An Investigation into the Present Condition and Biomolecular Activities of Bangladeshi Seaweed with Deadly Diseases: A review

By

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A thesis submitted to the Department of Mathematics and Natural Science in partial fulfillment of the requirements for the degree of
Masters of Science in Biotechnology

Department of Mathematics and Natural Science
BRAC University
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Declaration

It is hereby declared that

1. The thesis submitted is my original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Approval

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of Fall, 2019 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Masters of Science in Biotechnology on January 2024.

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Ethics Statement

Since this is a review paper, no animals or plants were used. Even no living material gets hurt. So, there are no ethical issues.

Abstract

The potential for therapeutic and nutraceutical applications of marine algae is unparalleled because they contain several novel molecules and other bioactive compounds. Many known and unknown marine algae are abundant in Bangladesh's coastal area, with a total of 119 genera having been identified thus far. In Bangladesh, Tribal communities utilize seaweed as food (salad, soup, jelly, etc.), and Seaweed collectors engage in an annual harvesting operation, extracting a substantial quantity ranging from 6 to 9 metric tons, to clandestinely smuggle their bounty to neighboring countries. *U. pinnatifida* (wakame), *P. palmate* (dulse), *Laminaria* sp (kombu), *E. bicyclis* (arame), *P. yezoensis, P. tenera* (Nori), kelp, *S. fusiforme* (hijiki), *Ulva (*aonori), are widely used in different cuisines. Recently, in the USA, two commercially available products containing lutein, Aztec Marigold and Tagetes have been introduced to the market, showcasing the growing recognition and utilization of these sources in the health and nutrition industry. Natural drugs are being developed by scientists to prevent and cure various fatal diseases, and seaweeds are among their most promising options because of their diverse metabolites (saturated/ unsaturated fatty acids, alkaloids, terpenoids, sulfated polysaccharides, polyphenols, amino acids, vitamins, minerals, pigments, etc.), inhibit various viruses, bacteria, protozoa, diabetes, cancer, tumors, and oxidants, inflammatory, as well as neuroprotective, and cardiovascular disease preventive. The U.S. Food and Drug Administration has given the green light for astaxanthin to be consumed by humans. The carrageenan-based nasal spray and the heparin spray are both safe and efficient in treating the common cold, pulmonary coagulopathy and swelling and is available in the market. Fucoidan is a safe and effective adjuvant, serve as a vaccine. This systematic review focuses on enormous research papers published on seaweeds found in Bangladesh, their metabolites, and their potential bioactivities against chronic and life-threatening diseases.

Keywords: Bangladesh Marine algae; secondary metabolites; Viral diseases; Cancer; Cardio–vascular diseases; anti diabetics;

Literature Search Methodology:

The latest compilation of seaweed species available in Bangladesh was conducted, focusing on marine algae. Additionally, the secondary metabolites of the most abundant seaweeds in Bangladesh were documented. Conducting an exhaustive examination of in vitro, in vivo, and clinical research literature, a comprehensive investigation was undertaken to scrutinize the potential anticancer, antiviral, antimicrobial, antidiabetic, antioxidant, anti-inflammatory, and cardiovascular disease-preventing attributes inherent in the metabolites derived from these marine algae. The search encompassed databases such as Scopus, Sci-Hub, PubMed, MDPI, Science Direct, Springer Link, and Web of Science, Google Scholar. The inclusive review includes peer-reviewed papers released up to February 2023, without any restriction on publication years.

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Table of Contents

Declaration **2**
Approval **3**
Abstract **5**
Acknowledgement **7**
Table of Contents **8**
Chapter 1 Introduction **14**
Chapter 2 Information about seaweed that occurs naturally in Bangladesh (current state): **15**
2.1 Distribution of seaweeds: 15
2.2 Bangladesh's seaweed species: 18
Chapter 3 ..... **30**
The Pharmacologically active components of Bangladeshi seaweeds: **30**
3.1 Polysaccharides: 33
3.1.1 Fucoidans 34
3.1.2 Laminarin: 35
3.1.3 Carrageenans: 37
3.1.4 Ulvans: 38
3.1.5 Algins/ Alginates/ Alginic acid: 38
3.2 Polyphenolic Compounds: 41
3.2.1 Phlorotannin: 41
3.2.2 Flavonoids: 42
3.3 Terpenes: 43
3.3.1 Sesquiterpenes: 46
3.3.2 Diterpenes: 46
3.3.3 Triterpenoids: 47
3.4 Steroid on Sterols: 48
3.5 Alkaloids: 48
3.6 Fatty Acids and Lipids: 51
3.7 Protein and Poly Peptides: 54
3.8 Glycerol: 54

3.9 Pigments:.....56
3.9.1 Chlorophyll:.....56
3.9.2 Carotenoids:.....58
3.9.2.1 β-Carotene:.....58
3.9.2.2 Astaxanthin:.....60
3.9.2.3 Fucoxanthin:.....61
3.9.2.4 Zeaxanthin and Lutein:.....62
3.9.3 Plycobiliprotein or Phicobilin:.....63
3.10 Vitamins, minerals, and others nutritional value:.....64
Chapter 4.....66
Bioactive compounds sourced from algae hold promise for potential therapeutic interventions against various life-threatening ailments:.....66
4.1 Antiviral activities:.....68
4.1.1 COVID-19 / SARS-CoV-2/Corona Virus:.....72
4.1.2 Influenza Virus:.....76
4.1.3 Dengue / DENV:.....80
4.2 Antibacterial activities:.....82
4.3 Anti-parasitic/Anti Protozoal activity:.....87
4.3.1 Malaria:.....89
4.4 Preventive and Protective agents for cardiovascular diseases (CVDs):.....90
4.5 Antidiabetic potentiality:.....96
4.6 Anticancer activities:.....98
Chapter 5 Conclusion:.....104
References……...105

List of Tables

Table 1: List of seaweed species that are available in Bangladesh.....18

Table 2: Various classes of algae-derived compounds showcase antiviral properties, each with unique mechanisms of action:.....70

Table 3: Extracted compounds from marine algae with antibacterial activities.....85

Table 4: Antiparasitic effect of marine algae and their mechanisms of action.....88

Table 5: The effects of some seaweed extracts on CVDs.....94

Table 6: Anticancer effect of different metabolites from different seaweeds 101

List of Pictures

Picture 1. *Sargassum sp* 16

Picture 2. *Hypnea sp* 16

Picture 3. *Ulva sp* 16

Picture 4. *Porphyra sp* 16

Picture 5. *Rosenvigea sp* 16

Picture 6. *Gracilaria sp* 16

Picture 7. *Padina sp* 17

Picture 8. *Palmaria sp* 17

Picture 9. *Undaria sp* 17

Picture 10. *Chaetomorpha sp* 17

List of Figures

Figure 1. Agar 31

Figure 2. beta- carotene..... 31

Figure 3. Lamenarin..... 31

Figure 4. Fucoxanthin 31

Figure 5. Fucosterol 31

Figure 6. Fucoidan 32

Figure 7. Flavinoid..... 32

Figure 8. Carrageenan..... 32

Figure 9. Porphyran 32

Figure 10. Phlorotannin 32

Figure 11. Caulerpin 32

Figure 12. Phytol..... 32

List of Acronyms

ACE- Angiotensin Converting enzyme

AIDS- Acquired immunoDeficiency Syndrome

ASFV- African Swine Fever Virus

AMP- Antimicrobial peptides

AMPK- Adenosine monophosphate activated protein kinase

Bcl- B cell lymphoma

CO-1- Cytochrome c oxidase subunit-1

COX2- cyclooxygenase- 2

CRP- c- reactive protein

DC- Dendritic cell

DHA- Docosahyexaenoic acid

DNA- deoxyribonucleic acid

DPA- Docosapentaenoic acid

DPP- dipeptidyl peptidase

DR- Death receptor

ELISA- enzyme linked immune-absorbent assay

EPA- 13 Eicosapengtaenoic acid

GADD- Growth arrest and DNA damage

GIP- Gastric inhibitory polypeptide

GLP- glucagon like peptide

GST- Glutathione S- transferase

GTC-FID- gas chromatography with flame- ionization detection

HBV- hepatitis B virus

HDL-C- High density lipoprotein cholesterol

HIF- hypoxia inducible factor

HIV- human immunodeficiency virus

HPLC-ELSD- high performance liquid chromatography with evaporative light scattering detection

HPV- human papillomavirus

HSV- herpes simplex virus

IFN- interferon

IgA- immunoglobulin A

IHD- Ischemic heart disease

IL- interleukins

iNOS- inducible nitric oxide synthase

IRSI- Insulin receptor substrate 1

JNK- c-Jun N-terminal kinase

LDL-C- Low density lipoprotein cholesterol

MAPK- Mitogen activated protein kinase

Mcl- Myeloid cell leukemia

MCP- Monocyte chemoattractant protein

MIC- minimal inhibitory concentration

MIP- Macrophage inflammatory protein

MMP- Matrix metalloproteinase

MRSA- Methicillin resistant *Staphylococcus aureus*

NF-κB- Nuclear factor kappa light chain enhancer of activated B cell

NK- Natural killer

NO- nitric oxide

NPs- nanoparticles

PGE-2- Prostaglandin E2

PI3K-AKT- Phosphatidylinositol 3- kinase and protein kinase B

PTP1B- Protein tyrosine phosphatase 1B

PUFA- polyunsatturated fatty acid

RNA- ribonucleic acid

ROS- Reactive Oxygen Species

RSV- Respiratory Syncytial virus

SOD- Superoxide dismutase

STD- Sexually transmitted diseases

TC- Total cholesterol

TG- triglycerides

TLR- Toll like receptor

TNF- Tumour Necrosis Factor

ULK- elegans uncoordinated- 51 like kinase

UV-B- Ultraviolet B

VHSV- Viral hemorrhagic septicemia virus

Chapter 1

Introduction

“Seaweed’’ is a colloquial term from the common name of countless species of microscopic, macroscopic, and multicellular algae that do not have root systems, flowers, leaves, stems, fruits, or seeds, generally grow and live attached to rock or other substrate below the high-water mark or remain drifted in the oceans (Borowitzka,1995). Marine algae offer distinct and cost-effective metabolites with commercial production potential. Various compounds derived from the marine environment are already in use, contributing to the development of drugs for treating conditions such as viral infections, neuropathic pain, and hypertriglyceridemia. Notable among these are marine-derived anticancer products like Adcetris, Halaven, Yondelis, and Cytosar-U (Pereria et al., 2019), Utilizing creams and cosmetics derived from seaweed is an effective approach to upholding skin health and enhancing beauty. These products contribute to accelerating epidermal regeneration, diminishing scars, providing moisture, revitalizing the skin, and promoting a fairer complexion (Scieszka et al., 2019). These aquatic species are currently gaining more and more recognition due to their bioactive metabolites, which have unmatched potential for a variety of pharmaceutical activities. The abiotic elements within the marine ecosystem, including temperature, nutrients, salinity, oxygen levels, solar energy, water clarity, tides, aerial exposure, and currents, significantly impact the production and release of bioactive chemical compounds by marine organisms. Due to their supplemental, nutritional, and pharmaceutical activities, all bioactive compounds found in marine macro algae hold great interest. Moreover, algae – derived bioactive molecules offer potential health benefits and diverse applications such as antibacterial,

antiviral, antidiabetic, anti-cancer, anti-protozoal, anti-inflammatory, antioxidant, and neuroprotective applications, etc (Alam et al., 2021).

