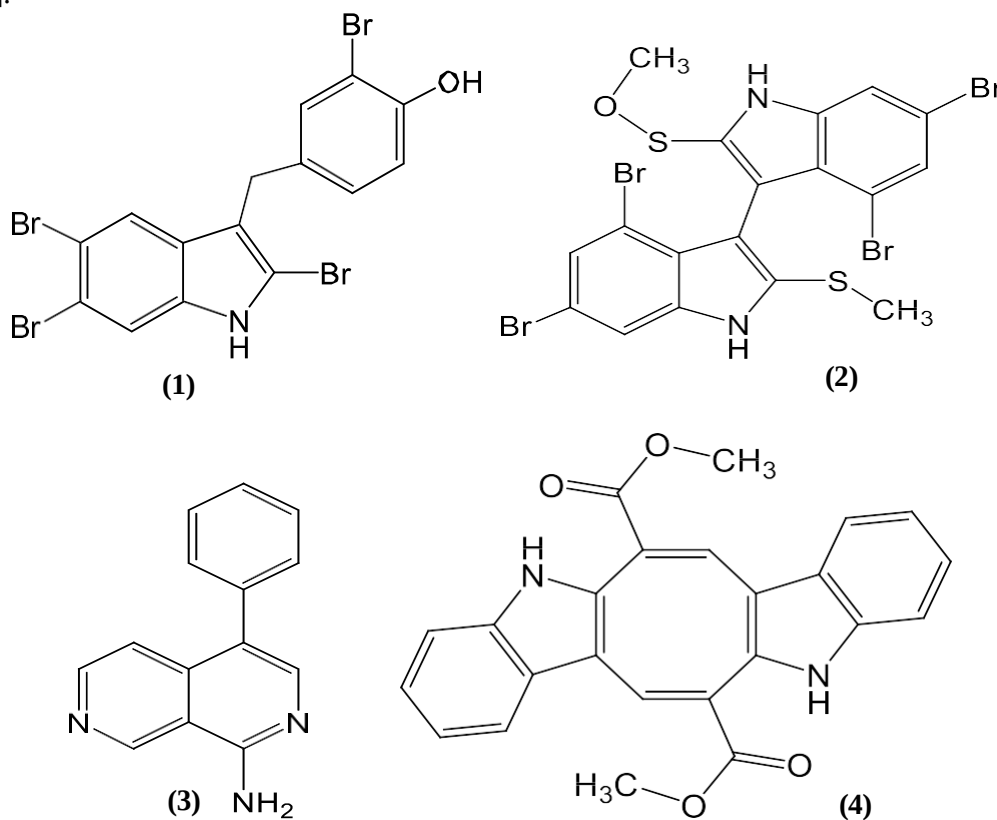


Figure 1. Structures of some seaweed alkaloids [20, 22]

Red seaweed produces certain alkaloids. Some red seaweeds produce indole alkaloid, such as caulerpin (dimethyl-6,13-dihydrodibenzo[b,i]phenazine-5,12-dicarboxylate methyl ester), including *Caloglossa leprieurii*, *Chondria armata*, *Colpomenia sinuosa*, *Eucheuma muricatum*, *Hypnea concornis*, *Laurencia majuscula* and *Laurencia cartilaginea* [23]. Lophocladine A and lophocladine B are a 2,7-naphthyridine alkaloid isolated from red alga *Lophocladia* sp. [24]. Lophocladine B (**4**) exhibits as anticancer (human leukemia cells) (HL-60, IC₅₀ 1 μ M) [20]. Caulerpin (**4**) belongs to indole group which have two indole functional groups that linked by an eight cyclic ring [25]. It has two carboxy groups within the ring. Caulerpin can isolated from some red seaweeds such as *Chondria armata*, *Laurencia dendroidea*, *Laurencia majuscula*, and *Caloglossa leprieurii*. Caulerpin suppresses hypoxia-inducible factor 1 (HIF-1), an essential target for cancer treatment, at concentration of 10 μ M [20].

Carotenoids

Red seaweeds are rich in carotenoids. Major carotenoids in red seaweeds are lutein and zeaxanthin (**5**). Some red seaweed carotenoids such as α -carotene, β -carotene, fucoxanthin (**6**), and violaxanthin (**7**) are found in low content [26]. A certain carotenoid with a unique structure, such as fucoxanthin has allene (C=C=C) group. In addition, fucoxanthin also has acetyl group (O-CO-CH₃) in the end cyclic structure [27]. The chemical structures of some seaweed carotenoids are shown in Figure 2.

