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# A review article of phytochemical constitutions of the Sargassum Genus

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**Abstract**

The bioactive secondary metabolites of Sargassum species have not been completely investigated, while, their major constituents are known and used in folk medicine.
Furthermore, several unique compounds have been isolated as meroterpenoids, pholorotanins and fucoidans from Sargassum species, which may be responsible for their medicinal activities. Other compounds such as phytosterols, sulfoglycolipids, and polyunsaturated fatty acids have been barely reported in this genus
This review focuses on the chemical constituents from sargassum species. The present review provides a significant clue for further research of the chemical constituents from the sargassum species as potential medicines. It is important to mention that the occurrences of classes of secondary metabolites in seaweeds are a point deserving consideration, because it may end up useful in prospects of pharmacologically active substances.

**Keywords:** Phytochemical, Sargassum Genus, Alginates, Meroterpenoids, Phlorotannins

## Introduction

Seaweeds are considered as a crucial source of polysaccharides presented in different phyla as Phaeophytes or brown seaweed (e.g., fucoidans), Rhodophytes or red seaweed (e.g., carrageenan), and Chlorophytes or green seaweed (e.g., ulvan) (Patel 2012) [51]. These polysaccharides are presented as a component of their cell wall/extracellular matrix which has a structural function. They provide strength and flexibility as well as allow them to adapt to a variety of water movements in which they grow. They also swell in water and preserve hydration (Rinaudo, 2008) [60].
Generally, brown seaweed sulfated polysaccharides (fucoidan)and alginates are comprising up to 45% dry weight, while cellulose only about 1–8% (Fig.2.3) (Rioux and Turgeon 2015) [61]. Their cell wall system model is mostly an assembly of two polysaccharide-based networks, the first layer composed of FCSPs interlocking a b- glucan scaffold, embedded in the second layer which made up of alginates and cross- linking polyphenols. Proteins, glycoproteins, halogenated and/or sulfated phenolic compounds known as phlorotannins, halide compounds such as iodide, and other ions as calcium, are additional components in their cell walls. Cell wall rigidity is likely controlled by the tuning of alginate fine structure, calcium ion bridging, and polyphenol cross-linking, while sulfated polysaccharides probably play a key role in the adaptation to osmotic stress (Deniaud-Bouët *et al*. 2014) [12].
*Sargassum* polysaccharides are belong to two main groups, fucoidan, alginate and laminaran. In general, *Sargassum* contains more alginate, and less fucodian and laminaran. The bioactive polysaccharides structures have not been totally characterized due to their complexity (L. Liu, *et al*., 2012) [42].

## Alginates

Alginate is a sodium, calcium, or magnesium salt of alginic acid (COOH vs. COONa for sodium alginate). Alginate is a linear polysaccharide consisting of β-D- mannuronic acid (M) and α-L-guluronic acid (G) bound with b-(1,4) (or a-(1,4) in GG block) (Fig.7). In general, mannuronic and guluronic acid ratio is 1:1, but these ratios may change, based on the age, seaweed species, season and the harvest place. The two monomers MM or GG type are called homogeneous block, while MG or GM blocks are called mixed blocks (Fig.1). According to the arrangement of the blocks, the glycosidic linkage position is called di-equatorial (MM), di-axial (GG), equatorial- axial (MG), or axial-equatorial (GM) (Rioux and Turgeon 2015) [61].

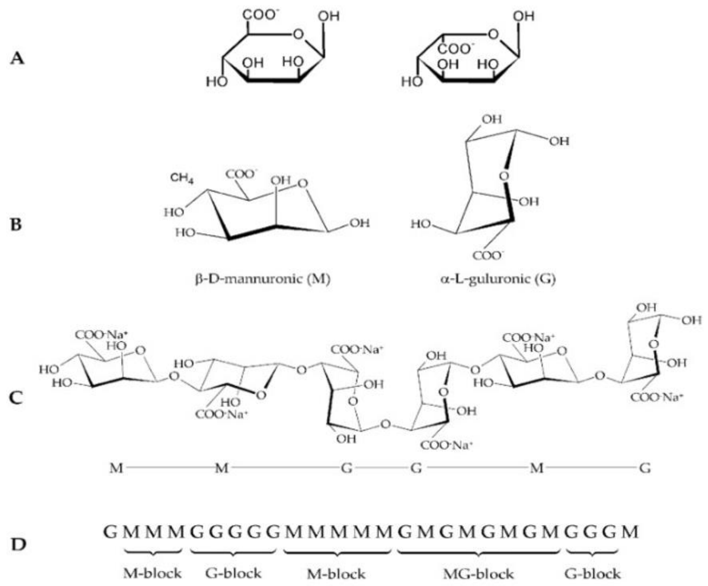


**Fig 1:** Structure of alginates: (A) alginate monomers, (B) chemical structure of monomers, (C) chain conformation, and (D) block distribution (Silva, *et al.*, 2017) [65].

Although, alginates have not any nutritional value, nowadays researchers revealed that, alginates isolated from *Sargassum* had anticancer (in vivo) (Torres, *et al.*, 2007: Fujihara and Nagumo, 1992) [71, 17], antiviral (in vitro) (Fenoradosoa, *et al.*, 2010) [16] and hypolipidemic (in vivo) effects (Fenoradosoa, *et al.*, 2010) [16].

*Sargassum* alginates have a wide range of molecular weights (13–330 kDa), which may rely on the species, season, age, part of seaweeds and the extraction procedure (L. Liu, *et al.*, 2012) [42]. *Sargassum* have been known as producers of alginates with varying M/G ratios) are mention in Table 1.

**Table 1:** Alginates composition (%) obtained from some Sargassum species

| Sargassum species | | M/G | $F_M$ | $F_G$ | FMG | FGG | FMM | η | Reference |
|---|---|---|---|---|---|---|---|---|---|
| *Sargassum vulgare* | HV | 1.27 | 0.56 | 0.44 | 0.01 | 0.43 | 0.55 | 0.04 | (Torres, *et al.*, 2007) [71] |
| | LV | 1.56 | 0.61 | 0.39 | 0.03 | 0.36 | 0.58 | 0.06 | |
| *Sargassum turbinarioides* | | 0.94 | 0.48 | 0.52 | 0.25 | 0.39 | 0.36 | 0.5 | (Fenoradosoa, *et al.*, 2010) [16] |
| *Sargassum angustifolium* | | 0.89 | 0.47 | 0.53 | 0.14 | 0.39 | 0.33 | 0.56 | (Gholamipoor, *et al.*, 2013) |
| *Sargassum muticum* | | 1.08 | 0.52 | 0.48 | 0.09 | 0.39 | 0.43 | <1 | (Mazumder, *et al.*, 2016) |
| *Sargassum natans* | | 0.47 | 0.32 | 0.68 | 0.07 | 0.61 | 0.25 | - | (Rhein- knudsen, *et al.*, 2017) |
| *Sargassum vulgare* | | 0.70 | 0.41 | 0.59 | 0.10 | 0.49 | 0.31 | - | |

M: manuronic acid; G: glucouronic acid; $F_{MG}=F_{GM}$; η: viscosity; HV&LV: high viscosity & low viscosity

Fucose-containing sulfated polysaccharides Generally, fucoidan is a water-soluble complex sulfated heteropolysaccharide and do not develop highly viscous solutions. It is composed of L-fucose, D -uronic acid, D -galactose, D -xylose, and L-fucose sulfate; with various proportions of each composed. It also contains other monosaccharides as, D-glucose and D -mannose.

Fucoidan backbone build of two chain structures, the main chain with α-L- fucopyranose linked by (1→3) and (1→4) and the branch chain with (1→3)-α-L- fucopyranose. Sulphate substitutions can be presented at the C-2 or C-4 (rarely on C- 3) positions of both skeletons. The composition and structure of fucoidan is dependent on seaweed species, geographic location, harvesting season, part used for extraction, and the extraction procedures (Kalimuthu and Kim 2015) [29]. Different chemical structures of fucoidans were proposed from certain *Sargassum* species as *Sargassum fusiforme* (Fig.5) (B. Li, *et al.*, 2006) and *Sargassum binderi* (Fig..2) (Lim, *et al.*, 2016) [41].