The Bangladeshi Coast has a variety of marine algae, particularly in St. Martin, Cox's Bazar, and Sundarbans Mangrove Forest. There are approximately 5000 metric tons of seaweed biomass accessible. Seaweeds are commonly available from October to April because of seasonal variations in water quality parameters, and they are most abundant from January to March (Hornsey and Hide, 1976). The utilization of seaweed in Bangladesh paints a unique economic landscape, where economically valuable applications appear to be relatively scarce. While the Mog or Rakhyine tribal community incorporates seaweed into their cuisine as sauce and salad, and an annual cohort of approximately 400 seaweed collectors on St. Martin's Island clandestinely harvests 6-9 metric tons of wet seaweed for smuggling purposes, broader economic avenues for seaweed utilization in the country seem limited (Sarkar et al., 2016).

Chapter 2

Information about seaweed that occurs naturally in Bangladesh (current state):

2.1 Distribution of seaweeds:

The six coastal districts of Bangladesh, Cox’s Bazar, Chittagong, Noakhali, Potuakhali, Shatkhira, and Bagerhat exhibit significant potential for seaweed cultivation. Particularly promising are Moheshkhali, Sonadia, Nuniachara, Inany, Teknaf, and Saint Martin’s Island, showing a high likelihood of hosting the highest number of seaweed varieties (Hossain et al., 2021). There were 197 seaweed species found on the Bangladesh coast, with 95 being red, 46 being green, and 56

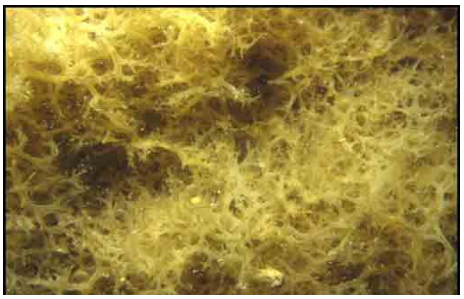
being brown (Islam et al., 2010). Recently, the Bangladesh Fisheries Research Institute released a species checklist featuring taxonomic descriptions for 132 seaweed species. Among these, 28 species are classified under Chlorophyta, 35 under Phaeophyta, and 69 under Rhodophyta (BFRF, 2011). However, Aftab Uddin (2019) confirmed the availability of 244 seaweed species in the coast water (Aftab Uddin, 2019).

Picture 1. *Sargassum sp*

Picture 2. *Hypnea sp*

Picture 3. *Ulva sp*

Picture 4. *Porphyra sp*



Picture 5. *Rosenvigea sp*

Picture 6. *Gracilaria sp*

Picture 7. *Padina sp*

Picture 8. *Palmaria sp*

Picture 9. *Undaria sp*

Picture 10. *Chaetomorpha sp*

The Sundarban Mangrove Forest benefits from a favorable climate, environmental conditions, and an extensive network of waterways, facilitating the natural growth of approximately 60 seaweed species. Notable species include *Boodliopsis sundarbanesis, Ulva sp, Catenella sp, Gelidium sp, Polysiphonia sp, Ceramium sp, Bostrychia sp, Compsopogon sp,* and more (Siddique et al., 2019). Cox's Bazar hosts around 155 seaweed species, thriving notably along the Shaplapur coast, Jaillapara, Shahparirdip in Teknaf, Nuniachara, Nazirartek in the Bakkhail-Moheshkhali river estuary, and the planted mangrove forest of Parabon region. The main species include *Hypnea musciformis* and *Enteromorpha intestinalis*. St. Martin's Island hosts around 140 seaweed species, distributed across its Western, Eastern, and Southern coasts. Notably, the Northern coast lacks seaweeds. The Southern coast features species such as *Sargassum coriifolium, Chaetomorpha moniligera, Gracilaria verrucosa,* and *Colpomenia sinuosa.* On the Eastern coast, species like

Sargassum coriifolium, Hypnea musciformis, Hypnea pannosa, and others are prevalent. Meanwhile, the Western coast exhibits species like *Gracilaria textorii, Hypnea musciformis, Petalonia fascia, Dictopteris divaricatum,* and more.

2.2 Bangladesh's seaweed species:

Chlorophyta-green algae, phaeophyta-brown algae, and Rhodophyta-red - red algae are the only 3 major divisions for about 265 seaweed species of 119 genera.

Table 1: **List of seaweed species that are available in Bangladesh**

No	Genus	Species	Division	Habit
1	*Asparagopsis*	*A.taxiformis* (Sea asparagus)	Rhodophyta	Macro alga with fluffy tufts thallus
2	*Acrochaetium*	*A. bengalicum*	Rhodophyta	Micro alga with loosely branched filaments
		A. crassipes		Micro alga with loosely branched filaments
		A. nurulislamii		Macro alga with filamentous
		A. polysporum		Macro alga with filamentous
		A. sagraeanum		Macro alga with filamentous
		A. zosterae		Macro alga with filamentous
3	*Actinotrichia*	*A. fragilis*	Rhodophyta	Macro alga with dichotomous branched filaments
4	*Acanthophora*	*A. specifera*	Rhodophyta	Macro alga with brittle, spiny thallus
5	*Amphiroa*	*A. fragilissima*	Rhodophyta	Macro alga with fragile calcified clumps thallus
		A. anceps		Macro alga with fragile calcified clumps thallus
		A. rigida		Macro alga with fragile calcified clumps thallus
		A. cryptarthrodia		Macro alga with fragile calcified clumps thallus

Table-1 continued

6	*Antithamnion*	*A. diverfens*	Rhodophyta	Macro alga with branched whorl-branchlets thallus
		A. cruciatum		Macro alga with branched whorl-branchlets thallus
7	*Antithamnio-nella*	*A. elegans*	Rhodophyta	Macro alga with branched whorl-branchlets thallus
		A. floccose		Macro alga with branched whorl-branchlets thallus
8	*Bostrychia*	*B. radicans*	Rhodophyta	Macro alga with prostrate or erect thallus
		B. tenella		Macro alga with prostrate or erect thallus
9	*Bangia*	*B. fuscopurpurea*	Rhodophyta	Macro alga with rapid growth filaments attached to small thallus
10	*Catenella*	*C. impudica*	Rhodophyta	Macro alga with irregularly branched thallus
		C. nipae		Macro alga with irregularly branched thallus
		C. repens		Macro alga with irregularly branched thallus
11	*Chrysymenia*	*C. okamura*	Rhodophyta	Macro alga with gelatinous single thallus
		C. agardhii		Macro alga with gelatinous single thallus
		C. Enteromorpha		Macro alga with gelatinous single thallus
12	*Ceramium*	*C. tenerrimum*	Rhodophyta	Macro alga with irregular branching thallus
		C. fastigiatum		Macro alga with irregular branching thallus
		C. gracillimum		Macro alga with irregular branching thallus
		C. brevizonatum		Macro alga with irregular branching thallus
13	*Callithamnion*	*C. corymbiferum*	Rhodophyta	Macro alga with free filamentous attaching small thallus
14	*Champia*	*C. parvula*	Rhodophyta	Small thallus with tufts or dense spherical clumps
15	*Callophyllis*	*C. rangiferina*	Rhodophyta	Macro alga with dichotomously branched thallus
16	*Centroceras*	*C. clavulatum*	Rhodophyta	Macro alga with dichotomously branched thallus

Table-1 continued

17	*Chondrus*	*C. crispus* (Irish moss)	Rhodophyta	Macro alga with dichotomously branched thallus
18	*Caloglossa*	*C. lerieuri*	Rhodophyta	Macro alga with dichotomously branched thallus
19	*Cottoniella*	*C. filamentosa*	Rhodophyta	Macro alga with threads like filaments
20	*Cthonoplastis*	*Cthonoplastis sp*	Rhodophyta	
21	*Crouania*	*C. attenuate*	Rhodophyta	Macro alga with decorticated thallus
22	*Dudresnaya*	*D. hawaiiensis*	Rhodophyta	Macro alga with gelatinous, bushy thallus
		D. Vertiallata		Macro alga with gelatinous, bushy thallus
23	*Dasya*	*D. Corymbifera*	Rhodophyta	Macro alga with soft hair on erect thallus
		D. pedicillata		Macro alga with soft hair on erect thallus
24	*Dermonema*	*D. pulvinatum*	Rhodophyta	Macro alga
25	*Dichotomaria*	*D. obtusata*	Rhodophyta	Macro alga with bushy thallus
26	*Eucheuma*	*E. cottonii*	Rhodophyta	Macro alga with apical meristem in thallus
		E. Subinosum		Macro alga with apical meristem in thallus
27	*Erythrocladia*	*E. Subintegra*	Rhodophyta	Macro alga with thallus of creeping filaments
		E. carnea	Rhodophyta	Macro alga with thallus of creeping filaments
28	*Goniotrichum*	*G. alsidii*	Rhodophyta	Macro alga with filaments
29	*Gracilaria*	*G. tenusstipitata* (ogonori)	Rhodophyta	Macro alga with solitary thallus
		G. textori		Macro alga with solitary thallus
		G. verrucose (ogonori)		Macro alga with solitary thallus
		G. coronopifolia		Macro alga with solitary thallus
		G. spinuligera		Macro alga with solitary thallus
		G.canaliculate (Bangladeshi ogonori)		Macro alga with solitary thallus
		G. Corticata		Macro alga with solitary thallus
		G. tikrahiae		Macro alga with solitary thallus
30	*Gellidium*	*G. amansii*	Rhodophyta	Macro alga with erect thallus
		G. pusillum		Macro alga with erect thallus
31	*Gelidiella*	*G. tenwssiona*	Rhodophyta	Macro alga with tuft thallus
		G. tenera		Macro alga with tuft thallus

Table-1 continued

32	*Gracilariopsis*	*G. longissimima* (Dragon beard algae)	Rhodophyta	Macro alga with erect thallus
33	*Galaxaura*	*G. fastigiate*	Rhodophyta	Macro alga with bushy thallus
		G. oblongata		Macro alga with bushy thallus
		G. rugosa		Macro alga with bushy thallus
34	*Ganonema*	*G. pinnatum*	Rhodophyta	Macro alga dichotomously branched thallus
35	*Gigartina*	*G. intermedia*	Rhodophyta	Macro alga with subdichotomously branched thallus
36	*Grateloupia*	*G. lanceolate*	Rhodophyta	Macro alga with large, soft, gelatinous blade on thallus
		G. livida		Macro alga with large, soft, gelatinous blade on thallus
37	*Halymenia*	*H. agardhii*	Rhodophyta	Macro alga with solitary or erect thallus
		H. dilatate		Macro alga with solitary or erect thallus
		H. venusta		Macro alga with solitary or erect thallus
		H. duchassaignii		Macro alga with solitary or erect thallus
		H. discoidia		Macro alga with solitary or erect thallus
		H. floridana		Macro alga with solitary or erect thallus
		H. floresia		Macro alga with solitary or erect thallus
		H. gelinaria		Macro alga with solitary or erect thallus
		H. maculate		Macro alga with solitary or erect thallus
		H. durvillei (dragon tongue)		Macro alga with solitary or erect thallus
38	*Hypnea*	*H. musciformis* (maiden hair)	Rhodophyta	Micro alga with bushy thallus
		H. esperi (maiden hair)		Micro alga with bushy thallus
		H. pannosa (maiden hair)		Micro alga with bushy thallus
		H. charoides		Micro alga with bushy thallus
		H. aspera		Micro alga with bushy thallus

