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Phytochemical and pharmacological properties of *Halimeda gracilis* (Marine seaweed): A Review

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Abstract
Since ancient times, marine seaweeds have been employed as a source of traditional food and medicine in Asian and other seacoast nations. *Halimeda gracilis* is a marine seaweed has ability to produce hydrocolloids which are used in food and cosmetic industries. Numerous investigations on this marine seaweed have been produced a wealthy of information regarding its biological activity in relation to the type of extract provide better activity. The plant has been utilized as an antioxidant, anti-diabetic, anti-bacterial, anti-bacterial, anti-plasmodial, anti-cancer, larvicidal, and spermicidal agent based on previous reports. The plant has discovered to be phytochemically abundant in tannins, phenols and phenolic derivatives, steroids, alkaloids, terpenoids, saponins, glycosides. The current review provides a summary of the state of understanding about morphology, their taxonomical classification, active chemical constituents and their chemistry, pharmacological activities and traditional applications.

Keywords: Seaweeds, *Halimeda gracilis*, morphology, chemical constituents, pharmacological activities, and traditional and medicinal uses

Introduction
Marine seaweeds have been consumed whole by East Asian populations for centuries, if not centuries, and can be found in many traditional recipe books. Furthermore, their human consumption in Western countries has increased in recent decades due to their association with improved human health. Some of the advantages of their consumption include a lower risk of cancer, lower blood pressure and blood sugar levels, and antiviral, anti-inflammatory, immunomodulatory, or neuro-protective properties [1, 2, 3].

Seaweeds have been used as a source of food and traditional medicine in Asian and other seacoast countries around the world since ancient times. Although their generalised value for human nutrition and health is already recognised, it is largely based on empirical evidence. Seaweeds are reservoirs of bioactive compounds that have yet to be fully utilised in a wide range of blue biotechnology applications, including functional foods and feeds, pharmaceutical, nutraceutical, cosmeceutical, and other high-end uses [4].

Seaweeds are basic autotrophic organisms with little or no cellular differentiation and complex tissue, particularly common around seashores, lakes, and other bodies of water [5]. Marine seaweeds are made up of 25000-30000 distinct species with a wide range of shapes and sizes [1]. Seaweed is the common name for variety of microscopic and multicellular marine algae in the Kingdom Protista that have no roots, stalks, leaves, flowers, fruits, or seeds and grow and live by attaching themselves to rocky formations or other hard substrate beneath water's surface or drifting in the sea [6]. seaweed species are found across the world's coastal climate zones, including tropical, temperature and polar areas [7, 8].

Based upon their color and pigmentation and depending upon taxonomic classification seaweeds are divided into 3 types:

- Rhodophyta (Red)
- Phaeophyceae (Brown)
- Chlorophyta (Red).

Brown seaweeds
Numerous health advantages might be shown. The primary marine carotenoid, fucoxanthin (fuco), is a crucial component of brown seaweed from a commercial standpoint. The seaweeds include sodium alginate and fuco, both of which have anti-inflammatory qualities. Animals consume brown seaweeds, which is utilized in animal feed more frequently than other types of algae. The most common genera include *Sargassum*, *Macrocystis*, *Ascophyllum*, and *Laminaria*.

Red seaweeds
These seaweeds are red in color due to the presence of pigments phycoerythrin and phycocyanin. The walls of algae made up of carrageenan and cellulose agar. Both polysaccharides having a lengthy chain are commonly used in industry. *Chondrus*, *Porphyra*, *Pyropia*, and *Palmaria* are some of the most known red algae genera.

Green seaweeds
The green color of these algae is due to the presence of chlorophyll-a, chlorophyll-b. The majority of green algae species are aquatic, living in both fresh water and marine habitats. Ulva is most frequently used seaweed. *Ulva*, *Cladophora*, *Enteromorpha* are most common genera [9].

Plant introduction
Halimeda gracilis is a marine edible seaweed belonging to the family: Halimedaceae, order: Bryopsidales, and class: Bryopidopyceae [10]. It has no synonyms and common names. The species are extensively spread in Gulf of mannar, Palk Bay and Southern coast of India [11]. The pant has a long history of usage in treatment of various conditions such as anti-cancer [11], anti-diabetic [12], antioxidant [14, 15, 16], anti-bacterial [15, 16], larvicidal [16], anti-coagulant[17], anti-plasmodial [13], and spermicidal activity [18].