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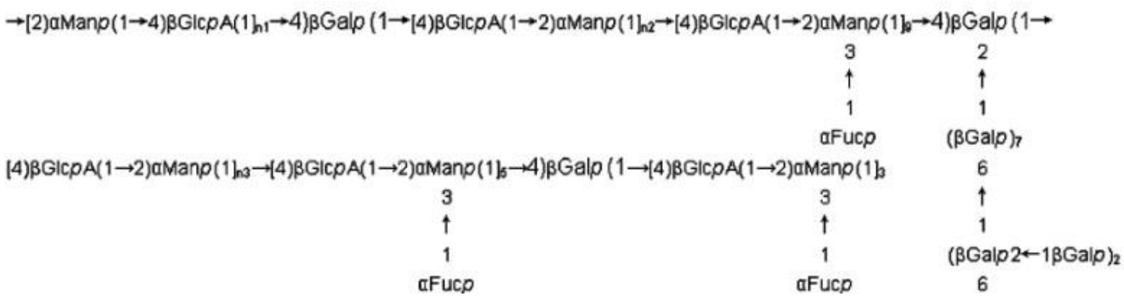


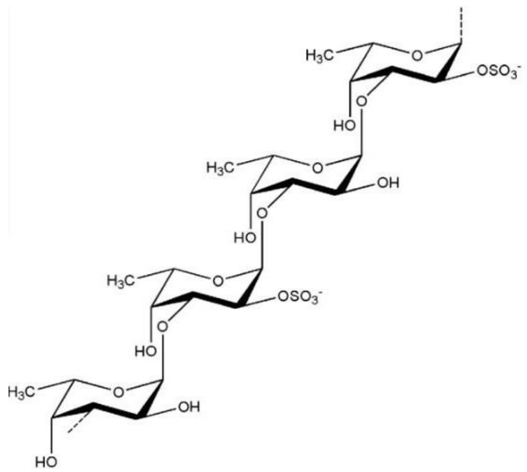



**Fig 2:** Presumptive model structure of fucoidan isolated from Sargassum binderi (Lim, *et al*., 2016) [41]

In general, the biological activity of sulphated polysaccharide is connected to their molecular weight, sugar type, sulphate content and sulphated position. Additionally, their molecular linkage type and geometry have a role in their activities (Suresh, *et al*., 2013 [69]; Zhuang, *et al*., 1995). W. Guan, *et al*., (2015) and Sanjeewa, *et al*., (2018) confirmed that the high molecular weight polysaccharides and high sulfated content had a significant anti-inflammatory activity (Sanjeewa, *et al*., 2018; G. Wu, *et al*., 2015). *Sargassum* fucoidans have wide spectrum of pharmacological activities including anticancer (Ye, *et al*., 2008) [75], antioxidant (Marudhupandi, *et al*., 2014) [43], anti-inflammatory (J. Y. Kang, *et al*., 2008 [30]; X. Liu, *et al*., 2016), antimicrobial (Ashayerizadeh, *et al*., 2019) [4], anticoagulant (Abdel-Fattah, *et al*., 1974; Dore, Faustino Alves, *et al*., 2013; Duarte, *et al*., 2001) [1, 14, 15], hypolipidemic (Kolsi, *et al*., 2017; Cuong, *et al*., 2014) [34, 11], immunomodulatory effect (Han, *et al*., 2017) [23], anti-vasculogenic (M. C. Chen, *et al*., 2015) [9], and liver and renal protective activities (Kuznetsova, *et al*., 2016; Chale-dzul, *et al*., 2019) [37, 8]. Moreover, *Sargassum* fucoidans have antiviral activity against many viruses as herpes simplex virus type-1 (HSV-1), type-2 (HSV-2) (Sinha, *et al*., 2010), hepatitis A virus (HAV) (Mohsen, *et al*., 2007) [46], coxsackie virus (CVB 3), human cytomegalovirus (HCMV) and human immunodeficiency virus type-1 (HIV-1) (Dinesh, *et al*., 2016; Zhu, *et al*., 2004) [13, 77]. Fucoidan from *Sargassum* spps. represent a clear structural variation due to its natural biodiversity. The same specific *Sargassum* spps. possibly contained different structural fucoidans. Some of them are represented in Table 2.

**Table 2:** Some Fucoidan compositions isolated from Sargassum species

| ***Sargassum* species** | | **Yield (%)** | **Suga r (%)** | **Sulfate (%)** | **Uronic acid (%)** | **Monosaccharide composition and mole ratio** | **M. wt (K.D a)** | **Reference** |
|---|---|---|---|---|---|---|---|---|
| *Sargassum tenerrimum* | | 31 | 59 | 2 | 9 | Fuc/Xyl/Man/Gal/Glc 73:15:Tr:9:3 | 30 | (Sinha, *et al*., 2010) |
| *Sargassum plagiophyllum* | | 23.7 | 63.3 | 21.9 | 12.6 | Fuc/Gal/Xyl/Man 70.8:13.5:2.5:11.2 | 35 | (Suresh, *et al*., 2013) [69] |
| *Sargassum swartzii* | FF1 | 21.4 | 61.8 | 19.2 | 17.6 | Fuc/Gal/Xyl/Man 51.5:19.2:5.1:12.9 | 45 | (Dinesh, *et al*., 2016) [13] |
| | FF2 | 44.8 | 65.9 | 24.5 | 13.4 | Fuc/Gal/Xyl/Man 58.5:16.3:3.3:14.3 | 30 | |
| *Sargassum pallidum* | SPC -60 | 0.69 | 83.75 | 4.18 | 32.53 | Rha/Fuc/Xyl/Man/Glc /Gal –:3.98:0.46: 2.58:1.00: 1.62 | 537 | (X. Liu, *et al*., 2016) |
| | SPC -70 | 0.44 | 84.10 | 6.84 | 34.78 | Rha/Fuc/Xyl/Man/Glc /Gal 0.35:5.91:0.44:3.52:1. 00:4.05 | 512 | |
| | SP H-60 | 0.96 | 82.47 | 3.84 | 29.14 | Rha/Fuc/Xyl/Man/Glc /Gal 0.09:1.27:0.17:0.92:1. 00:0.58 | 432 | |
| | SP H-70 | 0.80 | 83.12 | 6.85 | 20.05 | Rha/Fuc/Xyl/Man/Glc /Gal 0.31:3.88:0.40:2.29:1. 00:2.51 | 430 | |
| *Sargassum fusiforme* | | - | 16.8 | 20.8 | 34.6 | Fuc /Xyl/Man/ Gal /GlcA 36.6: 18.3: 7.0: 19.1: 19.1 | 47.5 | (Cong, *et al*., 2016) |
| *Sargassum henslowianum* | | - | 38..9 | 21.4 | 15.6 | Fuc/ Xyl /Gal/ Man/GlcA 41.8:16.8:10.5:17.4:13 .5 | 49.8 | (Han, *et al*., 2017) [23] |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *Sargassum vulgare* | 20.69 | 60.06 | 20.3 | 9.61 | Glc/Man/ Gal/Xyl/ Ara/ Mal 32.18: 30.20: 17.61: 7.54: 3.82: 1.22 | - | (Kolsi, *et al*., 2017) [34] |
| Sargassum polycystum | 12.17 | 62.96 | 27.53 | - | Fuc /Gal/Glc/Xyl/others 63.44:8.14:0.24:5.89:2 2.29 | - | (Fernando, *et al*., 2018) |

F: Fucoidan; Fucose (Fuc), Xylose (Xyl), Mannose (Man), Galactose (Gal), Glucose (Glc), Glucuronic acid (GlcA), Rhamnose (Rha), Trace (Tr), Maltose (Mal), fucoidan fractions (FF1and $FF_2$) SPC60, 70 and SPH60, 70 (Sulfated polysaccharides obtained from cold and hot water extraction and precipitated with 60%and 70%ethanol).

**Meroterpenoids**

Sargassum species are represented as abundant source of meroterpenoid compounds of the chromene class and related structures which often possessed a poly-prenyl chain linked to a hydroquinone or similar aromatic ring moiety. In 1983, Kikugh *et al.*, Sargtriol, α-Tocopherol (vitamin E) structurally related compound, was isolated from *Sargassum tortile* (Kikughi, *et al*., 1983) [33]. After that, several meroterpenoids, such as plastoquinones, chromanols and chromenes were isolated from different species (Table 3). Interestingly, chromenes can be obtained from the isolated plastoquinones through treating them with pyridine at room temperature under N2 atmosphere and had the biological activities of plastoquinones such as antioxidant and anticancer activities (Iwashima *et al*., 2005) [47].

Several studies showed that meroterpenoids, due to their ubiquitous range of chemical structure, provides promising pharmacological activities such as anticancer (Numata *et al*., 1992 [49]; Mori *et al*., 2005 [47]; J. I. Lee *et al*., 2013), antioxidant (Mori *et al.*, 2005; Iwashima *et al*., 2005) [47], antiviral (Iwashima *et al*., 2005) [47], anti-gastric ulcer (Mori *et al*., 2006), antimicrobial activity (Jung *et al*., 2008), anti-inflammatory activity (J. Lee *et al*., 2013; Gwon *et al*., 2018) and vasodilatation activity for cerebral vascular disease (Park *et al*., 2008) [50]. Many meroterpenoids were isolated from several *Sargassum* species are mention in Table 3.

**Phlorotannins**

Phlorotannins are basically polyphenolic compounds formed by dehydro-polymerizates of phloroglucinol units (1, 3, 5-trihydroxybenzene) (Fig 2.7) with different degrees of polymerization and a group of heterogeneous polymeric compounds sometimes with halogen or hydroxyl groups, present exclusively in brown seaweeds. Marine seaweeds have been revealed several low-, intermediate- and high-molecular weight of phlorotannins (M.wt up to 650 kDa). Phlorotannins are tannin derivatives consisting of several phloroglucinol units linked with each other in different ways resemble in their chemical properties and biological activity to tannins in vascular plants (J. Li *et al*., 2018) [40]. In general, phlorotannins concentrations are approximately more than 2% in temperate and tropical Atlantic and temperate Pacific regions. In some cases, these can accumulate up to 25–30% of thallus dry weight. Phlorotannins are presented soluble and stored in membrane bound vesicles called physodes or cell wall-bound forms. Phlorotannins form a complex with alginic acid when physodes fuse with the cell walls (Singh and Sidana, 2013) [67].