Table-1 continued

		H. boergesenii		Micro alga with bushy thallus
		H. valentiae		Micro alga with bushy thallus
		H. cornuta		Micro alga with bushy thallus
		H. flexicaulis		Micro alga with bushy thallus
39	*Helminthocladia*	*H. australis*	Rhodophyta	Micro alga with cylindrically branched thallus
40	*Herposiphonia*	*H. dendroidea*		Macro alga with prostrate delicate thallus
		H. tenella	Rhodophyta	Macro alga with prostrate delicate thallus
41	*Heterosiphonia*	*Heterosiphonia sp*	Rhodophyta	Macro alga with spongy thallus
42	*Himanthalia*	*H. elongata* (sea spaghetti)	Rhodophyta	Macro alga with button like thallus
43	*Hildenbrandia*	*H. rubra*	Rhodophyta	Micro alga with vertical filaments in perithallus
44	*Hydrolithon*	*H. onkodes*	Rhodophyta	Micro alga with lumpy growth dimerous thallus
45	*Jania*	*J. adhaerens*		Macro alga with small cushion like thallus
		J. ungulate		Macro alga with small cushion like thallus
		J. rubens	Rhodophyta	Macro alga with small cushion like thallus
46	*Kallymenia*	*K. cribosa*		Macro alga with fleshy thallus
		K. tasmanica		Macro alga with fleshy thallus
		K. rosea		Macro alga with fleshy thallus
		K. rubra	Rhodophyta	Macro alga with fleshy thallus
		K. perforate		Macro alga with fleshy thallus
47	*Kappaphycus*	*K. alvarezii* (sea moss/ cottonii)	Rhodophyta	Macro alga with tough, coarse fleshy thallus
48	*Liagora*	*L. albicans*		Macro alga with erect thallus
		L. ceranoides		Macro alga with erect thallus
		L. donaldiana		Macro alga with erect thallus
		L. hawaiiana		Macro alga with erect thallus
		L. perennis		Macro alga with erect thallus
		L. tetrasporifera		Macro alga with erect thallus
		L. valida		Macro alga with erect thallus
		L. viscida		Macro alga with erect thallus
		L. harveyiana		Macro alga with erect thallus
		L. ferinosa	Rhodophyta	Macro alga with erect thallus
49	*Laurrencia*	*L. obtuse*	Rhodophyta	Macro alga with tuft thallus

		L. pinnata		Macro alga with tuft thallus
		L. ceranoides		Macro alga with tuft thallus
50	*Lophocladia*	*L. trichociados*	Rhodophyta	Macro alga with filaments
		L. kuetzingii		Macro alga with filaments
51	*Lithothamnion*	*L. glaciala*		Macro alga with irregular, coral like thallus but fragile
		L. calcareum (mearl)	Rhodophyta	Macro alga with irregular, coral like thallus but fragile
52	*Lithophyllum*	*L. kotschyanum*		Macro alga with lamellae or protrusions makes adherent crusts
		L. okamurae	Rhodophyta	Macro alga with lamellae or protrusions makes adherent crusts
53	*Melobesia*	*M. confervicola*	Rhodophyta	Macro alga with unbranched spermatangial filaments.
54	*Messophylum*	*Messophyllum sp*	Rhodophyta	Micro alga
55	*Neurymenia*	*N. fraxinifolia*	Rhodophyta	Macro alga
56	*Nemalion*	*N. helmithoides*	Rhodophyta	Macro alga with fairly large erect thallus
57	*Porphyra (Nori)*	*P. umbilicalis*	Rhodophyta	Macro alga with sheet like thallus
		P. tenera		Macro alga with sheet like thallus
		P. yenzoensis		Macro alga with sheet like thallus
		P. deoica		Macro alga with sheet like thallus
		P. purpurea		Macro alga with sheet like thallus
		P. lacinitata		Macro alga with sheet like thallus
		P. leucosticte		Macro alga with sheet like thallus
		P. pseudolinearis		Macro alga with sheet like thallus
		P. indica		Macro alga with sheet like thallus
		P. vietnamensis		Macro alga with sheet like thallus
58	*Pterosiphonia*	*P. pennata*	Rhodophyta	Macro alga with bilaterally symmetrical thallus
59	*Palmaria*	*P. palmata* (dulse)	Rhodophyta	Macro alga with leathery thallus
60	*Polysiphonia*	*P. denudate*	Rhodophyta	Micro alga with fine-branched filaments
		P. mollis		Macro alga with fine-branched filaments
		P. harveyii		Macro alga with fine-branched filaments
		P. scheideri		Macro alga with fine-branched filaments
61	*Peyssonellia*	*P. polymorpha*	Rhodophyta	Macro alga with crust-like irregularly rounded thallus

62	*Scinaia*	*S. complanate*		Macro alga with dichotomously branched thallus
		S. japonica	Rhodophyta	Macro alga with dichotomously branched thallus
63	*Sacronema*	*S. jurcellatum*	Rhodophyta	Micro alga
64	*Struvea*	*S. anastomonas*	Rhodophyta	Micro alga with aseptate stipe thallus
65	*Solieria*	*S. robusta*	Rhodophyta	Macro alga with cylindrical thallus
66	*Spermotham-nion*	*S. repens*	Rhodophyta	Macro alga with filaments
67	*Tolypiocladia*	*T. glomerulata*	Rhodophyta	Macro alga with soft, bushy thallus
68	*Titanophycus*	*T. Validus*	Rhodophyta	Macro alga
69	*Tricleocarpa*	*T. cylindrica*		Macro alga with bushy thallus
		T. fragilis	Rhodophyta	Macro alga with bushy thallus
70	*Vanvorsita*	*V. coccinea*	Rhodophyta	Macro alga
71	*Falkenbergia*	*F. hillebrandii*	Rhodophyta	Macro alga
72	*Agarophyton*	*Agarophyton sp*	Rhodophyta	Micro alga with filaments
73	*Ascophyllum*	*A.nodosum* (goemon)	Phaeophyte	Macro alga with leathery thallus
74	*Colpomenia*	*C. peregrina*	Phaeophyte	Macro alga with hollow and crisp thallus
		C.ramosa		Macro alga with hollow and crisp thallus
		C. sinusa		Macro alga with hollow and crisp thallus
75	*Chnoospora*	*C. implexa*	Phaeophyte	Macro alga with creeping thallus
76	*Dictoyota*	*D. bratatresii*	Phaeophyte	Macro alga with small creeping thallus
		D. dichotoma		Macro alga with small creeping thallus
		D. divaricate		Macro alga with small creeping thallus
		D. friabilis		Macro alga with small creeping thallus
		D. patens		Macro alga with small creeping thallus
		D. ciliolate		Macro alga with small creeping thallus
		D. atomaria		Macro alga with small creeping thallus

		D. menstrualis		Macro alga with small creeping thallus
		D. flabellate		Macro alga with small creeping thallus
77	*Dictyopteris*	*D. australis*	Phaeophyte	Macro alga with erect thallus
		D. divarcatum		Macro alga with erect thallus
78	*Ectocarpus*	*E. breviarticulatus*	Phaeophyte	Micro alga with highly branched filaments
		E. rhodochortonoides		Micro alga with highly branched filaments
		E. siliculosus		Micro alga with highly branched filaments
79	*Eisenia*	*E. bicyclis*	Phaeophyte	Micro alga with branched and feathered stipe
80	*Feldmannia*	*F. columellaris*	Phaeophyte	Micro alga with filamentous tuft
		F. elachistaeformis		Micro alga with filamentous tuft
		F. india		Micro alga with filamentous tuft
		F. vaughani		Micro alga with filamentous tuft
81	*Giffordia*	*G. conifera*	Phaeophyte	Micro alga with filaments
		G. irregularis		Micro alga with filaments
		G. mitchellae		Micro alga with filaments
		G. rallsae		Micro alga with filaments
		G. thyrsoideus		Micro alga with filaments
82	*Hydroclathrus*	*H. clathratus* (sponge seaweed)	Phaeophyte	Macro alga with perforate thallus
		H. tenuis		Macro alga with perforate thallus
83	*Ishigae*	*I.okamurae*	Phaeophyte	Macro alga
84	*Isochrysis*	*I.galbana*	Phaeophyte	Micro alga with unicellular microtubular filamentous thalloid
85	*Lobophora*	*L. variegate*	Phaeophyte	Macro alga with erect ruffled thallus
86	*Macrocystis*	*M. pyrifera*	Phaeophyte	Macro alga with long braching blade
87	*Myriactula*	*M. arabica*	Phaeophyte	Macro alga
88	*Nannochloropsis*	*Nannochloropsis sp*	Phaeophyte	single cell algae
89	*Padina*	*P. australis*	Phaeophyte	Macro alga with leaf-like thallus
		P. tenuis		Macro alga with leaf-like thallus
		P. gymnospora		Macro alga with leaf-like thallus
		P. pavonica		Macro alga with leaf-like thallus
		P. boryana		Macro alga with leaf-like thallus

		P. usoehtunni		Macro alga with leaf-like thallus
		P. sanctae-crucis		Macro alga with leaf-like thallus
		P. tetratsromatica		Macro alga with leaf-like thallus
		P. vickersiae		Macro alga with leaf-like thallus
		P. arborescens		Macro alga with leaf-like thallus
		P. fraseri		Macro alga with leaf-like thallus
		P. antillarum		Macro alga with leaf-like thallus
90	*Petalonia*	*P. fascia*	Phaeophyte	Macro alga with leaf-like clustered thallus
91	*Rosenvingea*	*R. intricate*	Phaeophyte	Macro alga with erect thallus
		R. orientalis		Macro alga with erect thallus
		R. sanctae-cruicis		Macro alga with erect thallus
92	*Ralfsia*	*R. fungiformis*	Phaeophyte	Macro alga with erect thallus
93	*Spatoglossum*	*S. asperum*	Phaeophyte	Macro alga with large flattend thick coarse thallus
94	*Stypopodium*	*S. zonale*	Phaeophyte	Macro alga with smooth broad bladed thallus
95	*Sphacelaria*	*S. tribuloides*	Phaeophyte	Micro alga with filaments
		S. nova-hollandiae		Micro alga with filaments
96	*Sargassum*	*S. caryophyllum*	Phaeophyte	Macro alga with highly branched thallus
		S. flavicans		Macro alga with highly branched thallus
		S. ilicifolium		Macro alga with highly branched thallus
		S. piluliferum		Macro alga with highly branched thallus
		S. vulgare		Macro alga with highly branched thallus
		S. wightii		Macro alga with highly branched thallus
		S. coriifolium		Macro alga with highly branched thallus
		S. crassifolium		Macro alga with highly branched thallus
		S. oligocystum		Macro alga with highly branched thallus
		S. platycarpum		Macro alga with highly branched thallus
		S. myriocystum		Macro alga with highly branched thallus