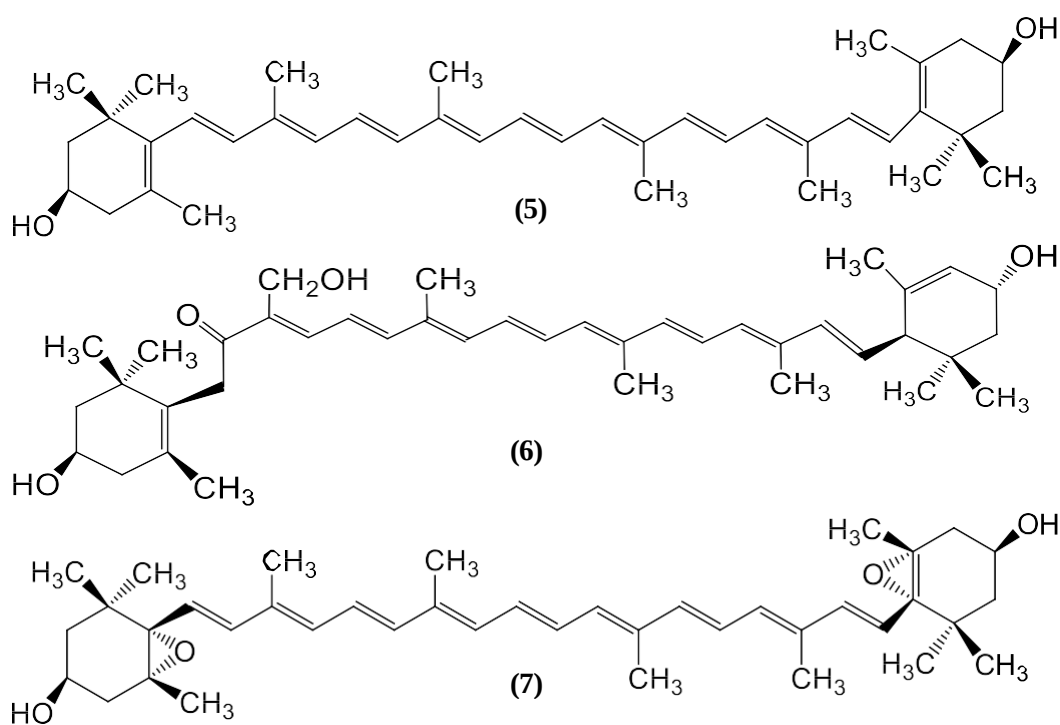


Figure 2. Structures of some seaweed carotenoids [28]

Seaweed carotenoids are generally located inside cell membranes in the chloroplast or accumulated in vesicles or cytoplasmic matrix [29]. Carotenoids are the most pigment distributed in nature, including red seaweeds, such as *Pyropia yezoensis* which belongs to Bangiales [30], *Gracilaria changii* [31]. Zeaxanthin is found as the main carotenoid in some species, such as *Gracilaria gracilis*, *Gracilaria vermiculophylla*, *Osmundea pinnatifida* and *Vertebrata lanosa*. Zeaxanthin from the rhodophyte *Porphyridium purpureum* has been demonstrated as an inducer of apoptosis of human melanoma cells [32].

Mycosporine-like amino acids (MAAs)

MAAs can be divided into two groups based on its substitution i.e. mono-substituted MAAs and di-substituted MAAs [33]. The structure of mono-substituted MAAs comprises a cyclohexanone with nitrogen substituent on the C₃ position [34]. The MAAs of this type from marine sources are mycosporine-glycin (**8**) and mycosporine-aurine. The di-substituted MAAs comprises a cyclohexenimine with glycine subunit on the C₃ and amino acid on the C₁. These type MAAs such as mycosporine-2-glycine, mycosporine-glycine-glutamic acid, porphyra-334 (**9**) and shinorine (**10**) [35]. It also contains amino alcohol (asterina-330 (**11**), palythanol) or enaminone chromophore (palythene (**12**), usujirene) [33]. Besides, the glycine unit can also be substituted by methylamine, including mycosporine-methylamine-serine and mycosporine-methylamine-threonine (**13**). The imine substituent of the cyclohexenimine ring system can also bind

sulphate esters (palythine-serine-sulphate) or glycosidic bonds (13-O- β -galactosyl-porphra-334) [34]. The chemical structure of some seaweed MAAs are shown in Figure 3.