Phlorotannins are crucial to the physiological integrity of seaweed and play a major role for chemical defense, protection against oxidative damage that occurs in response to changes in nutrient availability and UV radiation, interactions with other organisms or the abiotic environment, as well as being integral components of cell wall (Y. Li *et al*., 2017).

Generally, phlorotannins are classified into four subgroups relay on their inter- phloroglucinol linkages to (i) phlorotannins with ether linkage (fuhalols Fig.3, A and phlorethols Fig.3, B), (ii) with phenyl linkage (fucols Fig.3, C), (iii) with both ether and phenyl linkage (fucophlorethols Fig.3, D) and (iv) with dibenzo(1,4)dioxin linkage (eckols Fig.3,A) (Singh and Sidana, 2013) [67]. The difference between fuhalols and phlorethols by the presence of additional hydroxyl groups. Seaweed phlorotannins characterized by high complexity (Y. Li *et al*., 2017).

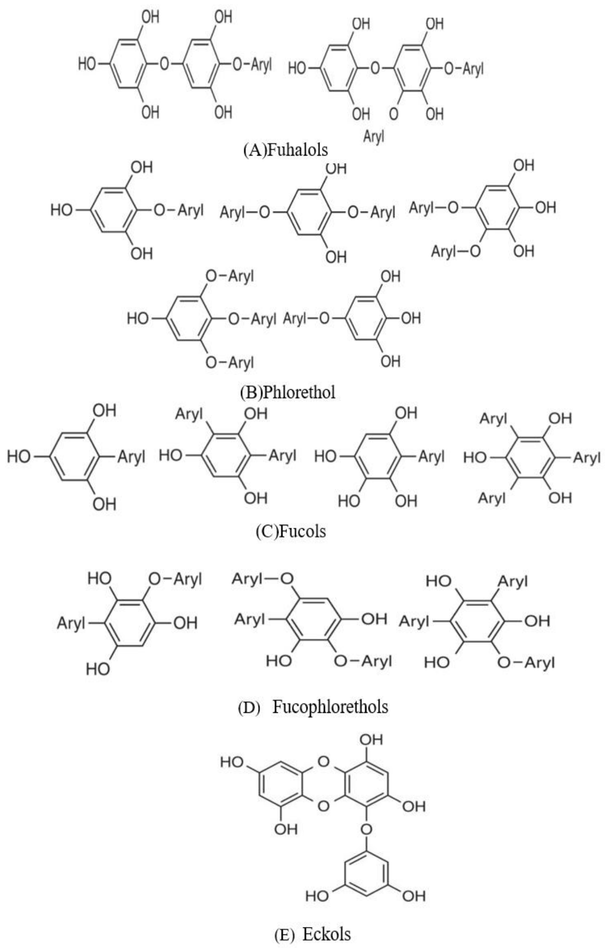



**Fig 3:** Phlorotannins subgroups adopted from Singh and Sidana, (2013) [67]

Several studies have reported that phlorotannins exhibited strong antioxidant (Nakai *et al*., 2006), antimicrobial, anti-proliferative, antitumor, anti-diabetic (Kawamura-konishi *et al*., 2012) [31], angiotensin converting enzyme-I (ACE I) inhibition, anti-inflammatory, matrix metalloproteinases

(MMPs) inhibition, hyaluronidase inhibition, tyrosinase inhibition, photo-protective, anticoagulant (Li *et al.*, 2018) [40] and anti-allergic activities (Maya Puspita *et al.*, 2019).

A large number of phlorotanins have been obtained from Sargassum genus including phlorethols, fuhalols and fucophlorethols. Although most of these phlorotanins were identified in *Sargassum spinuligerum* (K. W. Glombitza and Keusgen 1995 [20]; Keusgen and Glombitza, 1997), other species of *Sargassum* may also contain these polyphenols (L. Liu *et al.*, 2012) [42]. Several phlorotannins were isolated from different *Sargassum* species are mentioned in Table 3.

**Other bioactive compounds:**

*Sargassum* genus phytosterols, polyunsaturated fatty acids, glycolipids, bisnorditerpenes, farnesylacetones, arsenosugars, dipeptides, iodoamino acids, loliolides, octatrienes, etc have lesser reports compared to the meroterpenoids, phlorotanins, polysaccharides.

**I) Phytosterols:**

Phytosterols (plant sterols, PSs), which are crucial components of cell membranes, get a huge attention in the functional food industry because they have been exhibited reduction in the incidence of cardiovascular diseases (CVD). Sterols from *Sargassum* species have demonstrated anti-atherosclerotic. Saringosterol exhibits potent cholesterol lowering activity (Z. Chen *et al.*, 2014). Thunberol, a new sterol isolated from *Sargassum thunbergii* exhibited potential Type II-diabetes and obesity treatment via protein tyrosinase phosphatase 1B inhibition activity (He *et al.*, 2014) [24]. Other biological activities reported in *Sargassum* are anticancer activity (Tang *et al.*, 2002) [70], antiviral activities including Human Immuno-deficiency virus (HIV) (Tang *et al.*, 2002) [70], anti- inflammatory activity (J. Lee *et al.*, 2013), and anti-nociceptive activity (A. K. F. S. de Sousa *et al.*, 2015) [68]. Phytosterols are abundant in *Sargassum*, however, the functions of its phytosterols are barely reported (Z. Chen *et al.*, 2014). Some identified phytosterols are summarized in Table 3.

**II) Carotenoids**

Fucoxanthin is a marine carotenoid found in *Bacillariophyta* (diatoms) and brown seaweeds. Fucoxanthin, a xanthophyll, is responsible for the a very intense brown color of brown seaweed. Fucoxanthin has a unique structure including an unusual allenic bond, conjugated carbonyl, epoxide, and acetyl group within its molecule (Fig.4) (Mikami and Hosokawa, 2013) [44].

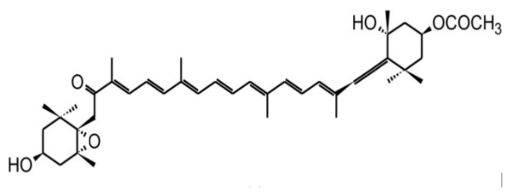



**Fig 4:** Fucoxanthin structure obtained (Mikami and Hosokawa, 2013) [44]

Many fucoxanthin and fucoxanthin derivatives have been isolated from different Sargassum species with several biological activities including antioxidant (Pramitha and Kumari, 2016) [58], anticancer (Satomi, 2012), anti-inflammatory (S. Heo *et al.*, 2012; E. J. Yang *et al.*, 2013 [74]; Pramitha and Kumari, 2016) [58], cytoprotective activity (S.-J. Heo *et al.*, 2008), and UV preventative activity (S. J. Heo and Jeon, 2009) [25]. Some isolated fucoxanthin and its derivative are mentioned in Table 3.

**III) Polyunsaturated fatty acids and glycolipids:**

Sargassum seaweeds are rich in fatty acids, which are known to play an essential role in cardiovascular health (CVH), particularly the polyunsaturated fatty acids (PUFAs). Long-chain omega-3 and -6 fatty acids such as eicosapentaenoicacid (EPA, 20:5n-3), arachidonic acid (AA, 20:4n-6) and docosahexaenoic acid (DHA, 22:6n-3) are particularly rich in some *Sargassum* species (L. Liu *et al.*, 2012) [42].

*Sargassum thunbergii, Sargassum marginatum* and *Sargassum confusum* contained glycolipids as the major lipid class followed by neutral lipids and phospholipids. The predominant fatty acid was palmitic acid (C16:0) among the three seaweed (Narayan *et al.*, 2004) [48]. Ginneken, *et al.*, (2011) [19] investigated the lipid contents of different seaweeds. Particulary, *Sargassum natans* predemonantly contained palmitic (C16:0) and oleic acids (C18:1, n-9) fatty acid together with eicosapentaenoic acids (EPA, C20:5, n-3), and docosahexaenoic acid (DHA, C22:6, n-3). The ratio of n-6: n-3 fatty acids found to be 0.55 (Ginneken *et al.*, 2011) [19] less than 10 which according to the WHO can prevent inflammatory, cardiovascular and neural disorders (Sanchez-Machado *et al.*, 2004) [63] *Sargassum fusiforme, Sargassum thunbergii, Sargassum pallidum,* and *Sargassum horneri* contained palmitic and stearic acid as a major saturated fatty acids (SFA) and monounsaturated fatty acids (MUFA) respectively, while the main polyunsaturated fatty acids (PUFAs) were linoleic, arachidonic, and eicosapentaenoic acid (Z. Chen *et al.*, 2016).