Fig 1: *Halimeda gracilis* (marine seaweed)

Morphology
Halimeda genus consist of thalli is clearly segmented and calcified. Calcium carbonate is deposited as aragonite, and calcification can be begun as early as 36 hours. Their segments are composed of 60-80% aragonite and are separated by non-calcified nodes. The thalli are made up of made up of siphons that ramify into medullary filaments that are surrounded by a cortex. The medullary filaments branch out trichotomously to form peripheral utricles, which stick together to enclose each segment's intersiphonal spaces. The precipitation of aragonite occurs in these spaces.
Halimeda has three distinct types of holdfasts that act as attachment points to the substrate. A few loose filaments grown at the ends or between the segments of the "sprawler" type. The matted holdfast in the "rock-grower," type is made up of branched filaments that secure the thallus to a rock surface. The final type is the "sand-grower" in which the filaments cling to fine sand particles and form a root-like structure. *Halimeda* is coenocytic and siphonous, which means that its cells are not divided by cross walls and instead form a continuous filament. This distinguishes the genus from Acetabularia, another calcified green seaweed genus [19].

Distribution: *Halimeda gracilis* is widely distributed in Palk Bay, Gulf of Mannar and Southern Coast of India [11]. In India especially Munaikadu [20], Rameswaram coastal area, Tamil Nadu [12]

Habitat
Marine includes sea water, seashores, and lakes etc.

Table 1: Taxonomic Classification

Kingdom	Plantae
Sub kingdom	Viridiplantae
Phylum	Chlorophyta
Class	Bryopsidophyceae
Order	Bryopsidales
Family	Halimedaceae
Genus	Halimeda
Species	*Halimeda gracilis* [10]

Traditional AMD medicinal uses
- *H. gracilis* has significant economic value due to its ability to produce hydrocolloids, which are used in food and pharmaceutical industries [15].
- It is a rich source of natural antioxidants such as carotenoids, myco-sporin like amino acids, and terpenoids, and it has numerous biomedical applications [21].
- Because of inhibition of cancer cell proliferation, it is used as an anti-cancer agent against breast cancer [11].
- It is used to treat variety of ailments, including anti-bacterial [15, 16], antioxidant [16, 14-15], anti-coagulant [17], larvicidal [16] and spermicidal properties [18].
- In a freshwater Zebrafish model, *Halimeda gracilis* chooranan is used to treat diabetics [12].

Active chemical constituents
1. The Methanolic extract of *Halimeda gracilis* yielded phenols and steroids [15].
2. From ethanolic extract of marine seaweed the compounds like alkaloids, flavonoids, proteins and sugars are obtained [18].
3. Chloroform, methanol, ethanol, acetone and water extracts of these seaweed contains alkaloids, terpenoids, steroids, tannins, saponins, quinones and glycosides [16].
4. The phytochemical constituents of Ethyl acetate extract and methanol extract of *Halimeda gracilis* were identified using data from LC-ESI-Q-TOF-MS^E such as molecular ion, fragment ion, chemical formula, and mass accuracy of less than 5 ppm. The total ion chromatogram results showed that 15 peaks were detected from ethyl acetate extract in positive mode and 17 peaks were observed from methyl *Halimeda gracilis* extract in negative mode, and the compounds were separated well in a very short period of time (22mins), indicating that the developed technique is ideal for separating bioactive compounds from marine seaweeds. The complete information of the compounds from marine seaweeds (*H.gracilis*) was gathered and obtained from the Dictionary of Natural Products [22], and a compound library was created with the compound name, molecular formula, chemical structure and molecular mass.

Based on the ToF-MS and MS/MS spectra 27 compounds were isolated belonging to the different classes of compounds including phenols, terpenes, sesquiterpenes, diterpenes, phenolic derivatives, cinnamic acid and its derivatives. The isolated compounds of *Halimeda gracilis* are Ascosalipyrone, Caulerprenylol A, Caulerpenyne-1, Chlorellatin A,

Communesin A, Cyclofarnesa-5(14), 8-diene-11, 15-dial, Flexilin, Glycerol 1-alkanoates-1, Haemotoporphrin, Oxytocin, Phaeophorbide B, Pheophytin B, Siphoxanthin, Stigmast-28-ene-3, 5, 6, 24-tetrol, Fucodiphlorethol A, Porphyrinolactone, Terretenin E, Phaeopytin A, Pleosporallin D, 2-Amino-4, 8-octadecadiene-1, 3-diol, 1, 16-Pentacosidiene, 3, 4-DHPEA-EDA, Caffeic acid, Caffeoyl tartaric acid, Carnosic acid, Coumaric acid, Ferulic acid, Isopropyl 3-(3, 4-dihydroxyphenyl)-2-hydroxypropanoate, p-Hydroxybenzaldehyde and Rosmanol were reported [10].