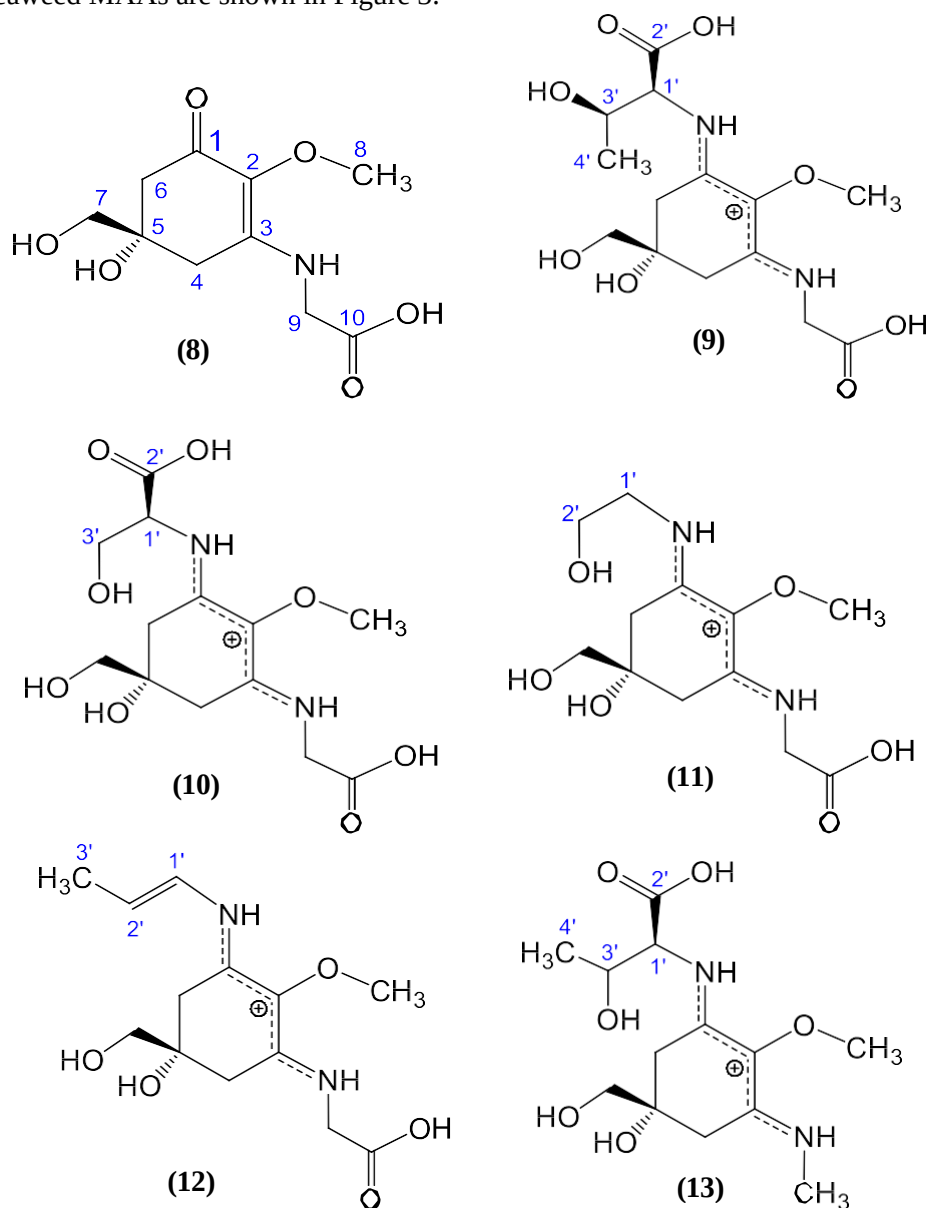


Figure 3. Structures of some seaweed MAAs [36]

The most abundant MAAs from red seaweeds are asterina-330, mycosporine-glycine, palythene, palythine, palythanol, porphyra-334, shinorine and usurijene (Orfanoudaki *et al.*, 2019). *Porphyra umbilicalis* mainly synthesizes asterina-330, palythine, palythanol, porphyra-334 and shinorine [37]. This study reported that the porphyra-334 content was 23%, while the asterina-330 content was 72% of the total MAAs. Based on this study, mycosporine-serinol can only be found in *Lichina pigmaea*. Porphyra-334 and shinorine from red seaweed have been reported as activators of the cytoprotective Kelch-like ECH-associated protein 1-nuclear factor erythroid 2 (Keap1-Nrf2) pathway. It means that these compounds can potentially be developed as therapeutic and chemopreventive agents [38].