Moreover, *Sargassum* species are abundant in glycolipids, which are functional lipids with nutritional significance. Glycolipids contain 1,2-diacyl-glycerol moiety with mono- or oligosaccharide groups linked at sn -3 position of the glycerol backbone.

The typical algal glycolipids include monogalactosyl-diacylglycerol (MGDG), digalactosyldiacylglycerol (DGDG) and sulfo-lipid, sulfoquinovosyldiacylglycerol (SQDG) Fig (12; 103,104,105, respectively adapted from (Pereira *et al.*, 2014) [52]. MGDG and DGDG contain one and two galactose molecules, respectively, and are uncharged at physiological pH, while SQDG carries a negative charge due to its sulfonic acid residue at position 6 of the monosaccharide moiety (Kumari *et al.*, 2013) [36].

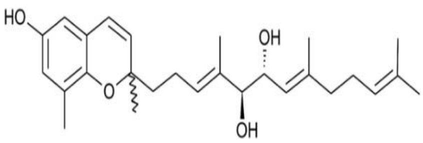
Glycoglycerolipids are predominantly located in chloroplasts where MGDGs and SQDG present in the thylakoid membranes and DGDGs are located mainly in the extraplastidial membrane and play an essential role in photosynthesis (Pereira *et al.,* 2014) [52]. Some biological activities of glycolipid reported in some *Sargassum* species including fibrinolytic activity (W. Wu *et al.*, 2009), anti-microfouling (Plouguerné *et al.*, 2010, 2020) [54, 56], and antiviral (Plouguerné *et al.*, 2013) [57].

**Table 3:** Some secondary metabolites isolated from Sargassum species

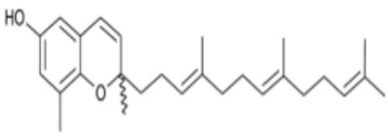
| ***Sargassum* species** | **Phyto-constituents** | **Reference** |
|---|---|---|
| | **Meroterpenoids compounds** | |
| *Sargassum tortile* | Sargatriol (1) | (Kikughi *et al*., 1983) [33] |
| | Sargaol (2) | |
| *Sargassum tortile* | Sargadiol-I (3) | (Numata *et al*., 1992) [49] |
| | Sargadiol-II(4) | |
| | Sargasal-I (5) | |
| | Sargasal-II (6) | |
| | Hydroxysargaquinone(7) | |
| *Sargassum autumnale* | Nahocol A(8) | (Tsuchiya *et al*., 1998) |
| | Nahocol A1(9) | |
| | Nahocol B (10) | |
| | Nahocol C (11) | |
| | Nahocol D1 (12) | |
| | Nahocol D2 (13) | |
| | Isonahocols D1(14) | |
| | Isonahocols D2(15) | |
| *Sargassum siliquastrum* | Sargachromanol A(16) | (Jang *et al*., 2005) |
| | Sargachromanol B(17) | |
| | Sargachromanol C(18) | |
| | Sargachromanol D(19) | |
| | Sargachromanol E(20) | |
| | Sargachromanol F(21) | |
| | Sargachromanol G(22) | |
| | Sargachromanol H(23) | |
| | Sargachromanol I(24) | |
| | Sargachromanol J(25) | |
| | Sargachromanol K(26) | |
| | Sargachromanol L(27) | |
| | Sargachromanol M(28) | |
| | Sargachromanol N(29) | |
| | Sargachromanol O(30) | |
| | Sargachromanol P(31) | |
| *Sargassum micracanthum* | Plastoquinone-1 (32) | (Mori *et al*., 2005) [47] |
| | Plastoquinone-2 (33) | |
| | Plastoquinone-3 (34) | |
| | Plastoquinone-4 (35) | |
| *Sargassum micracanthum* | (2R,8'S)-7',8'-dihy- dro-9'-oxo-γ –tocotrienol (36) | (Iwashima *et al*., 2008) |
| | (2R)-9'-oxo- γ -tocotrienol (37) | |
| *Sargassum siliquastrum* | Nahocols A (8) | (Jung *et al*., 2008) |
| | Nahocol A1(9) | |
| | Nahocol D1(12) | |
| | Nahocol D2(13) | |
| | Isonahocols D1 and D2(14&15) | |
| | Sargahydroquinoic acid (38) | |
| | Sargahydroquinone (39) | |
| *Sargassum yezoense* | Sargaquinoic acid (40) | (S. Kim *et al*., 2008) |
| | Sargahydroquinoic acid (39) | |
| *Sargassum micracanthum* | Sargaquinoic acid (40) | (Park *et al*., 2008) [50] |
| | Sargahydroquinoic acid (39) | |
| *Sargassum siliquastrum* | (9S,10S)-13-(3,4-dihydro-6-hydroxy-2,8-dimethy-2H-1-benzo-pyran-2-yl)-2,6,10-trimethyl-trideca- (2E,6E)-diene-4,5,10-triol (41) | (J. I. Lee and Seo, 2011) |
| | (9S,10R)-13-(3,4-dihydro-6-hydroxy-2,8-dimethy-2H-1-benzo-pyran-2-yl)-2,6,10-trimethyl-trideca- (2E,6E)-diene-4,5,10-triol (42) | |
| | 9-(3,4-dihydro-6-hydroxy-2,8-dimethy-2H-1-benzopyran-2-yl)- 2,6-dimethyl-(6E)-nonenoic acid (43) | |
| *Sargassum horneri* | Sargachromenol (44) | (J. Kim *et al*., 2012) |
| *Sargassum siliquastrum* | Sargaquinoic acid (40) | (G. Kang *et al*., 2012) |
| *Sargassum elegans* | Sargaquinoic acid (40) | (Ragubeer, Limson, and Beukes, 2012) |
| | Sargahydroquinoic acid (38) | |
| | Sargaquinal (45) | |
| *Sargassum siliquastrum* | Sargachromanol J (25) | (J. I. Lee *et al*., 2014) |
| | Sargachromanol Q(46) | |
| | Sargachromanol R(47) | |

| | | |
|---|---|---|
| *Sargassum micracanthum* | Sargachromenol (44) | (Madushan *et al*., 2016) |
| *Sargassum macrocarpum* | Tuberatolide B (48) | (Choi *et al*., 2017) |
| *Sargassum Macrocarpum* | Macrocarquinoids A(49) | (Niwa *et al*., 2021) |
| | Macrocarquinoids B(50) | |
| | Macrocarquinoids C(51) | |
| **Phlorotannins compounds** | | |
| *Sargassum muticum* | Phloroglucinol tri-acetate(52) | (Glombitzat *et al*., 1978) |
| | Diphlorethol penta-acetate(53) | |
| | Bifuhalol hexa-acetate (54) | |
| | Trifuhalol A octa-acetate(55) | |
| | Trifuhalol B octa-acetate(56) | |
| *Sargassum spinuligerum* | Diphlorethol pentaacetate (53) | (K. Glombitza *et al*., 1997) |
| | Triphlorethol-A- heptaacetate (57) | |
| | Trifuhalol-A octaacetate(55) | |
| | Tetrafuhalol-A undecaacetate (58) | |
| | Pentafuhalol-A tridecaacetate (59) | |
| | Hexafuhalol-A hexadecaacetate (60) | |
| | Fucophlorethol-B octaacetate (61) | |
| | Fucodiphlorethol-D decaacetate (62) | |
| | Fucotriphlorethol-B dodecaacetate (63) | |
| | Fucophlorethol-C octaacetate (64) | |
| | Fucodiphlorethol-E decaacetate (65) | |
| | Hydroxyfucophlorethol-A nonaacetate (66) | |
| | Hydroxyfucodiphlorethol-A undecaacetate (67) | |
| | Hydroxyfucotriphlorethol-A tridecaacetate (68) | |
| | Hydroxyfucotetraphlorethol-A pentadecaacetate (69) | |
| | Hydroxyfucopentaphlorethol-A heptadecaacetate (70) | |
| | Dihydroxyfucotriphlorethol-A tetradecaacetate (71) | |
| | Dihydroxyfucotetraphlorethol-A hexadecaacetate (72) | |
| | Trihydroxyfucopentaphlorethol-A nonadecaacetate (73) | |
| *Sargassum patens* | 2-(4-(3,5- dihydroxyphenoxy)-3,5-dihydroxyphenoxy) benzene-1,3,5-triol (DDBT) (74) | (Kawamura- konishi *et al*., 2012) [31] |
| **Phyto-sterols compounds** | | |
| *Sargassum acinarium* | Fucosterol (75) | (Kanias *et al*., 1992) |
| | Campesterol(76) | |
| *Sargassum carpophyllum* | 3b,28j-dihydroxy-24-ethylcholesta-5,23Z-dien(77) | (Tang *et al*., 2002) [70] |
| | 2a-oxa-2- oxo-5a-hydroxy-3,4-dinor-24-ethylcholesta-24(28)-ene (78) | |
| *Sargassum asperifolium* | Saringosterone (79) | (Ayyad *et al*., 2003) |
| | Saringosterol (80) | |
| *Sargassum oligocystum* | 22-dehydrocholesterol (81) | (Permeh *et al*., 2012) |
| | Cholesterol (82) | |
| | Fucosterol (75) | |
| | 29-hydro-peroxy-stigmasta-5,24(28)-dien-3β-ol (83) | |
| | 24-hydroperoxy-24-vinylcholesterol (84) | |
| | A mixture of 24(S)-hydroxy-24-vinylcholesterol and 24(R)-hydroxy- 24-vinylcholesterol (85) | |
| | Ostreasterol(24-Methylene-cholesterol) (86) | |
| *Sargassum fusiforme* | Fucosterol(75) | (Z. Chen *et al*., 2014; Zhen *et al*., 2015) |
| | Saringosterol (a mixture of 24(S)-saringosterol and24(R)-saringosterol) (85) | |
| | 24-Hydroperoxy-24-vinyl-cholesterol (84) | |
| | 29-Hydro-peroxy-stigmasta-5,24(28)-dien-3β-ol (83) | |
| | 24-Methylene-cholesterol (86) | |
| | 24-Keto-cholesterol (87) | |
| | 5α,8α-Epidioxyergosta-6,22-dien-3β-ol (88) | |