		S. filipendula		Macro alga with highly branched thallus
		S. arnaudianum		Macro alga with highly branched thallus
		S. swartzii		Macro alga with highly branched thallus
		S. tenerrimum		Macro alga with highly branched thallus
97	*Skeletonema*	*Skeletonema sp*	Phaeophyte	Diatom
98	*Undaria*	*U. pinnatifida* (wakame)	Phaeophyte	Macro, thallus
99	*Laminaria*	*L. japonica (kombu)*	Phaeophyte	Macro alga with large leathery thallus
		L. digitate (kombu breton)		Macro alga with large leathery thallus
		L. saccharina (kombu royal)		Macro alga with large leathery thallus
100	*Acetabularia*	*A.catyculus*	Chlorophyta	Macro alga with large and unicelluler root, stem and leaves
101	*Boodlea*	*B. composite*	Chlorophyta	Macro alga with erect filamentous thallus
102	*Bryopsis*	*B. indica*	Chlorophyta	Macro alga with filamentous bushy thallus
103	*Boodliopsis*	*B. sundarbanensis*	Chlorophyta	
104	*Chaetomorpha*	*C. aerae*	Chlorophyta	Micro alga with filaments
		C. brachygona		Micro alga with filaments
		C. gracilis		Micro alga with filaments
		C. linum		Micro alga with filaments
		C. moniligera		Micro alga with filaments
105	*Caulerpa*	*C. macrophysa*	Chlorophyta	Macro alga with rubbery thallus
		C. Mexicana		Macro alga with rubbery thallus
		C. peltate		Macro alga with rubbery thallus
		C. racemosa (sea grape)		Macro alga with rubbery thallus
		C. sertularoides		Macro alga with rubbery thallus
		C. taxifolia		Macro alga with rubbery thallus
		C. fergusonii (green feather)		Macro alga with rubbery thallus
		C. cactoides		Macro alga with rubbery thallus
		C. sealpelliformis		Macro alga with rubbery thallus

		C. okamurae		Macro alga with rubbery thallus
		C. chemnitzia		Macro alga with rubbery thallus
106	*Cladophora*	*C. echinus*	Chlorophyta	Macro alga with filaments
		C. patentiramea		Macro alga with filaments
		C. sakaii		Macro alga with filaments
		C. vagabunda		Macro alga with filaments
		C. crispula		Macro alga with filaments
		C. prolifera		Macro alga with filaments
		C. herpestica		Macro alga with filaments
		C. laetevirens		Macro alga with filaments
		C. gracilis		Macro alga with filaments
107	*Codium*	*C. geppei*	Chlorophyta	Macro alga with creeping thallus
		C. fragile		Macro alga with creeping thallus
		C. extricatum		Macro alga with creeping thallus
108	*Cladophorella*	*C. calcicole*	Chlorophyta	Macro alga with pseudodichotomously branched thallus
109	*Chlorella*	*Chlorella sp*	Chlorophyta	single cell algae
110	*Dictyosphaeria*	*D. cavernosa*	Chlorophyta	Macro alga with tough, solid cushion like thallus
111	*Enteromorpha* (aonori/ green string lattuce)	*E. clathrate*	Chlorophyta	Macro alga with filaments
		E. compressa		Macro alga with filaments
		E. intestinalis		Macro alga with filaments
		E. prolifera		Macro alga with filaments
		E. moniligera		Macro alga with filaments
		E. torta		Macro alga with filaments
112	*Halimeda*	*H. discoidea*	Chlorophyta	Macro alga with compact erect thallus
		H. opuntia		Macro alga with compact erect thallus
		H. gracilis		Macro alga with compact erect thallus
		H. minima		Macro alga with compact erect thallus
		H. tuna		Macro alga with compact erect thallus

113	*Halodula*	*H. universis*	Chlorophyta	Macro alga with root, erect stem and leaves.
114	*Lola*	*L. capillaris*	Chlorophyta	Micro alga
		L. implexa		Micro alga
		L. tortuosa		Micro alga
115	*Phyllodictylon*	*P. anastromosans*	Chlorophyta	Micro alga with filamentous, erect thallus
116	*Rhizoclonium*	*R. grade*	Chlorophyta	Macro alga with finely branched or filamentous
		R. hookeri		Macro alga with finely branched or filamentous
		R. kerneri		Macro alga with finely branched or filamentous
		R. riparium		Macro alga with finely branched or filamentous
117	*Tetraselmis*	*Tetraselmis sp*	Chlorophyta	single cell algae
118	*Ulva*	*U. lactuca* (sea lattuce)	Chlorophyta	Macro alga with flat and blade thallus
		U. intestinalis (gut weed)		Macro alga with flat and blade thallus
		U. compressa		Macro alga with flat and blade thallus
		U. conglobate		Macro alga with flat and blade thallus
		U. fasciata		Macro alga with flat and blade thallus
		U. reticulata		Macro alga with flat and blade thallus
		U. linza (mini sea lattuce)		Macro alga with flat and blade thallus
119	*Valoniopsis*	*V. pachynema*	Chlorophyta	Macro alga with stiff, coarse filamented thallus

Chapter 3

The Pharmacologically active components of Bangladeshi seaweeds:

Being readily accessible compared to synthetic products, natural origin products were once the cornerstone of the pharmaceutical armamentarium. In the last few decades, marine algae and their remarkable primary and secondary metabolites have gained recognition for their potent therapeutic properties, attributed to the diverse adaptation strategies that enable these algae to thrive in harsh conditions and produce a myriad of secondary metabolites (Dahms and Dobretsov, 2017), (Levasseur et al., 2020). The nutritional composition of algae is characterized by a spectrum of components, comprising lipids (1-5%), proteins (5-47%), polysaccharides (15-76%), and minerals (7-36%). Significantly, the protein content demonstrates considerable variability across different types of seaweeds: red seaweeds range from 10-30% of dry weight, brown seaweeds contain 5-15%, and green seaweeds display a diverse range of 3-47%, influenced by seasonal variations. The highest concentration is found during winter- early spring and the lowest during summer- early autumn. Marine algae have a high percentage of beneficial lipids and polyunsaturated fatty acids, even though their overall lipid content is low. Moreover, Seaweeds are abundant with pigments and vitamins including vitamins A, B, B12, D, E, K, and β-carotene. Seaweeds, rich in iodine, offer a preferable alternative to iodized salt and drugs in regulating thyroid hormone production. This is particularly beneficial for individuals facing mental health and thyroid issues due to iodine deficiency (Silva et al., 2020).

Due to their potential, marine chlorophytes, phaeophytes, and rhodophytes are already viewed as crucial assets in the drug industry. Further discussion delves into the actions or applications of certain naturally promising pharmacologically active products extracted from both macro and microalgae found in the marine environment of Bangladesh:

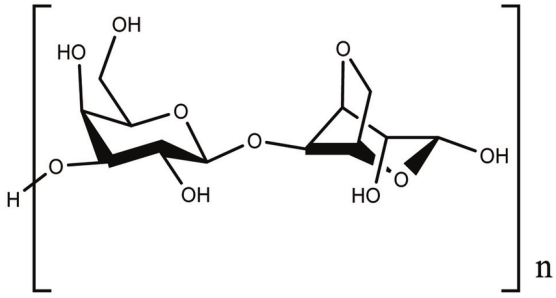


Figure 1. Agar

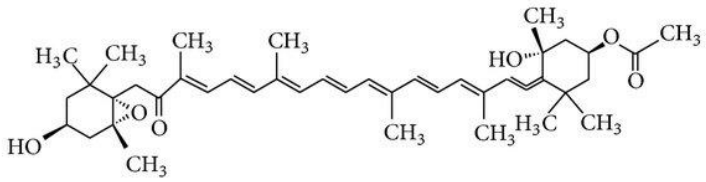


Figure 2. beta- carotene

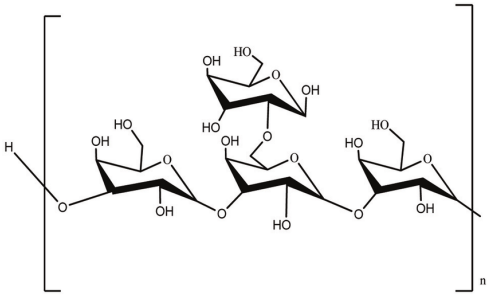


Figure 3. Lamenarin

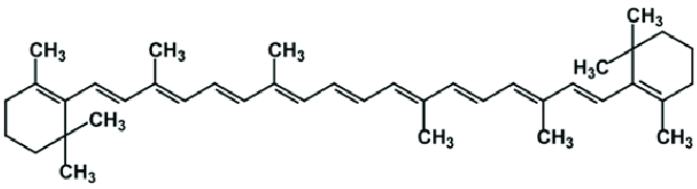


Figure 4. Fucoxanthin

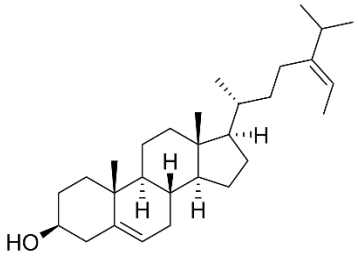


Figure 5. Fucosterol

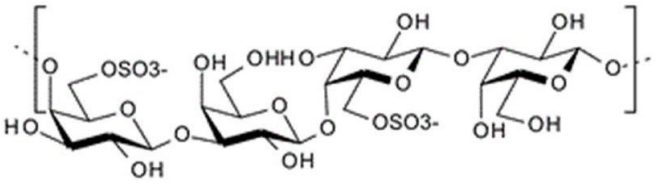


Figure 6. Fucoidan

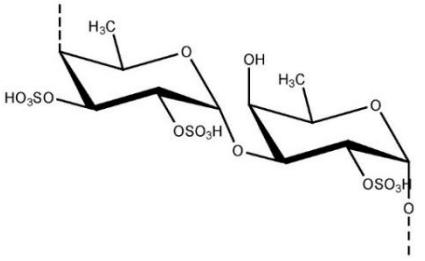


Figure 8. Carrageenan

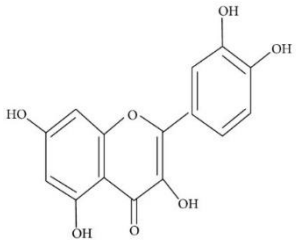


Figure 7. Flavinoid

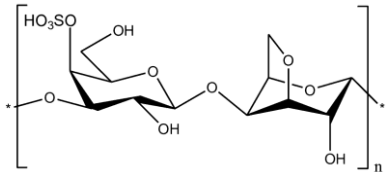


Figure 9. Porphyran

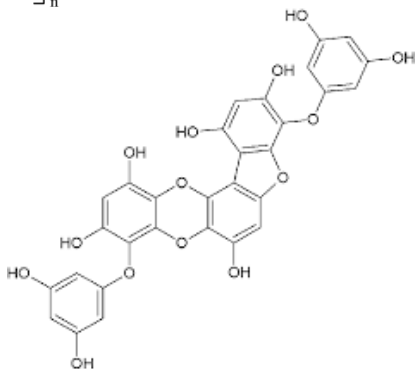


Figure 10. Phlorotannin

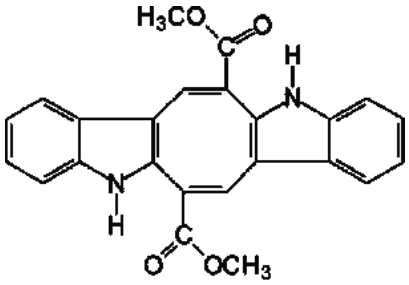


Figure 11. Caulerpin

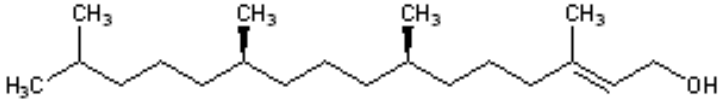


Figure 12. Phytol

3.1 Polysaccharides:

Constituting polymers of recurrent monomeric carbohydrate units interconnected through glycoside linkages, polysaccharides represent intricate molecular structures. Functioning as the primary structural components of the algal cell wall, these compounds contribute to its rigidity and strength, with marine algae predominantly featuring sulfated polysaccharides that distinguish them from plant polysaccharides (Bhowmick et al., 2020). These compounds constitute a category of biopolymers, with their content and structure subject to variation based on factors such as algae type, growth location, climatic conditions, harvesting season, extraction method, and various other influences (Hmelcov et al., 2018). On a dry weight basis, the carbohydrate content exhibited a considerable variation, ranging between 36% and 63% (Khan et al., 2016). The enzymatic degradation of sulfated polysaccharides entails a series of enzymes capable of cleaving glycosidic bonds and removing sulfate groups from the carbohydrate backbones (Helbert, 2017). Carbohydrates from Marine-derived like alginic acid, fucoidan, carrageenan, agar, etc., possess diverse bioactive properties, such as anticoagulant, anti-tumor, and immune-modulatory effects. These compounds are promising for applications in drug delivery, wound management, and regenerative medicine, contributing to their significance in medicinal and nutraceutical fields (Amorim, 2012). The sulfated polysaccharides found in algae serve as natural mimics of heparan sulfates. Fucoidans and carrageenans can imitate the actions of endogenous factors, regulating the functions of microorganism systems by interacting with crucial cell and enzyme receptors. Additionally, they can bind to various receptors on host cell surfaces, competing with viruses for glycoprotein receptors (Wang et al., 2012)