Phycobiliproteins

Phycobiliproteins are a photosynthetic pigment that has been given the characteristic colour of red seaweeds [39]. Phycoerythrin (**14**) constitutes chromophores which absorb in the bright pink region (540-570 nm), phycocyanin (**15**) absorbs in the dark cobalt blue region (610-620 nm), while allophycocyanin (**16**) (Figure 4) absorbs in the brighter aqua blue region (650-670 nm) [40]. In red algae, these phycobiliproteins chromophores gather together with protein referred to as phycobilisome [41]. Phycoerythrin is visually seen as red color. Phycocyanin, namely phycoerythrocyanin and R-phycocyanin appears purple, while C-phycocyanin appears deep blue. Besides, allophycocyanin seems greenish blue. In the marine red algae, R-phycoerythrins are the most abundant phycobiliprotein chromophores [42].

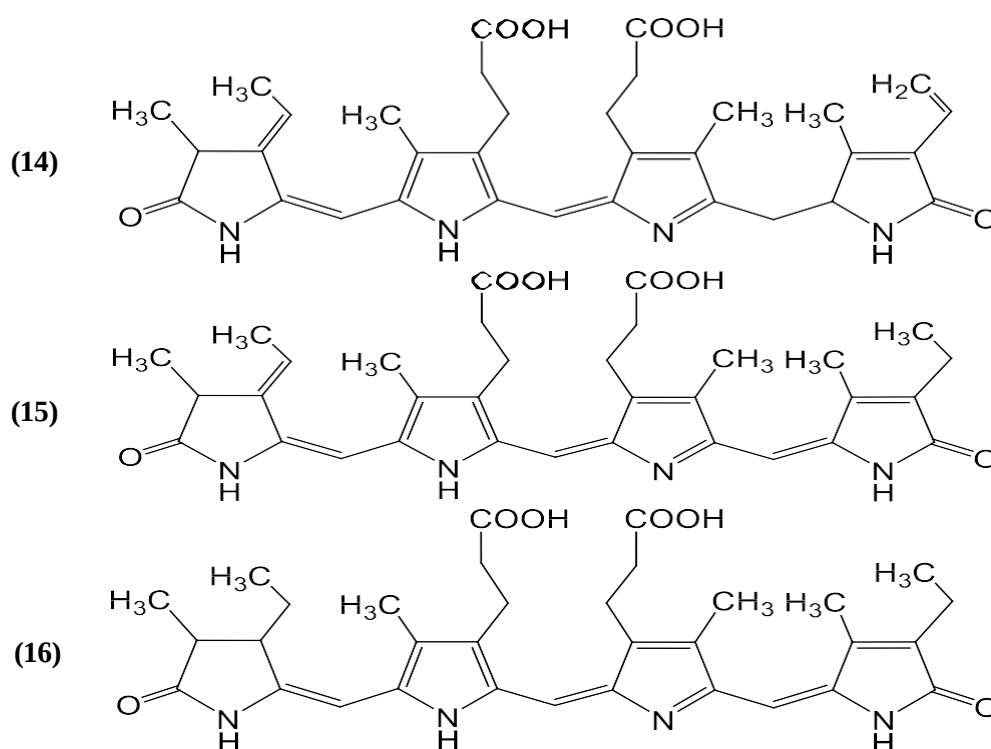


Figure 4. Structures of some phycobiliproteins [40]

Phycobiliproteins are primarily found in cyanobacteria and red algae (Rhodophyta). Rhodophyta as a source of phycobiliproteins include *Kappaphycus alvarezii* [42], and *Polyshiponia urceolata* [41]. *Chondrus crispus*, *Palmaria palmata* and *Porphyra dioica* have been found to contain phycocyanin and phycoerythrin [43]. *Porphyridium cruentum* is a source of phycobiliprotein, primarily B-phycoerythrin. The content is about 42% of all colorant proteins [44]. A previous study has shown that R-phycoerythrin isolated from the red seaweed *Portieria hornemannii* revealed cytotoxic effects against the HT-29 cell line with IC₅₀ values ranging from 77 to 98 µg/ml [45].

Polyphenol

Red seaweed commonly contains polyphenol constituents. These compounds include bromophenol, terpenoids and tichocarpols. The red seaweeds which consist of bromophenol include *Odonthalia corymbifera*, *Rhodomela confervoides*, *Symphycladia latiuscula* [46-47]. Terpenoids constituent can be obtained from *Callophycus serratus* and *Laurencia* sp. Tichocarpols (phenylpropanoid derivatives) are polyphenol obtained from red seaweed *Tichocarpus crinitus* [48]. *Vidalia obtusiloba* contains bromophenol i.e. vidalols A (17) and B (18) (Figure 5) [49]. Marine macroalgae which include red seaweed commonly consist of polyphenol such as flavonoids, rutin, quercetin, catechol, and myricetin [37].