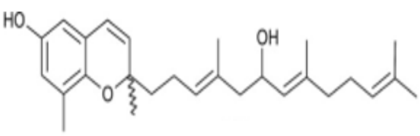
| | | |
|---|---|---|
| *Sargassum thunbergii* | Thunberol (89) | (He *et al*., 2014) [24] |
| | 24-ethylcholesta-4,24(28)-dien-3-one (90) | |
| | Stigmasta-5,28-dien-3b-ol (91) | |
| | Cholesta-5,14-dien-3b-ol (92) | |
| | Cholesta-5,23-dien-3b,25-diol (93) | |
| *Sargassum glaucescens* | Fucosterol(75) | (Payghami *et al*., 2015) |
| | 24(S)-hydroxy-24-vinylcholesterol and 24(R)-hydroxy-24-vinylcholesterol mixture (85) | |
| | Stigmasterol (94) | |
| | β-sitosterol (95) | |
| | Cholesterol (82) | |
| *Sargasuum horneri* | Phytol (96) | (Xia *et al*., 2019) |
| | Fucosterol (75) | |
| | Saringosterol(80) | |
| **Carotenoids compounds** | | |
| *Sargassum siliquastrum* | Fucoxanthin (97) | (S.-J. Heo *et al*., 2008; S. J. Heo and Jeon, 2009) |
| *Sargassum siliquastrum* | Trans-(6'R) fucoxanthin (97) | (S. Heo *et al*., 2012) |
| | 9'-cis-(6'R) fucoxnathin (98) | |
| | 13-cis and 13'-cis-(6'R) fucoxanthin mixture (99 and 100) | |
| *Sargassum elegans* | Fucoxanthin (97) | (Ragubeer*et al*., 2012) |
| *Sargassum muticum* | Apo-9‟-fucoxanthinone (101) | (E. Yang *et al*., 2013) [74] |
| *Sargassum plagyophyllum* | Trans-fucoxanthin (97) | (Jaswir *et al*., 2013) |
| **Glycolipids** | | |
| *Sargassum horneri* | Monogalactosyldiacylglycerol (102) | (Hossain *et al*., 2003) |
| | Digalactosyldiacylglycerol (103) | |
| | Sulfoquinovosyldiacylglycerol (104) | |
| *Sargassum pallidum* | Monogalactosyldiacylglycerol (102) | (Sanina *et al*., 2004) |
| | Digalactosyldiacylglycero (103) | |
| | Sulfoquinovosyldiacylglycerol (104) | |
| *Sargassum fulvellum* | 1-O-palmitoyl-2-O-oleoyl-3-O-(α-D-glucopyranosyl) -glycerol,where $R_1$=palmitoyl $R_2$=oleoyl l (102) | (W. Wu *et al*., 2009) |
| | 1-O-myristoyl-2-O-oleoyl-3-O-(α-D-glucopyranosyl) – glycerol, R2: $R_1$=myristoyl $R_2$=oleoy (102) | |
| *Sargassum muticum* | Galactoglycerolipids (MGDGs) where $R_1$ and $R_2$= fatty acids esters (102) | (Plouguerné *et al*., 2010) [54] |
| *Sargassum vulgare* | 1,2-di-O-palmitoyl-3-O-(6-sulfo-α-D- quinovopyranosyl)-glycerol(SQDG) where R and R'= palmitic acids esters (104) | (Plouguerné *et al*., 2013) [55] |
| *Sargassum vulgare* | Monogalactosyldiacylglycerols (102) | (Plouguerné *et al*., 2020) [56] |
| | Digalactosyldiacylglycerols (103) | |
| | Sulfoquinovosyldiacylglycerols (104) | |



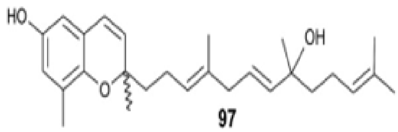

(1) Sargatiol



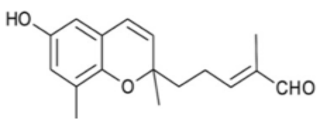

(2) Sargaol



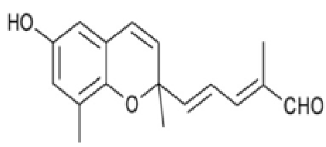

(3) Sargadiol-I



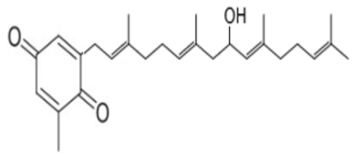

(4) Sargadiol-II



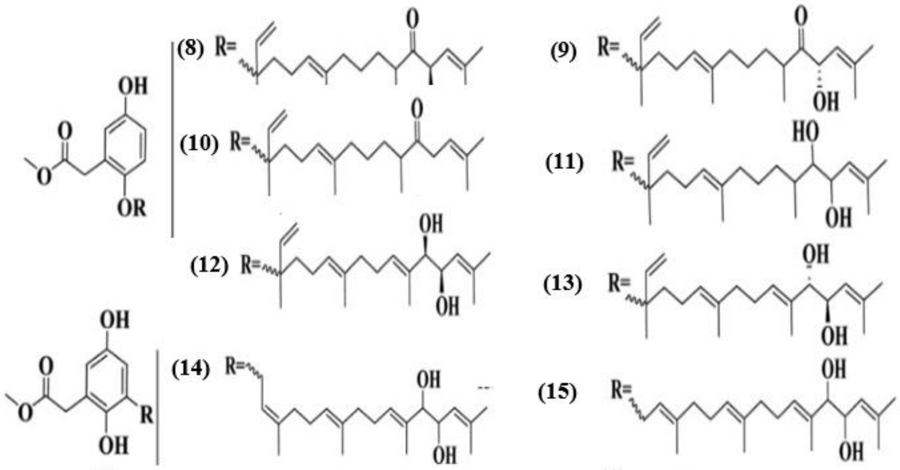

(5) Sargasal-I

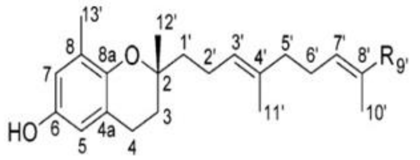



(6) Sargasal-II

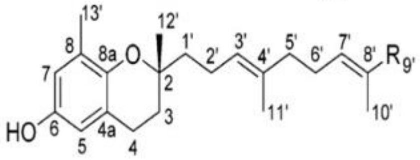


(7) Hydroxysargaquinon

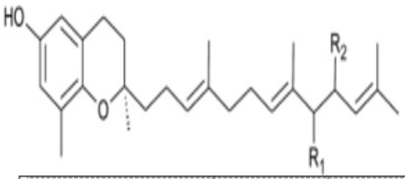




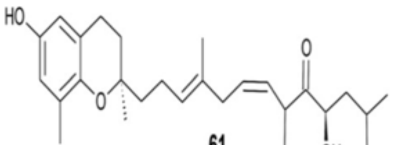
(16) Sargachromenol A; R=CHO



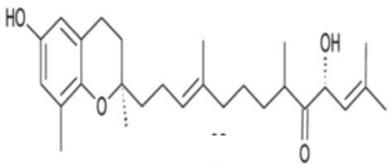
(17) Sargachromenol B; R=CH2OH



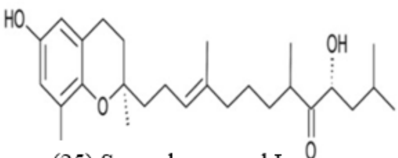
| Sargachromenol | -R1 | -R2 |
|---|---|---|
| C(18) | -OH(*R*) | -H |
| D(19) | -OH(*R*) | -OH(*S*) |
| E (20) | -OH(*R*) | -OH(*R*) |
| F(21) | -OMe | -OH(*S*) |
| G(22) | =O | -OH(*S*) |
| K(26) | -OH(*R*) | =O |