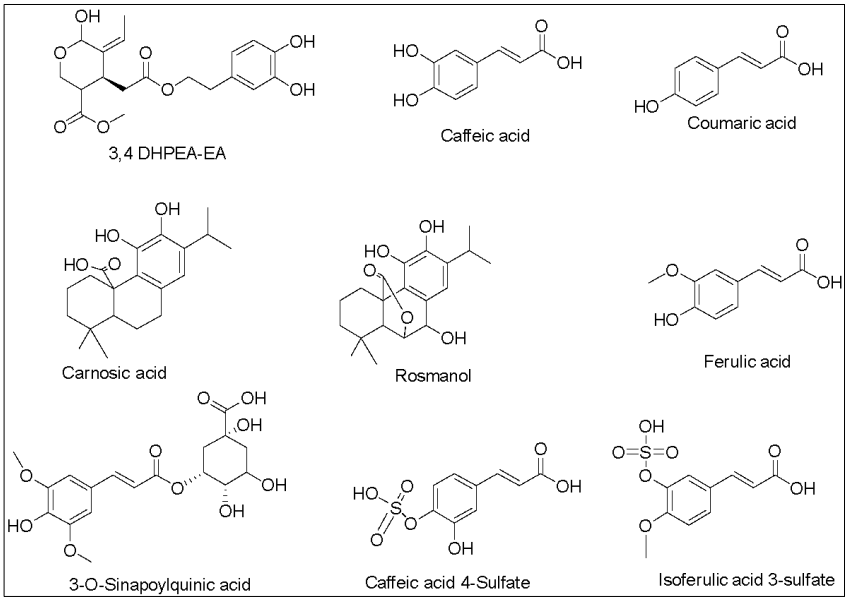

Fig 2: Structures of isolated compounds from *Halimeda gracilis* using UPLC-Q-TOF-MS[E.]

Pharmacological activities

Acute toxicity and anti-diabetic activity

In Zebra fish model, a methanolic extract of *Halimeda gracilis* (MEHG) was assessed for acute toxicity and anti-diabetic activity.

In an acute toxicity study, zebra fish were divided into six groups of 8 fish each and dosed with 6.25, 12.5, 25, 50, and 100mg/L MEHG concentrations, except for normal control fish, and observed for mortality, morbidity, and other behavioral changes in zebrafish at 0, 24, 48, 72, and 96 hours intervals. The results show that MEHG treatment does not cause mortality, morbidity.

In the anti-diabetic study, diabetics were induced using Streptozocin (STZ) according to body weight (0.35mg/g) for 19 days, with the exception of the normal control group intraperitoneal injection. The Zebrafish were divided into six groups of eight each: control, positive, diabetic zebrafish (three doses of MEHG given orally), and standard control (treated with metformin). On the 20th and 21st days, the fishes were fasted for 12 hours, and blood samples were collected through the caudal fin and analyzed for blood glucose levels. The result shows that when test groups were compared to the control group, there was a significant reduction in both fasting and postprandial blood glucose levels, as well as significant changes in pancreatic-beta cells regeneration and vacuolization [12].

Anti-bacterial and Antioxidant activity

The purpose of this study was to determine the antibacterial and antioxidant activity of green algae *Halimeda gracilis*. Utilizing the maceration process and a rotary evaporator to concentrate, extraction was carried. *H. gracilis* methanol extracts were tested against Staphylococcus aureus and Escherichia coli. *H. gracilis* methanol extract created an inhibitory zone against the test micro-organisms that had a 10 mm and 6 mm diameter, respectively. After liquid-liquid partition (water: ethyl acetate), the inhibitory zone of *H. gracilis* was exclusively visible in ethyl acetate fraction with diameters of 6 mm and 7.501.71 mm, respectively. Methanol extracts and ethyl acetate fractions of *H. gracilis* used in antioxidant tests have IC50 values of 290.49 ppm and 375.50 ppm, respectively [15].

Spermicidal activity

In this context, testing of crude ethanolic extract of Indian seaweeds *in vitro* male contraceptive effects against typical human sperm is done. Twelve seaweeds in total were tested for *in vitro* spermicidal potential. *Halimeda gracilis*, one of these twelve seaweeds, completely inhibited human spermatozoa at a concentration of 10 mg ml^{-1} in 20 seconds, and its EC50 value was 2.05 mg ml^{-1} in 20 seconds. The sperm was totally immobilized for 20 seconds, according to the dose and time-dependent spermicidal assay. The exposure of H. gracilis extract caused damaged to the sperm's plasma membrane. Using *H. gracilis* extract in MTT experiment, 88.5% of samples were cytotoxic. The LC50 value of *H. gracilis* extract against Artemia salina, when tested for cytotoxicity, was 34.8 g ml^{-1} [18].