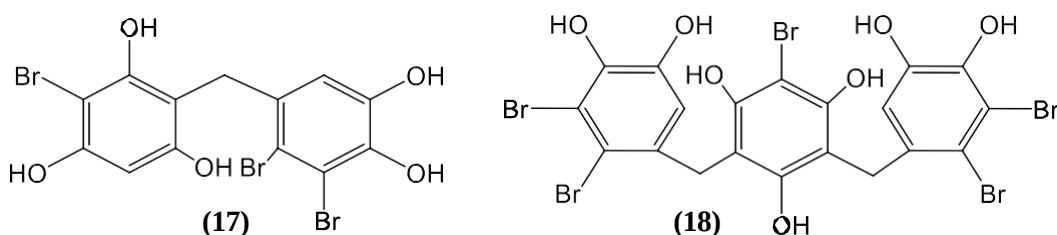


Figure 5. Structures of some polyphenols [49]

Red seaweed *Eucheuma cottonii* is rich in polyphenols which has an activity as breast tumour protective through by inducing apoptosis, improving oxidative status and downregulating the endogenous active estrogen biosynthesis [50]. 3-bromo-4,5-dihydroxy benzoic acid methyl ester and 3-bromo-4,5-dihydroxy-benzaldehyde isolated from *Rhodomela confervoides* belong to bromophenols that act as anticancer [49].

Carrageenan

Carrageenans consist of about fifteen forms based on the position, number of sulphate groups, and 3,6-anhydrogalactose content [51]. The types of carrageenans are beta (β), iota (ι), kappa (κ), lambda (λ), mu (μ), nu (ν) and theta (θ). Carrageenans are hydrophilic sulphated linear galactans, which can be extracted from red seaweeds. *Chondrus*, *Eucheuma*, *Fulcellaria*, *Gigartina*, *Hypnea Kappaphycus* and *Irridae* are red seaweeds which are the sources of carrageenans [52]. Carrageenans content in these seaweeds can reach up to 50% of the dry weight. Carrageenan extracted from *Eucheuma spinosum* mostly consists of ι -carrageenan. The natural sources of λ -carrageenan are *Gigartina* sp. and *Chondrus* sp. [53]. Red seaweed of the Phyllophraceae, such as *Gymnogongrus torulosus* (*Anhfeltia torulosa*) is a major source of ι -carrageenan [54]. Carrageenan extracted from *Kappaphycus alvarezii* (*Eucheuma cottonii*) is mainly composed of κ -carrageenan. This species also contains the other types i.e. ι -, λ -, ν - and μ -carrageenan [55]. Kappa/iota-carrageenan and iota/kappa-carrageenan produced from *M. pacificus* and *A. flabelliformis* revealed cytotoxic effects against some solid tumors at the concentration < 1 mg/mL and induced apoptosis [56]. The chemical structure of carrageenans is shown in Figure 7.