3.1.1 Fucoidans

Highly sulfated and typically possessing a branched structure, fucoidans represent a distinct class of polysaccharides found in marine environments (Kusaykim and Zvyagintseva, 2014). Fucoidans are commonly present in brown seaweeds, Oligosaccharides are obtained from the hydrolysis of fucoidans (contain glucose, galactose, fucose, mannose, uronic acid, xylose, and other monosaccharides, di or tri-saccharides unit, linked together and to the main chain by different types of glycosides bonds) (Raposo et al., 2015). The intricate structure of fucoidans poses challenges in establishing a direct correlation between their polysaccharide composition and biological actions. This complexity hinders the design of universal pharmaceuticals or drug-like substances for the treatment of specific diseases. Sulfated polysaccharide Fucoidans, extracted from *C. okamurans* prevents biofilm formation, in addition to the gastric mucosa and expression of other virulent factors that are involved in its infection process. Due to their minimal toxicity and biocompatible characteristics, these fucoidans are well-suited for use in nutritional supplements, proving effective in treating and eradicating *H. pylori* infections (Besednova et al., 2015). Fucans, Galactans, and galactofucans from brown and red seaweeds, with varying structures, sulfation levels, and molecular weights, have proven effective in inhibiting both HSV-1 and HSV-2 infections (Harden et al., 2009). Fucoidans treatment lessened flu symptoms' severity and alleviated lung pathology. Investigating the antiviral effects of fucoidan from *L. japonica* against the H5N1 influenza virus revealed its ability to suppress the virus's infection properties (Mekarenkova et al., 2010). Human skin melanoma cell lines and colon cancer cells were treated with fucoidan from *S. hornerii* and *C. costata*, and it demonstrated antitumor activity (Ermakova et al., 2011). Fucoidans also exhibited antitumor activities in the breast carcinoma cell by the influence of epithelial-mesenchymal transition (Hsu et al., 2013). Fucoidans from *C. okamurans*

induce apoptosis, exhibiting anti-proliferative effects in myeloid cancer and leukemia cell lines, suggesting their potential as alternative therapeutics for adult T-cell leukemia (Wijesekara et al., 2011). Fucose from brown algal cell walls modulates metastasis, atherosclerosis, and angiogenesis, in human lymphoma cell lines, involving the activation of caspase-3 and downregulation of kinase (Aisa et al., 2005). The antiadhesive characteristics of fucoidans may elucidate their anti-metastatic effects, as they are capable of hindering the adhesion of tumor cells to platelets, thereby reducing the potential for neoplastic cell proliferation (LI et al., 2008). Sulfated polysaccharides derived from *E. kurome* exhibit a correlation between higher anticoagulant activities and specific structural features, where fucans with greater molecular weight and an elevated content of both fucans and sulfate groups demonstrate the most pronounced anti-coagulant effects compared to those with lower molecular weight (Rocha et al., 2005). Fucoidan's anti-inflammatory capabilities in hypercholesterolemic rats have been documented, fucoidan extracted from *S. wightii* and commercial fucoidan from *F. vesiculosus*, obtained through hot water extraction, resulted in a reduction of inflammatory biomarkers such as C-reactive protein and TNF-α in both cardiac tissue and plasma (Preetha et al., 2010). Derived from two separate macroalgae species, *Dictoyta sp* and *Turbinaria sp*, the extracted fucoidan exhibited a capacity to inhibit HIV, suggesting the prospective application of these compounds from marine sources in the advancement of strategies targeting viral infections (Sanniyasi et al., 2019).

3.1.2 Laminarin:

Laminarin, a sulfated polysaccharide derived from brown algae, demonstrated growth inhibition against *Micrococcus luteus, Escherichia coli, Salmonella typhimurium, Salmonella enterica, Klebsiella pneumoniae* and *Pseudomonas aeruginosa*, with MIC values ranging from 20 to 40

mg/ml. Furthermore, the application of cream containing laminarin demonstrated effective in vivo Tissue regeneration in rats, characterized by Wound closure, regeneration of epithelial cells, and full restoration of skin tissue (Sellimi et al., 2018). The utilization of ultrasound-assisted extraction and purification for laminarin from *L. hyperborea* and *A. nodosum* revealed extensive antibacterial activity against both gram-positive and gram-negative bacteria, accompanied by significant antioxidant properties (Kadam et al., 2015). Given Laminarin's potent antioxidant properties, it has the potential to safeguard human health against injuries caused by reactive oxygen species (ROS), which may contribute to conditions like neurodegenerative diseases, cancer, inflammatory, and diabetes, as well as aging-related disorders including Alzheimer's and cardiovascular diseases. Laminarin has the potential to decrease the appearance of metastasis in vivo by inhibiting the activity of heparanase, an enzyme involved in the breakdown of the principal polysaccharide constituent within the basal membrane and extracellular matrix. The regulation of this enzyme's expression is acknowledged to be associated with the process of tumor metastasis (Chattopadhayay et al., 2010). Furthermore, this product has been employed to bolster and augment the immune system. Laminarin extracted from *E. bicyclis* displayed anticancer effects by impeding cell proliferation, prompting apoptosis, and causing cell cycle arrest at the sub-G1 phase in cell lines associated with ovarian clear cell carcinoma and papillary serous adenocarcinoma (Bae et al., 2020). Laminarin and its sulfated counterpart demonstrated promising in vitro anticancer potential against human malignant melanoma cells. Furthermore, these substances showcased a suppressive impact on the formation of colonies in human colon cancer cell lines and displayed cytotoxic properties against a diverse range of carcinoma cell lines. Additionally, activation of Caspase- 3, Caspase- 6, Caspase- 7, Caspase- 8, and Caspase- 9 and increased release of cytochrome were observed following the treatment with Laminarin and its analogs (Ji et al., 2013)

3.1.3 Carrageenans:

Carrageenans, belonging to the category of sulfated polysaccharides found in red algae, feature a chemical structure characterized by a disaccharide repeating unit composed of two D-galactose residues linked by β-1,4 glycosidic bonds. The assembly of these units into polysaccharides occurs through α-1,3 bonds (Yermak et al., 2014). Substituents can be other monosaccharides (mannose, xylose), sulfate, methoxy, and pyruvate groups, the pattern of sulfation dividing carrageenan into different families, for example, in C-2 for λ-carrageenan and C-4 for κ-carrageenan. Red seaweeds are good sources of κ-carrageenan (*E. spinosa*, *K. alvarezii*), t-carrageenan (*E. spinosa*), λ-carrageenan (*C. crispus*, *G. skottsbergii*) (Funami et al., 2007). Of the various biological properties exhibited by these sulfated polysaccharides, their antiviral, immunomodulatory, anticoagulant, antitumor, and anti-ulcer activities are currently the most noteworthy. A variety of eukaryotic cell proteins are interacted with by sulfated polysaccharides, resulting in a multi-directional impact on the body's immunomodulators. The immunostimulatory properties of carrageenan extracted from *Chondrus* sp, revealed that variants with lower molecular weights exhibited enhanced efficacy in stimulating the immune system (Zhou et al., 2004). The significant soluble fiber, carrageenan, is noteworthy as the intake of Products enriched with dietary fiber derived from macroalgae is recorded to foster health advantages. These advantages encompass the mitigation of conditions like colon cancer, type II diabetes, obesity, and cardiovascular diseases (Jimenez- Escrig and Sanchez, 2000). Brief carrageenan supplementation notably influenced the lipid profile in ischemic heart disease patients. Prophylactic use of carrageenan as a dietary supplement in the comprehensive therapy of IHD patients led to a significant decrease of 16.5% in plasmatic total cholesterol (TC) levels and 33.5% in LDL-cholesterol (LDL-C) compared to initial measurements (Sokolva et al., 2014). Certain types of carrageenan, with no significant anticoagulant properties

or cytotoxicity, may be suitable for use in vaginal lubricant gels and as coatings for condoms, given their virucidal activity against HIV and other STD-associated viruses, including HPV (Raposo et al., 2015). They can be transformed into porous structures, membranes, or fibers, serving diverse biomedical purposes, alongside their function as hydrogels (Popa et al., 2011). Carrageenan is acknowledged for eliciting robust inflammatory and carcinogenic effects. However, some carrageenan stimulates the activity of macrophages, while others inhibit macrophage activities (Wijesekara et al., 2011). Directly targeting alveolar macrophages with carrageenan is an intriguing possibility. Clinical trials have been completed for t-carrageenan, and a nasal spray based on it is now available in Europe for the treatment of viral infections in the human respiratory tract. Nasal congestion symptoms, such as runny nose, cough, and sneezing, are significantly reduced by this sulfated polysaccharide (Ludwig et al., 2013). Due to their high molecular weight, carrageenans are unable to pass through the body's barriers. Consequently, they establish a physical barrier in the nasal cavity, effectively preventing respiratory viruses, including the flu virus. Carrageenan types (λ, κ, t) hinder the interaction between viruses and cells, inhibiting the formation of syncytium induced by influenza A viruses (Damonte et al, 2004). Inflectional animals' respiratory organs have a reduced spread of the virus due to Carrageenan's effect on the surface epithelium

3.1.4 Ulvans:

The structural integrity of the green algae cell wall is primarily attributed to polysaccharides, wherein L-rhamnose 3-sulfate is commonly linked to disaccharide modules, with a notable preference for association with Ulvabiouronic acid unit A, Ulvabiuronic acid unit *B, ulvabiose* unit A, or ulvabiose unit B, thereby forming a complex and robust matrix. The predominant recurring disaccharide units identified in ulvan are ulvanobiouronic acid-3 sulfate, characterized by the

presence of either glucuronic acid or iduronic acid, constituting a repetitive and structurally integral motif within the ulvan polysaccharide framework (Lahaye and Robic, 2007) (Lahaye and Ray, 1995) The Ulvaceae family, known for its production of ulvans, exhibits distinct and wide-ranging pharmacological applications, including potential uses in formulating functional foods.