Anti-cancer activity

The compounds such as DHPEA-EA [23], coumaric acid [26], caffeic acid [24], Carnosic acid [25], ferulic acid [27] and Rosmanol [28] are major compounds for anti-cancer activity. The MTT assay was performed to test *in vitro* cytotoxic effect of MHG and EAHG against breast cancer cells MDA-MB-231. Cells that had been cultured overnight were treated with varying concentrations of crude extract for 24 hours (0-100 ug/mL) the cytotoxic impact was seen in dose dependent manner, as the concentrations of these two extracts grew along with their potential cytotoxicity. At higher concentrations (100 ug/mL), EAHG and MHG respectively inhibited 95% and 100% of growth. And triggered apoptosis against skin cancer cells by producing an excessive amount of ROS, harming the mitochondrial membrane and nuclear

components. Furthermore, the results of the western blot analysis shown that the EAHG and MHG upregulate the apoptotic proteins Bax, Cyto C, p21, p53, Caspase 9 and Caspase 3 while downregulating the oncoproteins PI3K, AKT, p-AKT, BcL2. Together, the EAHG and MHG exhibited excellent anticancer activity against breast cancer by targeting the intrinsic apoptosis and PI3K/AKT signaling pathways [11].

Conclusion

Marine seaweeds are traditionally used as sea vegetables, due to their nutritional value and the potential use as functional ingredients, in Asian countries than in the western countries, H. gracilis has excellent biomedicial applications as per previous reports.

Based upon the different types of extracts of *Halimeda gracilis* used to reported various pharmacological activities like anti-bacterial, anti-diabetic, antioxidant, anti-plasmodial, anti-cancer, larvicidal and spermicidal activity and secondary metabolites like tannins, phenols, glycosides, steroids, alkaloids, proteins, sugar and quinones. Among major compounds isolated from *Halimeda gracilis*, 3, 4 DHPEA-EA, Caffeic Acid, Carnosic acid, Ferulic acid, Coumaric acid And Rosmanol are well-known compounds for anti-cancer activity.