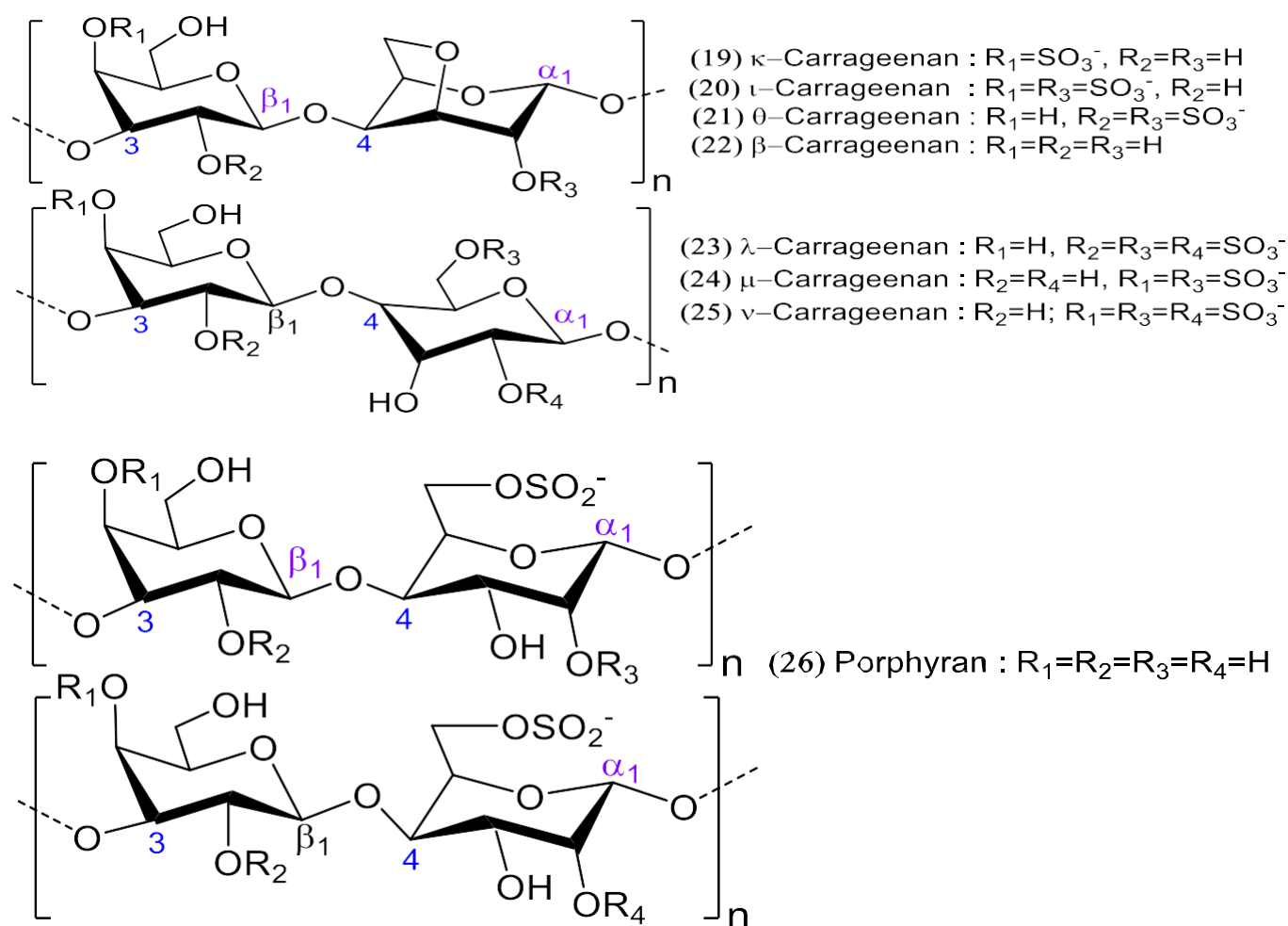


Figure 7. Chemical structures of carrageenans and agar precursor [52-53]

Porphyran

Porphyran (26) (Figure 7) is a linear polysaccharides with basic structure composed of alternating 3-linked β -D-galactose and 4-linked 3,6 anhydro- α -L-galactose residues. L- and D-galactose are linked by α -1,3 and β -1,4 glycosidic linkages [57]. Porphyran is a precursor of agar [53]. The structure of porphyran is varied, from species to species. Porphyran isolated from *Porphyra vietnamensis* consists of 6-O-methyl-D-galactose and 3,6 anhydro-L-galactose units [58]. Porphyran extracted from *Porphyra umbilicalis* consists of 4-linked 6-O-sulfo- α -L-galactopyranose and 3-linked 6-O-methyl- β -D-galactopyranose residues.

The content of sulphated disaccharide units in this species is 49%. The porphyran isolated from *Porphyra capensis* has structure of alternating 3-linked β -D-galactose and 4-linked α -L-galactose-6 sulphate or 3,6 anhydro- α -L-galactose

units. The alternating 3-linked β -D-galactopyranosyl and 4-linked α -L-galactosyl 6-sulphate residues constituted a type of backbone from porphyran which are extracted from *Porphyra haitanensis* [57].

Porphyran is a polysaccharide obtained from the cell wall and intercellular regions of red seaweed from the genus *Porphyra* sp. such as *Porphyra capensis*, *Porphyra haitanensis*, *Porphyra umbilicalis*, *Porphyra vietnamensis*, *Porphyra yezoensis*. *Porphyra* known as nori or laver [57-59, 53]. Porphyran can also be obtained from the genus *Pyropia* sp. such as *Pyropia yezoensis*. Porphyran is a polysaccharide that may be used in medical development. Porphyran showed inhibit tumor necrosis factor- α (TNF- α) secretion by LPS-stimulated RAW 264.7 cells [60]. Porphyran has also been reported as anti-cancer and hypolipidemic [61].