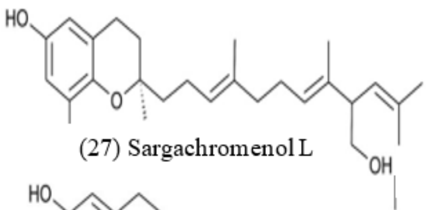
(23) Sargachromenol H



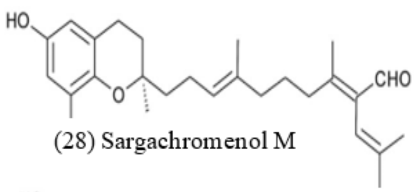
(24) Sargachromenol I



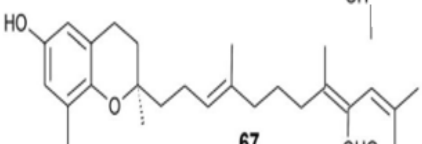
(25) Sargachromenol J



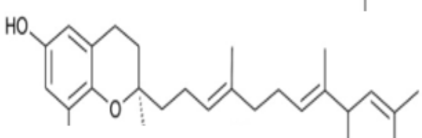
(27) Sargachromenol L



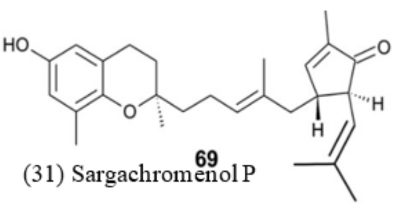
(28) Sargachromenol M



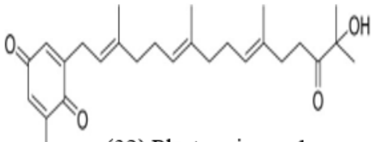
(29) Sargachromenol N



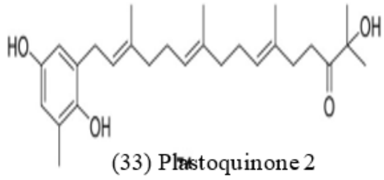
(30) Sargachromenol O



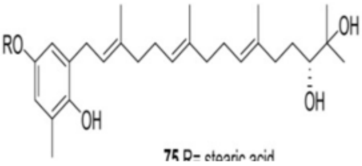
(31) Sargachromenol P



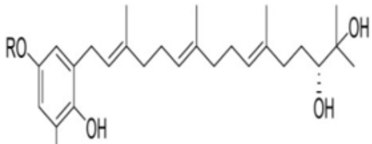
(32) Plastoquinone 1



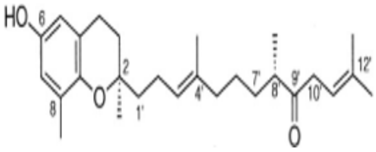
(33) Plastoquinone 2



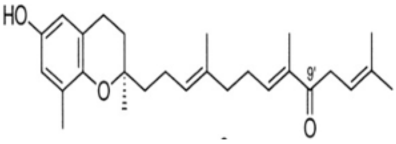
(34) Plastoquinone 3|;R= stearic acid



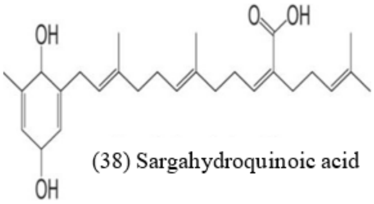
(35) Plastoquinone 4; R= oleic acid



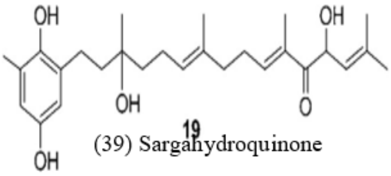
(36) 7',8'-dihydro-9'-oxo-d-tocotrienol



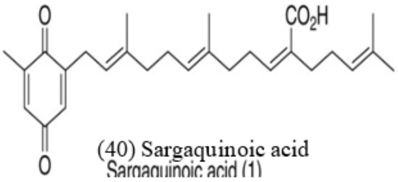
(37) 9'-oxo-d- tocotrienol



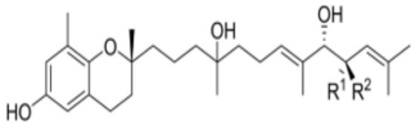
(38) Sargahydroquinoic acid



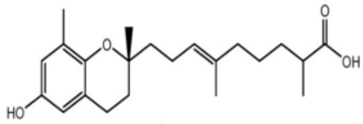
(39) Sargahydroquinone



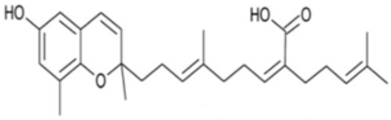
(40) Sargaquinoic acid



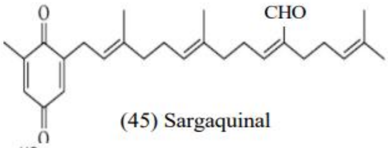
(41) R1=H, R2=OH,
(42) R1=OH, R2=H



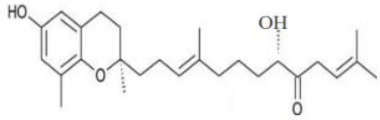
(43) 9-(3,4-dihydro-6-hydroxy-2,8-dimethy-2H-1-benzopyran-2-yl)-2,6-dimethyl-(6E)-nonenoic acid