Ulvan derived from *U. rigida* stimulates the production of nitric oxide and enhances the synthesis of cytokines in macrophages (Raposo et al., 2015). Strong antioxidant power is exhibited by ulvans from *U. fasciata*, characterized by lower sulfate content, while the antioxidant activity in *E. linza* and other seaweeds is dependent on sulfate. The primary antioxidant action of ulvan is achieved by either scavenging free radicals like superoxide, hydroxyl, and 1,1-diphenyl-2-picrylhydrazyl (DPPH) or by preventing their formation (Wang et al., 2014). After four weeks of orally administering ulvan from *U. fasciata* to hypercholesterolemic rats, no adverse effects were observed, and a notable reduction in serum lipid levels, including TC, TG, LDL-C, and VLDL-C, was noted (Borai et al., 2015). Intragastric administration of ulvans from *U. lactuca* in hypercholesterolemic rats significantly increased HDL-C levels by 180% compared to oral administration (Hassan et al., 2011). Ulvans derived from *Ulva spp.* demonstrate anti-peroxidative properties, effectively shielding liver tissue against hyperlipidemia and providing protection to injured tissues from the detrimental effects of oxidative stress. SOD and catalase were regulated, vitamins E and C were increased, glutathione was reduced, and the levels of aspartate and alanine transaminases in the rat's liver were reduced by these sulfated polysaccharides (Sathivel et al., 2008). *U. ohnoi* administration resulted in a substantial 29 mmHg reduction in systolic blood pressure, a 24% decrease in the ultimate body fat mass, and enhancement in insulin sensitivity and glucose utilization (Kumar et al., 2015). Porous structures, including hydrogels, nanofibers, and particle membranes, can be produced from ulvans, derived from green algae, rendering them

promising candidates for medical applications like wound dressing, tissue engineering, and drug delivery. A 253 KDa high molecular weight ulvan from *U. lactuca* has shown inhibitory effects on the neurotropic flavivirus JEV by blocking its adsorption and cell penetration (Shah et al., 2020).

3.1.5 Algins/ Alginates/ Alginic acid:

Alginic acid is a polysaccharide that is derived from the cell wall of brown algae and is commonly known as algin. A stimulating antitumor effect of nanoparticles was observed in mice bearing H22 tumors whose contained alginic acid (Mondal et al., 2020). This polysaccharide also interacts with carcinogenic substances and heavy metals found in the intestine, working to transform these toxic compounds into non-harmful forms (Fedorov et al., 2013). Algins exist in versatile formulations, presenting themselves in both acidic and salt configurations. Alginic acids manifest as linear polymers comprising two distinct uronic acids, namely β-D-mannuronic acid and α-L-guluronic acid, intricately woven into a complex molecular structure (Dominguez, 2013).

Alginates extracted from macroalgae find diverse applications, including scaffolding for ligaments, controlled drug release, tissue engineering, cell encapsulation, regeneration of various human tissues, and even the preparation of dental molds. Alginate fibers are also extensively employed in wound management (de Jesus Raposo, 2015). Alginate is a material that can be used as a component in scaffolds for the engineering of heart valves and cardiac tissues (Hockaday et al., 2012). Arthritic rats induced with Type II collagen exhibited elevated levels of inflammatory marker enzymes, including Lipoxygenase (5-LOX), Cox-2, myeloperoxidase (MPO), and xanthine oxidase (XO), along with increased concentrations of CRP and rheumatoid factor (RF). The activities of these enzymes and proinflammatory cytokines (TNF-α, IL-1 β, and IL-6) were significantly reduced by alginic acid (Kumari and Kurup, 2013). Algin demonstrated a significant

reduction in paw edema in collagen-induced arthritic rats, indicating its potential to mitigate inflammation within joints by reducing erythema and soft tissue swelling. The selection of agar as the chondrogenic material for poly-L lectic scaffolds was made due to its chondrogenic potential (Gong et al., 2007).

3.2 Polyphenolic Compounds:

Polyphenols, including flavonoids, phenolic acids, tannins, anthocyanidins, catechin, epigallocatechin, epicatechin, lignin, and Gallic acid, are abundantly accumulated in algae, with notable concentrations of phloroglucinol and its polymer phlorotannin. Green and red algae, in particular, exhibit a substantial presence of flavonoids, bromophenols, and phenolic acids. Phlorotannin is predominantly present in brown algae, with lower concentrations in red algae (1.8%-3.2%), and even fewer amounts are found in green algae (Machu et al., 2015). Algae primarily produce these compounds as secondary metabolites, consisting of a variety of chemical compounds connected to multiple hydroxyl groups and bonded to benzene rings (Waterman and Mole, 1994). Polyphenolic compounds possess the ability to decrease the mitotic index and diminish the cellular proteins essential for the proliferation and formation of cancer cell colonies. The edible seaweed *P. palmata*, abundant in polyphenols with potential antioxidant and anticancer properties, inhibits xenobiotic metabolizing enzymes, disrupting the mitotic process in the telophase and causing cell division disruption (Khalifa et al., 2019). These compounds have garnered acclaim for their commendable anti-allergic, antidiabetic, antioxidant, radioprotective effects, and antitumor, as well as their prowess in combating fungal infections, and malaria, and exhibiting remarkable anticancer properties, collectively underscoring their multifaceted and positive impact on diverse biological systems. The antibacterial properties imparted by polyphenols through interacting with multiple sites of bacterial cells like disrupting membrane

permeability, inhibiting enzymes of different metabolic pathways, binding to surface adhesive molecules, etc (Bhowmick et al., 2020).

3.2.1 Phlorotannin:

Exclusive to brown algae, phlorotannins are phenolic compounds composed of dehydro-oligomers or dehydro-polymers of phloroglucinol with molecular weights ranging from 126-650 kDa. They display diverse molecular arrangements, including variations in the structure linkages between phloroglucinol units (aryl-aryl or di-aryl ester bonds) and the number of hydroxyl groups (Freile-Peleguin and Robledo, 2013). Physodes inside algal cells contain them and they are produced through the acetate-malonate pathway, accounting for up to 25% of their dry weight (Ragan et al., 1986). Phlorotanins have been found to contain various compounds, including eckol, diekol, phlorofucofuroeckol A, phloroglucinol, and others (Li et al., 2011).

Phlorotannins, through their antibacterial prowess, engage in intricate interactions with bacterial enzymes integral to essential metabolic pathways and membrane proteins, thereby disrupting oxidative phosphorylation processes and precipitating the lysis of bacterial cells, underscoring a multifaceted mechanism of action in their antibacterial activity. Oligomeric phlorotannins from *F. vesiculosus,* comprising 3-8 Phloroglucinol units, exhibited a significant bacteriostatic impact on pathogenic Gram-positive bacteria like *S. aureus* and *S. pneumoniae*, in contrast to the tested Gram-negative bacteria (Bogolitsyn et al., 2019). The antibacterial activity of Phlorotannins from *E. bicyclis* was found against *Propionibacterium acnes,* which is resistant to antibiotics. The deleterious impact of algal phlorotannins extends across the spectrum of microbial life, as these compounds exhibit the capability to inflict damage and induce mortality in both aerobic and anaerobic bacteria, reflecting their broad-spectrum antibacterial efficacy. Phlorotannins from *L. digitata* were studied for their effects on a mixed anaerobic microbial culture. Exposure to

phloroglucinol caused membrane dysfunction, leading to the detachment of the cytoplasmic membrane from the cell wall in bacterial cells. Phlorotannins and their derivatives are proposed to play a role in the advancement of naturally sourced antibiotics, effectively targeting multidrug-resistant bacteria. Indications suggest that phlorotannins and their derivatives may play a role in the creation of naturally derived antibiotics targeting multidrug-resistant bacteria. Notably, eckol, phlorofucofuroeckol A, and dieckol, all phlorotannins, could potentially demonstrate ACE-I inhibitory activity. This is significant as ACE-I inhibition is an established strategy in hypertension treatment (Hierholzer et al., 2013), (Jung et al., 2006). Phlorotannins from *Sargassum japonica* and *Sargassum hornerii* show strong antioxidant activity, while those from *Halimeda sp* effectively protect against LDL oxidation. Additionally, in an animal model, phloroglucinol, eckol, and dieckol demonstrated the ability to inhibit acetic acid-induced hyperpermeability and carboxymethyl cellulose-induced migration of leukocytes (Kim et al., 2012). Phlobotannin, typically found in higher plants, has been observed in seaweeds such as *S. coriifolium, S. wightii*, and *H. musciformis* collected in Bangladesh (Widner-Wells et al., 1998). The combination of fucofuroekol-A from *E. bicyclis* with streptomycin synergistically affects *Listeria* strain, which is a common causative agent of various severe diseases linked to the consumption of contaminated foods (Kim et al., 2017).

3.2.2 Flavonoids:

Flavonoids stand out as crucial natural phenolic compounds, valued for their diverse biological and chemical activities, which encompass free radical scavenging and antioxidant properties (Kahkonen et al., 1999). Excessive ROS can cause oxidative stress, linked to incurable conditions like Alzheimer's, chronic fatigue syndrome, autism, Parkinson's, infection, cancer, and heart failure. Removing ROS is crucial to defend against these diseases, and flavonoids (powerful

natural antioxidants) play a key role in boosting immunity, and can also be used for antitumor activities (Sobuj et al., 2020) (Aziz et al., 2020). Flavon-3-ols, encompassing catechins present in various red algae, hinder telomerase activity in colon cancer cells (HT29) and monoblastoid leukemia cells, resulting in cellular demise. Telomerase is crucial for preserving the termini of telomeres 30 in cancer cells, a characteristic absent in normal cells (Yoshei et al., 2000). *S. wightii* stands out as a botanical entity rich in flavonoids, contributing substantively to its antioxidant activity and affirming its potential as a source of compounds that can counteract oxidative stress (Kumari and Kurup, 2013). Flavonoids extracted from *G. gracilis* and *N. oculata* have exhibited noteworthy antioxidant capabilities against specific respiratory viruses. The significance of this activity lies in its capacity to diminish the production of ROS, leading to a reduction in inflammation. Consequently, it contributes to the alleviation of lung and tissue damage while concurrently preserving the functionality of the epithelial tissue (Alam et al., 2021). Flavonoids from *G. tenuistipitata* and *P. tetrastromatica* neutralize excess free radicals, protecting cellular structures. Maintaining a balance of antioxidants is vital for overall well-being, and in this regard, flavonoids may outperform synthetic antioxidants (Sobuj et al., 2021). Flavonoids have versatile applications in skincare, featured in moisturizers, protective agents, body ointments, face masks, anti-aging products, radical scavengers, and formulations targeting immune stimulation, histamine-related inflammation, and issues like age spots and skin elasticity. They also play a role in oral care and maintaining skin texture (Pereira, 2018). The mitotic index is reduced, and the levels of cellular proteins crucial for cancer cell proliferation and colony formation are diminished by flavonoids (Khalifa et al., 2019).

The extracted gallic acid derived from *G. acerosa* emerges as a bioactive agent exhibiting efficacy against *S. aureus*, a pathogenic bacterium associated with food-borne toxicoinfective incidents,

thereby presenting a rationale for its potential application in mitigating the gastrointestinal distress characterized by symptoms such as diarrhea and vomiting (Estevinho et al., 2008).

3.3 Terpenes:

Terpenes are hydrocarbon compounds formed from 5- carbon isoprene units assembled to generate a vast range of skeletons, which are used by various enzymes to conjugate functionality and alter oxidation. These cyclic molecular can be categorized as monoterpenes, diterpenes, triterpenes, tetraterpenes, sesquiterpenes, and sesterterpenes based on the isoprene units it contains (Kandi et al., 2015). While terrestrial plants typically synthesize these compounds through mevalonic acid-dependent pathways, algae employ mevalonic acid-independent pathways for terpene synthesis (Bhowmick et al., 2020).