Lipid

Lipid has substituent on the sterol side chain at the C₂₄ position which comprises nine or ten atom carbons, while the side chain of cholesterol consists of eight atom carbons [62]. The nucleus of sterol consists of four rings, a hydroxyl group at C₂ and side chain. Rings A and D play role an important role in the function of sterol, whereas the OH group at C₃ in ring A, contributes to hydrogen-bond interaction. The C₄ takes part in conformation of ring A. The number and position of double bonds in the nucleus have an effect on the shape of sterol. The stereo chemistry of alkyl at the C₂₄ position contributes to intermolecular contacts of phytosterols (27) (Figure 8) [63]. Compounds of 22-dehydrocholesterol, cholesterol, oleic acid and stigmasterol are lipid isolated from *Gracilaria salicornia*. Constituent of (22E)-cholesta-5,22-dien-3 β -ol-7-one is phytosterols isolated from *Hypnea flagelliformis*. This molecule contains carbonyl group in ring B [64].

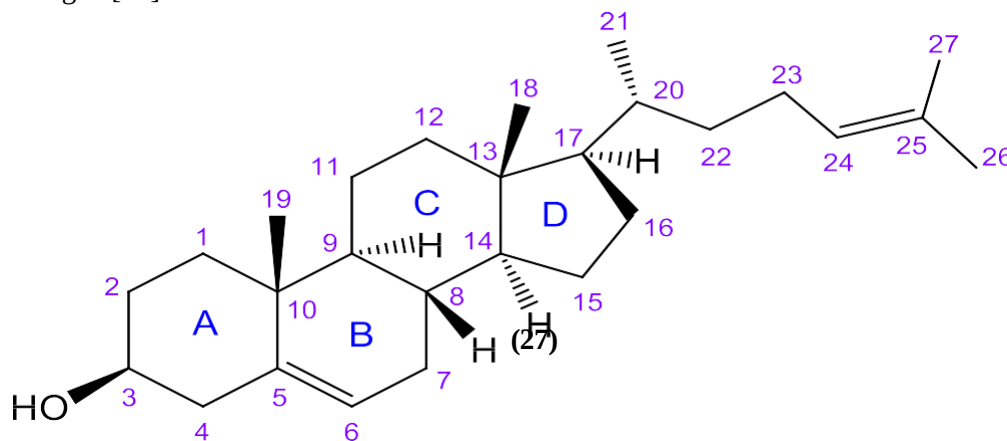


Figure 8. Chemical structure of phytosterol [63]

Red seaweed produces many biologically active phytochemicals including lipid. The content of lipid in *Gracilaria* seaweed is 1.98% of the dry weight. Red seaweed *Gracilaria gracilis* contains lipid, fatty acids and sterol [65]. *Chondrus crispus* is red seaweed which contains galactolipids [66]. *Solieria chordalis* contains total lipid of 2.96%, glycolipid of 38.50% and phospholipid of 23.70%, while *Solieria robusta* contains total lipid 2.80% of the dry weight [67]. A sterol fraction containing cholesterol, β -sitosterol and campesterol from red macroalgae, *Porphyra dentata*, significantly decreased the reactive oxygen species and arginase activity of myeloid derived-suppressor cells in tumor-bearing mice [68].

In summary, red seaweeds represent a promising natural source of diverse bioactive compounds with notable anticancer properties. As shown in Table 1, these compounds, ranging from sulfated polysaccharides and polyphenols to alkaloids and phycobiliproteins, exert anticancer effects through multiple mechanisms.

Future Directions and Limitations

Bioactive compounds of red seaweeds have demonstrated promise in fighting against cancer. More investigation is required before clinical use. Some investigations are still needed to evaluate the successful effects of red seaweed compounds as an anticancer. This process includes preclinical study, specific (marker compounds) and non-specific standardization of red seaweed extracts, examining the seaweed chemicals' mechanisms of action as an anticancer, formulation, and toxicity study of red seaweed extracts [69]. Red seaweeds constitute an edible macroalgae which can be consumed as a nutraceutical [70]. Nutraceutical supplements taken in large quantities on a daily basis may not be safe and may have harmful side effects. Therefore, it is important to separate the preventive dose from the therapeutic dose. A therapeutic dose solely stops the proliferation of cancer cells, but a prophylactic dose protect both healthy and malignant cells [71].