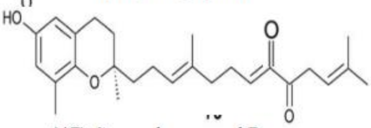
(44) Sargachromenol



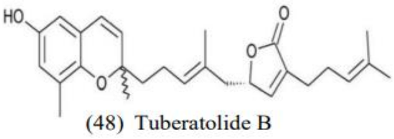
(45) Sargaquinal



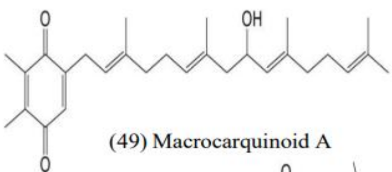
(46) Sargachromenol Q



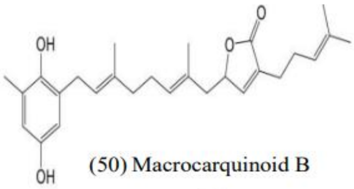
(47) Sargachromenol R



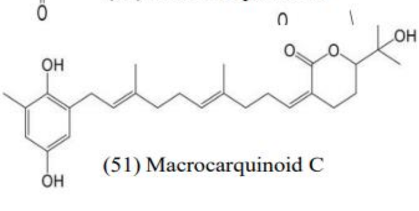
(48) Tuberatolide B



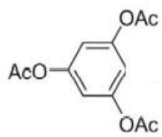
(49) Macrocarquinoid A



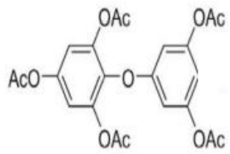
(50) Macrocarquinoid B



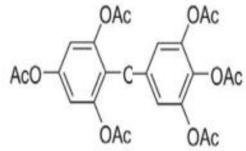
(51) Macrocarquinoid C



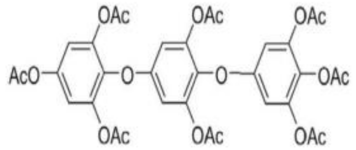
(52) Phloroglucinol tri-acetate



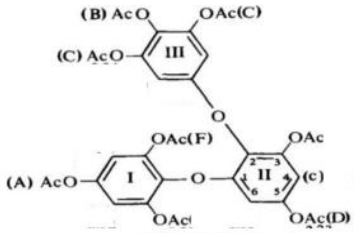
(53) Diphlorethol



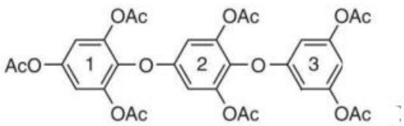
(54) Bifuhalol



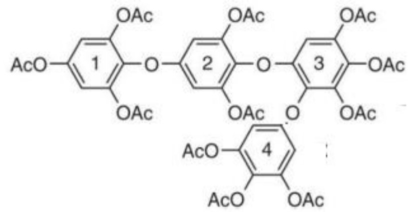
(55) Trifuhalol A



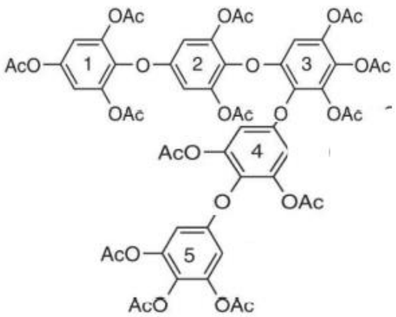
(56) Trifuhalol B



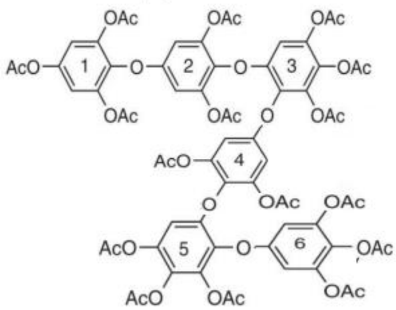
(57)Triphlorethol A



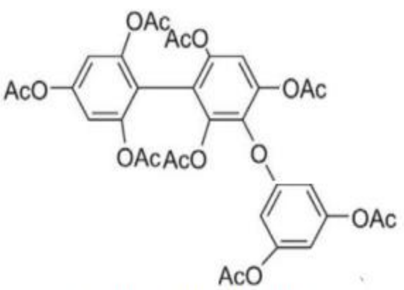
(58)Tetrafuhalol A



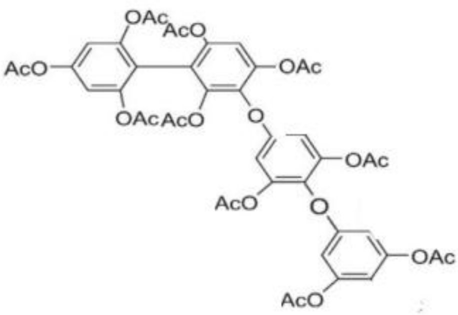
(59)Pentafuhalol-A



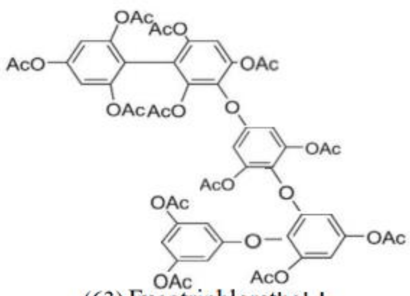
(60)Hexafuhalol-A



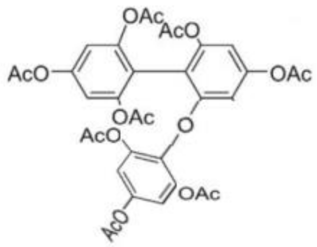
(61) Fucophlorethol-B



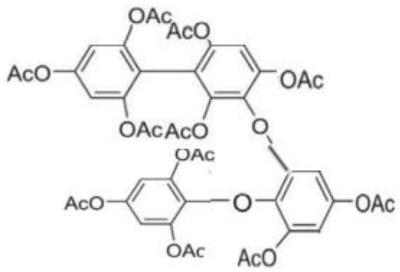
(62) Fucodiphlorethol-D



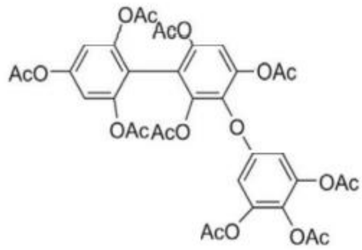
(63) Fucotriphlorethol-E



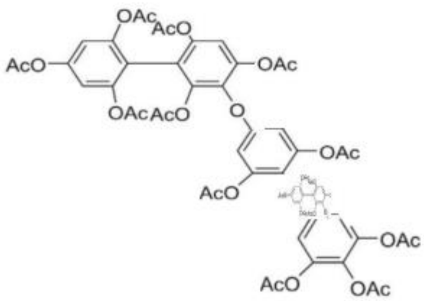
(64) Fucophlorethol-C



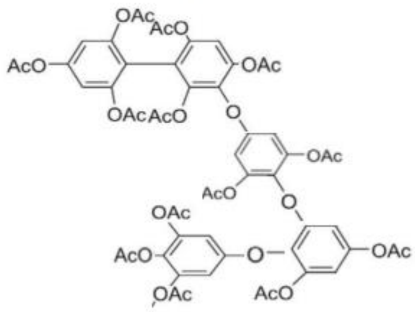
(65)Fucodiphlorethol-E



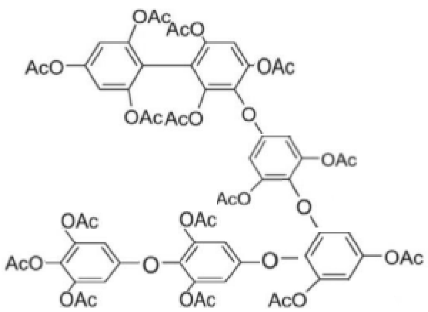
(66) Hydroxyfucophlorethol-A



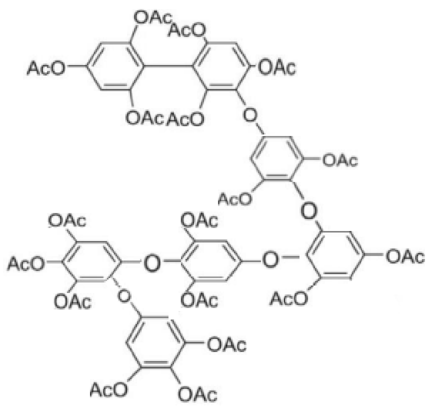
(67) Hydroxyfucodiphlorethol-D



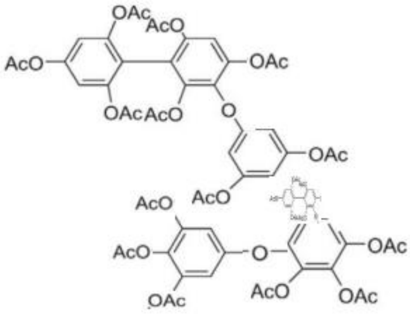
(68) Hydroxyfucotriphlorethol-A



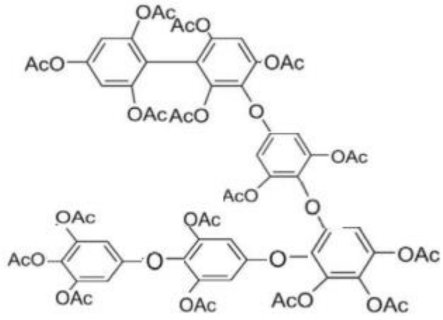
(69) Hydroxyfucotetraphlorethol-A



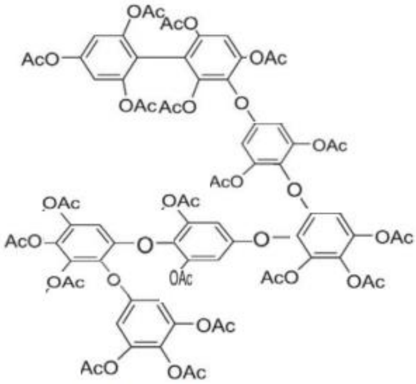
(70) Hydroxyfucopentaphlorethol-A



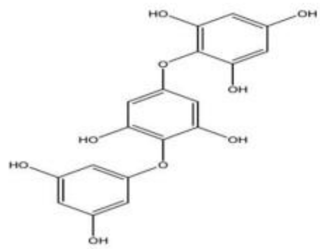
(71) Dihydroxyfucotriphlorethol-A



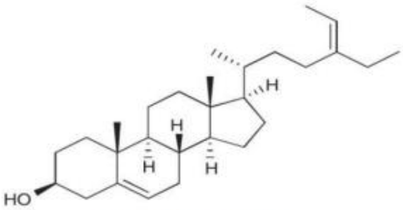
(72) Dihydroxyfucotetraphlorethol-A



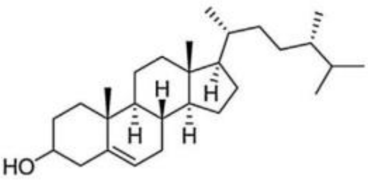
(73) Dihydroxyfucopentaphlorethol-A



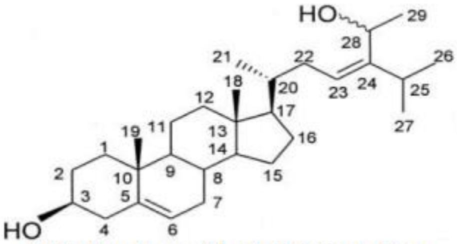
(74)DDBT



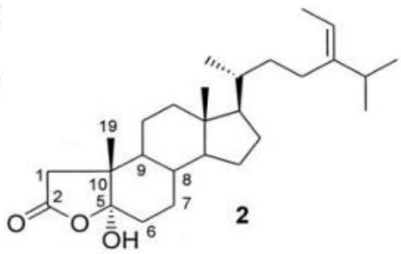
(75) Fucosterol



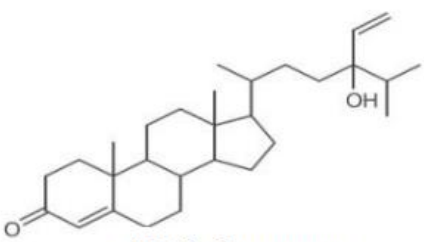
(76) Campesterol



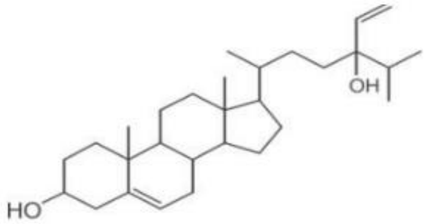
(77) dihydroxy-24-ethylcholestadien



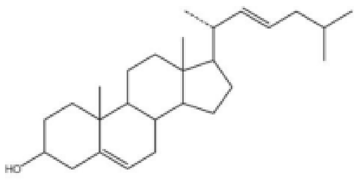
(78) 2a-oxa -5a-hydroxy-3,4-dinor-24-ethylcholesta-24(28)-ene