Brominated terpenes sourced from diverse algae display broad-spectrum activity against viruses, bacteria, and malaria, with Bromophycolides J-Q, extracted from *C. serratus*, exhibiting notable antibacterial effectiveness against *MRSA*, *Enterococcus*, and *M. tuberculosis* (Lane et al., 2009). Isolated from *S. coronopifolius*, sphaerane bromoditerpenes and sphaerodactylomelol have been found to inhibit the growth of *S. aureus*, *E. coli*, and *P. aeruginosa*, demonstrating highly specific anti-proliferative properties. Strong antimalarial activity against chloroquine-resistant *P. falciparum* was observed with 12S-hydroxybromosphaerodiol and Sphaerococcenol A, two other bromoditerpenes from the same algae (Rodrigeues et al., 2015) (Etahiri et al., 2001). Present in the chlorophyll of *Halimeda sp*, *Sargassum sp*, *Kappaphycus sp*, and *Padina sp*, the diterpene alcohol Phytol has exhibited inhibitory effects on both α-glucosidase and DPP-4, thereby revealing substantial therapeutic potential for individuals with diabetes (Chin et al., 2019). Derived from Sargassum sp, the meroterpenes sargachromanols J and R exhibit growth-inhibiting effects on colon cancer cells, whereas Sargachromanol E from the same source induces apoptosis in the colon

cancer cell line. S. zonale's zona quinone acetate was also effective in preventing the growth of colon cancer cells. Fubenatolide B, obtained from a distinct Sargassum species, demonstrated inhibitory effects across different cancer cell lines, including breast, colon cancer, and lung, through the induction of apoptotic cell death (Zbakh et al., 2020). *H. tuna* derived habitual, a novel diterpene aldehyde, showed effects against Coronavirus in vitro (Koehn et al., 1991). Brominated diterpenes, specifically Isopargurene and its partner, derived from *J. rubens*, exhibited potent antihelmintic activities against *Allolobophora sp*, surpassing the efficacy of the reference drug mebendazole (Awad, 2004).

3.3.1 Sesquiterpenes:

Sesquiterpenes consist of three isoprene units, the backbone of the C15 carbon. The varied properties exhibited by these compounds indicate activity against multiple targets, thereby opening new avenues for therapeutic applications. Neophytadiene, isolated from *U. lactuca*, demonstrates activity against drug-resistant bacterial strains such as *K. pneumonia, S. aureus*, and *E. coli* (Anjali et al., 2019). Caulerpal A and B, in conjunction with caulerpin extracted from *C. taxifolia*, have been recognized as inhibitors of human protein tyrosine phosphatase, showcasing properties indicative of anti-cancer activity (Mao et al., 2006). Two sesquiterpene derivatives, namely guai-2-en-10α-ol and guai-2-en-10α methanol, isolated from *U. fasciata*, exhibited significant inhibition of Vibrio growth (Chakraborty et al., 2010). The G1 phage of the triple-negative breast cancer (TNBC) cell line is affected by guai-2-en-10α-ol, which leads to both apoptosis and cell cycle arrest (Laxmi et al., 2018). The anticancer activity of Laurinterol, which was isolated from *L. okamurae*, was manifested in melanoma cells by a p53-dependent pathway (Kim et al., 2008). The isolation of four fresh sesquiterpenes from L. obtusa and their evaluation against multidrug-resistant bacteria strains, such as *S. aureus, E. faecalis and P. aeruginosa* was carried out (Bawakid

et al., 2017). Iso-obtusol derived from *L. majuscule* demonstrated comparable antimicrobial efficacy against *S. epidermis, K. pneumonia, and Salmonella sp,* when compared to commercial antibiotics (Vairappan, 2003). Debromolaurinterol, elatol, allolaurinterol, obtusol and deschloroelatol, demonstrated anti-Mycobacterium activities against *M. tuberculosis, M. avium,* and *M. bovis,* with obtusol also exhibiting activity against *L. amazonensis* and mentioned efficacy against *T. cruzi* (Veiga-Santos et al., 2010).

3.3.2 Diterpenes:

Four units of isoprene, the backbone of C20 are called diterpene. Anti-inflammatory properties have been demonstrated in lipopolysaccharide-stimulated cells for Neorogioltriol, a brominated diterpenoid derived from *Laurencia sp* (Chatter et al., 2011). Dolabelladienetriol, sourced from *Dictyota* sp, demonstrates efficacy against both promastigotes and intracellular amastigotes of *L. amazonensis*. Furthermore, it exhibits effectiveness in reducing amastigotes within HIV-1-infected human macrophages, showcasing its potential in addressing diverse infections (Soares et al., 2012). (12Z)-cis-maneonene-D and (12E)-cis-maneonene-E, isolated from *L. obtusa,* actively regulate apoptosis in neutrophils, inhibiting inflammatory responses (Ayyad et al., 2011). In *P. pavonica*, β-sitosterol [(3B)-stigmasta-5-en-3-01] is utilized in steroid synthesis, and concurrently, Campesterol reduces the permeability of biomembranes (Salem et al., 2014).

3.3.3 Triterpenoids:

Triterpenoids are composed of 6 isoprene units. Squalene, isolated alongside α-tocopherol from *C. racemosa*, demonstrates antifungal properties. Dwarkenoic acid, obtained from Codium sp along with various sterols (stigmasta-5,25-dien-3β-7α-diol, stigmasta-5,25-dien-3β-ol, androst-5-

en-3β-ol, ergosta-5,25-dien-3β-ol, etc.), exhibits notable inhibition of enzymatic α-glucosidase. Loliolide and isololiolide were extracted from *U. prolifera* (Shah et al., 2020).

3.4 Steroid on Sterols:

Sterols, characterized by their intricate organic nature, features a core structure constructed from four fused rings, underscoring the fundamental architecture that defines these biochemically significant molecules. The polarity is conferred by the hydroxyl (-OH) groups at the third position of ring A, while the aliphatic chains contribute to the overall nonpolar nature. Sterols, pivotal lipid entities, are ubiquitously present in the cellular composition of all eukaryotic organisms, underscoring their indispensable role in fundamental biological processes. The composition of phytosterols, which are derived from plants, is usually complex (Bhowmick et al., 2020). Sterols are distributed across various algal classes, with red algae being rich in Desmosterol, Cholesterol, and its derivatives, brown algae containing Fucosterol and its derivatives, and green algae harboring 24-ethyl cholesterol and ergosterol. Steroidal compounds, in comparison to nonsteroidal anti-inflammatory drugs, exhibit the utmost potency in terms of anti-inflammatory activity, highlighting their superior efficacy in modulating inflammatory responses within biological systems (Souto et al., 2011). Antileishmanial activity against *L. infantum* and *L. amazonensis* can be achieved through the use of fucosterol from *L. vadosa* (Becerra et al., 2015). Antibacterial activity of sterols is manifested through their interaction with the negatively charged phosphate groups in the bacterial membrane. This interaction initiates lipid exchange, inducing distortion in membrane composition and instability in osmoregulation, ultimately culminating in cell lysis (Kavita et al., 2014). Fucosterol, extracted from *T. triquatra, L. obtusa, and, U. lectuca* demonstrated antibacterial efficacy against *B. cereus, B. subtilis, K. pneumoniae, E. coli, S. aureus and P. aeruginosa.* The antibacterial activity increased with higher doses of fucosterol (Deyab,

2013). Iyengadione, an antibacterial steroidal-glycoside, along with newly discovered iyengaroside A and B, was isolated from *Codium sp.* Cholesterol galactoside from the same source also showed activity against *K. pneumonia.* Apoptosis can be induced in breast cancer cells by using the sterol from *C. fragile* (Alves et al., 2018). *C. racemosa* has the most active PTPIB inhibitory properties called (23E)-3b-hydroxy-stigmasta-5, 28-oxostigmastic steroid, 23dien-28-one (Yang et al., 2015). Gathered from St. Martin Island in Bangladesh, *Rosenvingea* is abundant in steroids, saponin, and steroidal glycosides. It demonstrates both antimicrobial and antioxidant properties, while maintaining low cytotoxicity, indicating its promise as a candidate for the formulation of anti-proliferative agents in cancer research (Alim et al., 2021).

3.5 Alkaloids:

Alkaloids represent a class of naturally occurring synthetic organic compounds, constituting a diverse group of heterocyclic molecules characterized by alkali-like properties and featuring a distinctive attribute of possessing at least one nitrogen atom within their structural framework (Mondal et al., 2020). Pelletier defines alkaloids as cyclic organic compounds that incorporate nitrogen in a reduced oxidation state, exhibiting a restricted occurrence within living organisms (Shah et al., 2020). Marine algae contain four groups of alkaloids, which are phenylethylamines, indoles, halogenated indoles, and other alkaloids (Khalifa et al., 2019). Morphine, extracted from the terrestrial plant *Papaver somniferum*, holds the distinction of being the inaugural alkaloid isolated from this source, while Hordenine claims the title of the first alkaloid discovered within the marine alga *P. nervosa*, marking significant milestones in the exploration of alkaloid diversity across botanical and marine realms (Guven et al., 1970). The bioactive compounds, including alkaloids, in *H. boergesenii* were found to have moderate antioxidant activity (Dewinta et al., 2019). The ethanolic extract from Rosenvingea sp demonstrated significant inhibitory effects in

vitro against three Gram-positive and four Gram-negative bacteria. Notably, it produced the highest zone of inhibition in one Gram-positive and two Gram-negative bacteria. Alkaloids identified through phytochemical screening were implicated in hindering bacterial cytokinesis, revealing the intricate mechanism behind the extract's bactericidal activity (Alim et al., 2021). The inhibitory effects against *P. aeruginosa, K. pneumonia, B. subtilis, S. aureus, E. coli, S. typhimurium, S. epidermidis,* etc. varied among green algae (*U. lactuca*, *Codium sp*), brown algae (*D. membranacea, S. vulgare*), and red algae (*Gelidium sp*), as a result of differences in their alkaloid content (Bhowmick et al., 2020). Lophocladine A and B, extracted from *Lophocladia spp*, effectively exhibited growth inhibitory activity against various cancer cell lines (Gross et al., 2006). Racemosins A and B, obtained in conjunction with caulerpin from *C. recemosa*, demonstrated a neuro-protective effect against Aβ25-35-induced damage in SH-SY5Y cells. In comparison to epigallocatechin gallate (EGCG), they exhibited a notable increase in cell viability, registering a 14.6% improvement (Shah et al., 2020) Within the domain of anti-inflammatory and analgesic medications, alkaloids emerge as effective agents for mitigating chronic and intense pain. Distinguished among these are several isoquinoline alkaloids—barbamine, berberine, and cepharanthine—each exerting its anti-inflammatory effects by acting as antagonists (Gonzalez-Barnadas et al., 2020). Indanoestrol A and B, along with Caulerprenyolol B, demonstrated a noteworthy level of antimycotic efficacy, exhibiting moderate activity against pathogenic fungi including *Trichophyton rubrum, Candida glabrata*, and *Cryptococcus neoformans*, thereby underscoring their potential as agents for combating fungal infections (Shah et al., 2020).