Table 1. Several classes of compounds in red seaweeds species and their anticancer activities

Class of compounds	Example of compounds	Example of source (Red Seaweed)	Biological activity
Alkaloids	Lophocladine B	<i>Lophocladia</i> sp.	a. Cytotoxic effect against solid cancer and hematological malignancies. b. IC ₅₀ values = 3.1 μ M (MDA-MB-435) and 1 μ M (HL-60) c. Induce apoptosis and cell cycle arrest d. Act as a microtubule inhibitor
	Caulerpin	<i>Caloglossa leprieurii</i> , <i>Chondria armata</i> , <i>Colpomenia sinuosa</i> , <i>Eucheuma muricatum</i> , <i>Hypnea concornis</i> , <i>Laurencia majuscula</i> , <i>Laurencia cartilaginea</i> , <i>Laurencia dendroidea</i>	a. IC ₅₀ values $\geq$ 20 μ M against several solid tumor cells b. Inhibits HIF-1 (anti-cancer target, effective at 10 μ M) c. Repress metastatic MDA-MB-231 cells migration
Carotenoids	Zeaxanthin	<i>Porphyridium purpureum</i>	a. Induces apoptosis in human melanoma cell line (A20258) with IC ₅₀ value of 40 μ M b. Promotes chromatin condensation, induces the A2058 cells accumulation (in sub-G1 phase) and triggers DNA fragmentation
Mycosporine-like amino acids (MAAs)	Shinorine Porphyra-334	<i>Porphyra umbilicalis</i> , other red seaweeds	a. Cytoprotective effect by stimulating and activating Keap1-Nrf2 cytoprotective pathway
Phycobiliproteins	R-Phycoerythrin	<i>Portieria hornemannii</i>	a. Cytotoxic effects against the HT-29 cell line b. IC ₅₀ values ranging from 77 to 98 μ g/ml
Polyphenols	Bromophenols	<i>Odonthalia corymbifera</i> , <i>Rhodomela confervoides</i> , <i>Symphyclocladia latiuscula</i>	a. Cytotoxic effect against various cancer cell lines (IC ₅₀ values $\leq$ 15 μ M)
	Polyphenols (catechin, rutin, and quercetin) in the methanolic extract	<i>Eucheuma cottonii</i>	a. Antiproliferative effect against MCF-7 cells, induces apoptosis, and downregulates the endogenous oestrogen biosynthesis
	3-bromo-4,5-dihydroxy benzoic acid methyl ester; 3-bromo-4,5-dihydroxy-benzaldehyde	<i>Rhodomela confervoides</i>	a. Cytotoxic effect against several cancer cell lines (A549, Bel-7402, and KB) with IC ₅₀ ranging from 12.5–40.1 μ M
Carrageenans	Carrageenans and Their Oligosaccharides	<i>Mastocarpus pacificus</i> <i>Ahnfeltiopsis flabelliformis</i>	a. Cytotoxic and antiproliferative activity against several cancer cell lines (HCT-116, DLD-1, HT-29, HEK-923) b. Induce apoptosis
<u>Porphyran</u>	<u>Porphyran</u>	<i>Pyropia yezoensis</i>	a. Cytotoxic effect against the RAW264.7 cell line at the concentration $< 1000 \mu\text{g mL}^{-1}$ b. Antiproliferative effect against colorectal and gastric cell lines c. Promoting apoptosis and cell cycle arrest
Lipid/cholesterol	Sterol fraction that contains some bioactive compounds (campesterol, cholesterol, β -sitosterol)	<i>Porphyra dentata</i>	a. Antiproliferative effect against 4T1 cells b. Antitumor growth in 4T1 cell-implanted tumor BALB/c mice b reduced ROS & arginase in MDSCs of tumor-bearing mice

Conclusion

This review presents bioactive compounds from red seaweeds, including alkaloids, carotenoids, mycosporine-like amino acids, phycobiliproteins, polyphenols, carrageenan, porphyran, and lipids. It is well known that red seaweeds are a valuable source of bioactive substances with a wide range of bioactivities, especially those related to the prevention and treatment of cancer. Mechanistically, red seaweed compounds act by inhibiting cell proliferation, inducing apoptosis, and arresting the cell cycle, disrupting microtubule function, modulating oxidative stress responses, or influencing immune pathways. Among these, apoptosis induction and oxidative stress modulation appear to be the most commonly reported and potentially clinically relevant mechanisms. Looking forward, research on red seaweeds is expected to focus on pinpointing the particular bioactive substances that contribute to these effects, elucidating their modes of action, and assessing their efficacy and safety in further intricate biological systems. Comprehensive studies at both preclinical and clinical stages will be essential to fully establish their therapeutic potency. Moreover, the investigation and exploration of innovative formulations and delivery systems may enhance the effectiveness of therapies derived from red seaweeds. In summary, red seaweeds represent a promising and natural source of anticancer, offering significant potential for advancing strategies in cancer prevention and treatment. Unlocking the full potential of these remarkable marine resources requires ongoing research in this field.

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Declarations

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