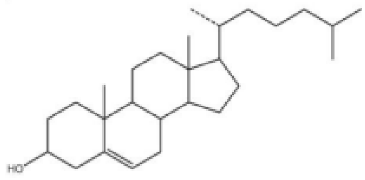
(79) Saringosterone



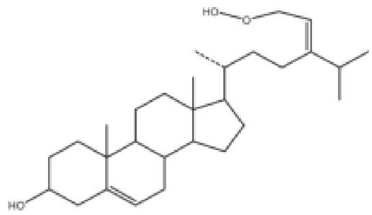
(80) Saringosterol



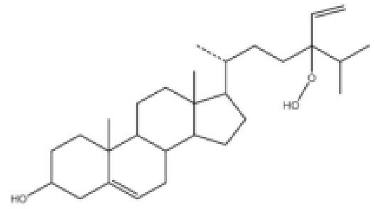
(81) 22- dehydrocholesterol



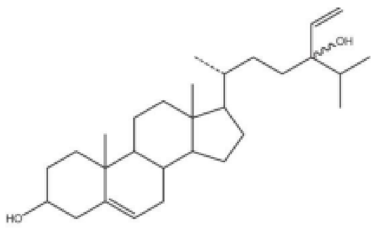
(82) Cholesterol



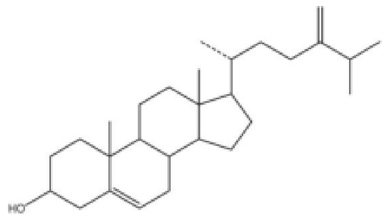
(83) 29-hydroperoxystigmasta-5,24 (28)-dien-3β-ol



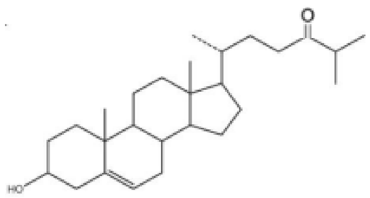
(84) 24-hydroperoxy-24-vinylcholesterol



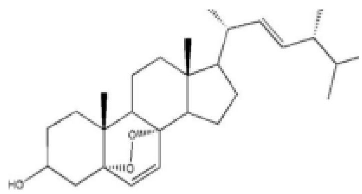
(85) 24(S) and 24(R)-hydroxy-24-vinylcholesterol



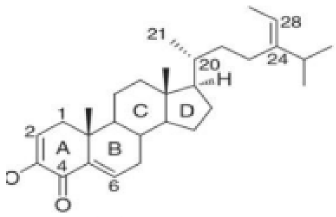
(86)Ostreasterol



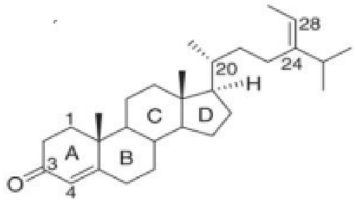
(87)24-KetoCholesterol



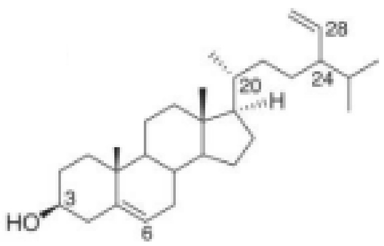
(88) 5α,8α-Epidioxyergosta-6,22-dien-3-ol



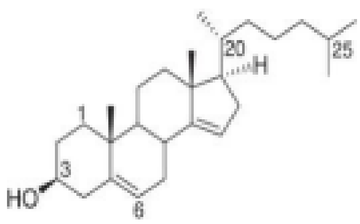

(89) Thunberol




(90) 24-ethylcholesta- 4,24-dien-3-one




(91) Stigmasta-5,28-dien-3b-ol




(92) Cholesta-5,14-dien-3b-ol

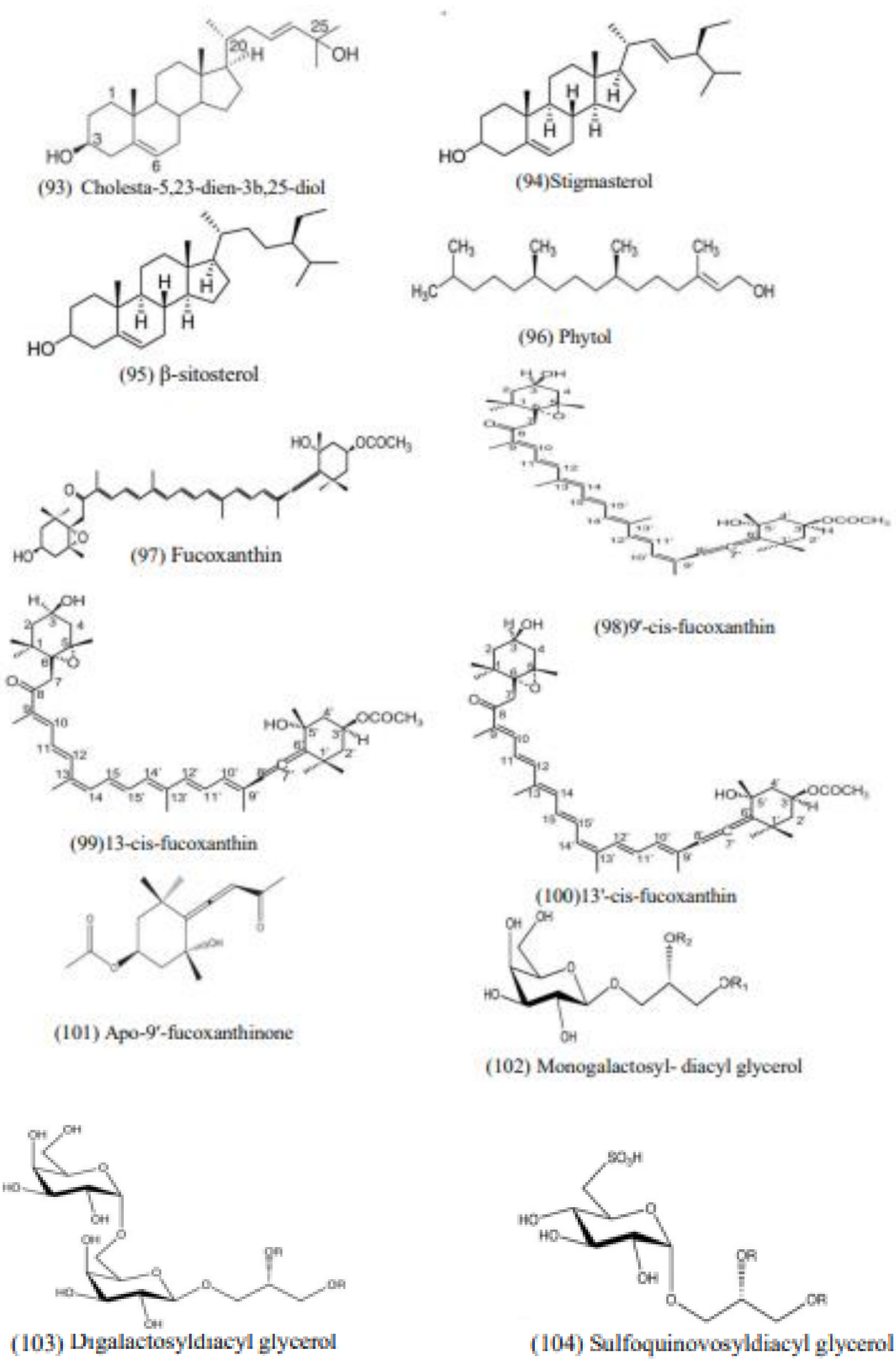



**Fig 5:** Chemical structure of Sargassum species secondary metabolites that mentioned in Table 3

Marine environment constitutes nearly more than half of the worldwide, so they are presented a wide resource for new bioactive substances and it is considered the largest remaining reservoir of natural products. Due to the extreme environmental conditions to which they are exposed marine organisms are adapted to different environmental factors and developed defense strategies resulted to a significant level of structural and chemical diversity of compounds. These compounds are originated from different metabolic pathways and are structurally different from terrestrial plants compounds(Hamed *et al.*, 2015) [22]. The exploitation of these organisms for pharmaceutical purposes has essential role for discovery of new drugs with biomedical application(Carte, 1996; El Gamal, 2010) [7, 18]

**Conclusion**

Seaweeds are considered as a renewable reservoirs with enormous potential for the production of an unlimited variety of bioactive compounds due to their wide ecological diversity, competitive adaptation environmental conditions. Marine environment is an extraordinary reservoir of bioactive natural products, many of them exhibit a novel structural features not found in terrestrial plant natural products. The numbers of novel marine metabolites are increasing every year, indicating that the marine organisms are potentially productive sources of highly bioactive secondary metabolites that may lead to the development of new pharmaceutical agents In the present review, we systematically summarized the phytochemical screening of the genus Sargassum.

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**Conflict of interest**
The authors declare that they have no competing interests.

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