References

1. Lopez-Santamarina A, Miranda JM, Mondragon ADC, Lamas A, Cardelle-Cobas A, Franco CM. Potential use of marine seaweeds as prebiotics: A review. Molecules. 2020;25(4):1004.
2. Cian RE, Drago SR, Sanchez de Medina F, Martínez-Augustin O. Proteins and carbohydrates from red seaweeds: evidence for beneficial effects on gut function and microbiota. Marine drugs. 2015;13(8):5358-5383.
3. de Borba Gurpilhares D, Cinelli LP, Simas NK, Pessoa Jr, A, Sette LD. Marine prebiotics: Polysaccharides and oligosaccharides obtained by using microbial enzymes. Food Chemistry. 2019;280:175-186.
4. Lopes D, Rey F, Leal MC, Lillebø AI, Calado R, Domingues MR. Bioactivities of lipid extracts and complex lipids from seaweeds: Current knowledge and future prospects. Marine Drugs. 2021;19(12):686.
5. Peñalver R, Lorenzo JM, Ros G, Amarowicz R, Pateiro M, Nieto G. Seaweeds as a functional ingredient for a healthy diet. Marine Drugs. 2020;18(6):301.
6. McHugh DJ. A guide to the seaweed industry. 2003.
7. McHugh DJ. A guide to the seaweed industry FAO Fisheries Technical Paper 441. Food and Agriculture Organization of the United Nations, Rome, 2003, 110.
8. Sarkar MSI, Kamal M, Hasan MM, Hossain MI. Present status of naturally occurring seaweed flora and their utilization in Bangladesh. Research in Agriculture Livestock and Fisheries. 2016;3(1):203-216.
9. El-Beltagi HS, Mohamed AA, Mohamed HI, Ramadan KM, Barqawi AA, Mansour AT. Phytochemical and potential properties of seaweeds and their recent applications: A review. Marine Drugs. 2022;20(6):342.
10. Guiry MD. AlgaeBase. World-wide electronisc publication, National University of Ireland, Galway (Taxonomic information republished from Algae Base with permission of MD Guiry). 2019.
11. Ramalingam V, Kumar NN, Harshavardhan M, Kumar HMS, Tiwari AK, Babu KS. Chemical profiling of marine seaweed *Halimeda gracilis* using UPLC-ESI-Q-TOF-MSE and evaluation of anticancer activity targeting PI3K/AKT and intrinsic apoptosis signaling pathway. Food Research International, 2022, 111394.
12. JV SA, Nayaka SR, Usha NS, Subha V, Manimekalai K, Syed M. Acute Toxicity Study and Antidiabetic Activity of Marine Alga-*Halimeda gracilis* Chooranam (HGC) In Freshwater Zebrafish Model. Biomedical and Pharmacology Journal. 2021;14(3):1647-1653.
13. Ravikumar S, Jacob Inbaneson S, Suganthi P. Seaweeds as a source of lead compounds for the development of new antiplasmodial drugs from South East coast of India. Parasitology research. 2011;109(1):47-52.
14. Widowati R, Handayani S, Suprihatin ILR. Phytochemicals and antioxidant of methanol extract of Gracilaria salicornia, *Halimeda gracilis*, *Halimeda macroloba*, and Hypnea asperi from Tidung Island coastal region. European Journal of Molecular & Clinical Medicine. 2021, 8(01).
15. Basir A, Tarman K, Desniar D. Antibacterial and antioxidant activity of green algae *Halimeda gracilis* from Seribu island district. Jurnal Pengolahan Hasil Perikanan Indonesia. 2017;20(2):211-218.
16. Suganya S, Ishwarya R, Jayakumar R, Govindarajan M, Alharbi NS, Kadaikunnan S. New insecticides and antimicrobials derived from *Sargassum wightii* and *Halimeda gracilis* seaweeds: Toxicity against mosquito vectors and antibiofilm activity against microbial pathogens. South African Journal of Botany. 2019;125:466-480.
17. Shanmugam M, Mody KH, Ramavat BK, Murthy A, Siddhanta AK. Screening of Codiacean algae (Chlorophyta) of the Indian coasts for blood anticoagulant activity. 2002.
18. Prakash S, Ravikumar S, Reddy KVR, Kannapiran E. Spermicidal activity of Indian seaweeds: an *in vitro* study. Andrologia. 2014;46(4):408-416.
19. Wikipedia contributors. Halimeda. In Wikipedia, The Free Encyclopedia. 2022, November 19. Retrieved 10:14, December 8, 2022.
20. Srinivasan R, Sengali Ragunath K, Karuppiah V, Radhesh Krishnan S, Gracy M. Isolation and screening of seaweed associated microbes for development of marine based agri–inputs. Seaweed Res Utiln. 2017;39:39-46.
21. Silva AMO, Novoa AV, Gutierrez DD, Mancini-Filho J. Seaweeds from Halimeda genus as sources of natural antioxidants. J. Anal. Pharm. Res. 2017;5(6):1-5.
22. CRC press, Taylor. Francis Group, Pubmed, Pubchem, Chemspider etc.
23. Nardi M, Baldelli S, Ciriolo MR, Costanzo P, Procopio A, Colica C. *Oleuropein aglycone* peracetylated (3, 4-DHPEA-EA (P)) attenuates H2O2-mediated cytotoxicity in C2C12 myocytes via inactivation of p-JNK/pc-Jun signaling pathway. Molecules. 2020;25(22):5472.
24. Rajendra Prasad N, Karthikeyan A, Karthikeyan S, Venkata Reddy B. Inhibitory effect of caffeic acid on cancer cell proliferation by oxidative mechanism in human HT-1080 fibrosarcoma cell line. Molecular and cellular biochemistry. 2011;349(1):11-19.
25. El-Huneidi W, Bajbouj K, Muhammad JS, Vinod A, Shafarin J, Khoder G. Carnosic acid induces apoptosis and inhibits Akt/mTOR signaling in human gastric cancer cell lines. Pharmaceuticals. 2021;14(3):230.
26. Hu X, Yang Z, Liu W, Pan Z, Zhang X, Li M. The anti-tumor effects of p-coumaric acid on melanoma A375 and B16 cells. Frontiers in Oncology. 2020;10:558414.

27. Gao J, Yu H, Guo W, Kong Y, Li Q, Yang S. The anticancer effects of ferulic acid is associated with induction of cell cycle arrest and autophagy in cervical cancer cells. Cancer Cell International. 2018;18(1):1-9.
28. Moore J, Yousef M, Tsiani E. Anticancer effects of rosemary (*Rosmarinus officinalis* L.) extract and rosemary extract polyphenols. Nutrients. 2016;8(11):731.