3.6 Fatty Acids and Lipids:

The sustenance of membrane integrity and cellular organization is contingent upon the incorporation of fatty acids as indispensable constituents within the membranes of virtually all biological entities, highlighting their pivotal role in fundamental cellular processes. Fatty acids are liberated from algal cells under specific conditions when the cell undergoes a loss of integrity. This phenomenon appears to be associated with defensive responses against predators and pathogenic bacteria. Marine microalgae and macroalgae stand as formidable reservoirs of a diverse array of fatty acids, encompassing the likes of Eicosapentaenoic, Hexadecanoic, Hexadecatrienic, Palmitoleic, Palmitic, Myristic, Eicosanoic acid, Stearic, Oleic, Linoleic, α-linolenic, γ-linolenic, 9-hexadecenoic, 10-octadecenoic, and 13-Octadecenoic. The intricate orchestration of fatty acid biosynthesis unfolds through the enzymatic conversion of acetyl coenzyme A (acetyl-CoA) into malonyl-CoA, a pivotal reaction presided over by the multifaceted enzyme acetyl CoA carboxylase. Anchored within this intricate biochemical tapestry is a principal pathway for acetyl-CoA genesis, emanating from the metabolic intricacies of 3-phosphoglycerate (3-PG), the primary yield of carbon dioxide fixation (Wang et al., 2009). The most effective strategy for boosting the content of natural lipids in algae is to limit nitrogen (Guschina and Harwood, 2006) (Richmond 2004). Lipids predominantly consist of polyunsaturated fatty acids, with a particular emphasis on ω-3 and ω-6 variants, elucidating the prevalence and significance of these essential fatty acids in the composition of lipid molecules. The lipid content in seaweed, ranging from 0.12% to 6.73% dry weight, primarily consists of glycolipids, phospholipids, and non-polar glycolipids, with phosphatidylglycerol predominating in green algae, phosphatidylcholine in red algae, and a combination of phosphatidylcholine and phosphatidylethanolamine in brown algae, while the major glycolipids include digalactosyldiacylglycerides, sulfoquinovosyldiacylglycerides and

monogalactosyldiacylglycerides (Plougerne et al., 2014). The concentrations of Fatty acids and lipids in red and brown algae tend to be higher.

The utilization of ω-3 PUFA extracted from *Enteromorpha* demonstrates potential in addressing conditions such as hemorrhoids, parasitic diseases, goiter, cough, bronchitis, reduced fever, and pain alleviation (Aditya et al., 2016). ω-3 fatty acids reduce cholesterol and fat levels in the bloodstream while purifying the lining of blood vessels. The application of ω-3 fatty acids serves as a therapeutic approach for inflammatory rheumatoid arthritis, heart disease, coronary conditions, and immunodeficiency diseases (Shah et al., 2020). Biologically active compounds, represented by three derivatives of monounsaturated fatty acids (MUFA), encompassing a keto-type C18 fatty acid, a corresponding shorter chain C16 acid, and an amide derivative, were successfully extracted from *U. lactuca*, thereby highlighting the diverse nature of the bioactive constituents present in this marine organism (Wang et al., 2013). Isomalyngamide A and Isomalyngamide A-1, fatty-acid amines from *L. majuscula*, inhibited breast cancer cell proliferation, while Jamaicamides A, B, and C, fatty acids from the same source, showed cytotoxicity to human lung and mouse neuroblastoma cell lines (Chang et al., 2011) (Edwards, 2004). In a study involving 485 healthy participants, supplementation with algal oil, abundant in the (n-3) fatty acid DHA, exhibited a significant impact on cardiovascular risk factors by reducing serum TG and elevating both HDL-C and LDL-C (Bernstein et al., 2012). The lipid profile obtained from *C. muelleri* demonstrated antimicrobial efficacy, and the examination of the fraction through HPLC-ELSD and GC-FID unveiled the existence of components such as monoglycerides, diglycerides, triglycerides, DPA, and free fatty acids (Mendiola et al., 2007). Chlorellin, a blend of fatty acids, was the initial antibacterial compound identified in *C. vulgaris*, yet it impeded the growth of the culture. Similarly, unsaturated and saturated long-chain fatty acids extracted from *S.*

costatum exhibited inhibitory activity against *Vibrio spp.* (Guedes et al., 2011). Antibacterial activity against various Nosocomial bacteria such *as P. aeruginosa, , S. aureus, B. cereus, B. subtilis, E. coli, and K. pneumonia* was observed in oleic acid and palmitic acid derived from *T. triquatra, U. lactuca,* and *L. optusa*. The combination of oleic and palmitic acid exhibited the most pronounced antibacterial efficacy against all tested bacterial strains (Deyab, 2013). Punicic acid, classified as a conjugated linoleic acid, has been recognized for its diverse biological benefits, encompassing properties that promote weight management, support diabetes management, exhibit anti-inflammatory effects, demonstrate antioxidant activity, and contribute to lipid profile improvement. (Aruna et al., 2016). PUFA ethyl esters isolated from *L. okamurai* exhibited activity against *C. glabrata*, displaying moderate efficacy with an MIC80 of 4 μg/mL, in comparison to the reference drugs amphotericin B (MIC80=1 μg/mL), fluconazole (MIC80=2 μg/mL), and ketoconazole (MIC80=0.5 μg/mL) (Falkenberg et al., 2018). hexadecanoic acid, 9-hexadecanoic acid, 10-octadecenoic acid, 13-Octadecanoic acid, and eicosanoic acid found in *G. edulis* inhibited *Aeromonas hydrophila* and *Vibrio spp* (Kasanals et al., 2019) Fatty acids in seaweeds, particularly from *S. horneri*, are rich sources of beneficial long-chain ω-3 and ω-6 PUFAs, including EPA and DHA. These lipids have been shown to positively impact serum levels of EPA, TC, TG, and the LDL-C/HDL-C ratio in KK-Ay mice (Sasaki et al., 2011). *Phorphyra spp* and *C. crispus* stand out for their valuable content of polyunsaturated fatty acids (PUFAs), soluble fiber, and sterols, collectively contributing significantly to human health by actively participating in the reduction of cholesterol levels, thus imparting potential preventive effects against heart diseases. The member of *Porphyridium* is used for the commercial production of arachidonic acid and pigments. ω-3 PUFAs play a vital role in various neurological functions, including neurogenesis, neurotransmission, and safeguarding against oxidative stress-induced cerebral damage. DHA and

EPA are integral in the therapeutic approaches for conditions such as atherosclerosis, cancer, rheumatoid arthritis, Alzheimer's disease, and more (Barneina et al., 2011).

3.7 Protein and Poly Peptides:

Algae, rich in proteins, constitute a substantial portion of essential amino acids including methionine, valine, trypsin, leucine, lysine, alanine, phenylalanine etc. The synthesis of peptide compounds in marine species has been greatly influenced by the action of enzymes during hydrolysis. Two main known groups of functionally active proteins present in algae are phycobiliprotien and lectins. Phycobiliproteins, stable fluorescent proteins found in red algae (e.g., phycoerythrin, phycocyanins, allophycocyanin), and lectins, ubiquitous carbohydrate-binding proteins and glycoproteins (proteins with attached sugar chains through glycosylation, forming crucial sugar-protein conjugates) play crucial roles in biological processes (Stangel et al., 2011). Lectins play a role in the initial defense against bacteria and viruses, exhibiting potential anticancer, anti-inflammatory, and anti-HIV properties. Meanwhile, cyclic and linear peptides demonstrate diverse activities, including cytotoxicity, antimicrobial effects, specific ion channel blocking, and antitumor capabilities. Numerous marine peptides have undergone successful evaluations and are now accessible in the market as formulated drugs with various trade names. One example is Polydioscamide A, known for its anti-tumor properties (Mondal et al., 2020). Seaweed protein hydrolysates, found in *P. palmata, U. pinnatifida, C. microphysa, Sargassum sp,* and *P. yezoensis*, comprise an intricate blend of bioactive peptides with ACE-I inhibitory properties (Beaulien, 2019). However, the ability to target ACE-I seems to be improved by the presence of Tyr residues in dipeptides (Suetsuna et al., 2004). *P. palmata*'s renin-inhibitory attributes persist in bread as a bioactive component, with 4% enrichment post-baking, showcasing enhanced renin-inhibitory capacity without compromising the bread's texture or sensory properties

(Fitzgerald et al., 2014). The rich presence of essential amino acids in *P. palmate* (valine, methionine, and leucine) akin to ovalbumin, and in *U. rigida* (valine, leucine, and phenylalanine), comparable to legumes, makes them ideal food supplements. On the other hand, *Arthospira sp, Chlorella sp, and D. salina*, renowned for their high protein content and nutritional value, are incorporated into human nutrition diets (Kim and Kang, 2011). Anti-proliferative effects are observed through secretory pathway inhibition, microfilament disruption, and other intracellular mechanisms in active peptides isolated from *Lyngbya spp.* (Costa et al., 2012). Lyngbyabellin B, a cyclic depsipeptide from *L. majuscula*, and Apratoxin A both induce cytotoxic effects against human Hela cervical carcinoma cells by inhibiting the cell cycle (Khalifa et al., 2019). AMPs exhibit a broad spectrum of activity against pathogenic bacteria by leveraging their amphiphilic nature. This property enables interactions with both nonpolar and polar sites on the bacterial cellular membrane, forming pores that lead to additional leakage and disruption of bacterial cells (Lordan et al., 2011). Protein-concentrated fractions from *T. suecica*, modified in amino acid residues (Lysine and alanine), exhibit potent antibacterial effects against *MRSA, B. cereus*, and *E. coli*, demonstrating enhanced activity without cytotoxicity on human cell lines. *Saccharina sp* proteins, obtained via trypsin hydrolysis, inhibit *S. aureus* growth. Lectin HR L40 from *H. renschii*, highly specific to (1,3)-bound monosaccharide residues on HM-N-glycans, binds to influenza A/H3N2/Udom/72 virus hemagglutinin, effectively inhibiting the infectious process in cells (Mu et al., 2017). A novel and distinctive lectin, KAA-2, identified in *E. serra* and *K. alvarezii*, exhibits exceptional specificity for high-mannose glucans in the trisaccharide core of carbohydrates. This unique lectin demonstrates promising antiviral activity against the influenza virus by recognizing high-mannose glucans within the glycoproteins composing the spikes of the virus (Hori et al., 1990). Both prohealing and anti-ulcerogenic activities can be achieved with

lectin. In rats, a lectin that is extracted from *G. changii* is effective in preventing acute gastric mucosal injury caused by EtOH, and it also helps in ulcer healing.

3.8 Glycerol:

Glycerols, categorized as neutral lipids, undergo augmented accrual in algae when subjected to nitrogen-limiting conditions, acknowledged as an exceedingly effective tactic for augmenting the levels of neutral lipids. The prevalent structure of these lipids predominantly consists of triglycerides marked by an elevated degree of saturation (Sara et al., 2014). A recently discovered compound, galactosyl glycerol-lipids, features an α-1,6-galactose and glycerol backbone connected to an ether-linked phytol, originating from the marine green alga *U. pertusa*. Monogalactosyl diacylglycerols, exemplified by 1-eicosapentaenoyl-2-lindenoyl-3-galactosylglycerol derived from *C. racemosa*, have demonstrated both cytotoxic and anti-inflammatory activities in macrophage cells. This compound, in conjunction with β-sitosterol, chlorophyll a, and unsaturated hydrocarbons, showcases multifaceted bioactive properties (Ragasa, 2015). From the same species, an exceptional antiviral compound, sulfoquinovosyl diacylglycerol, displayed remarkable activity against HSV-2, exhibiting an inhibitory concentration of 50% (IC-50) at 15.6 µg/ml against both typical and clinical HSV-2 strains. However, it demonstrated only modest antiviral effects against HSV-1.

3.9 Pigments:

Natural pigments, highlighted among functional ingredients in marine algae, play crucial roles in algae's photosynthetic and pigmentation metabolism. They additionally showcase diverse beneficial biological activities, including antioxidant, anti-inflammatory, anti-carcinogenic, anti-angiogenic, anti-obesity, and neuroprotective effects (Pangestuti and Kim, 2011). Algal pigments

fall into three main classes—Chlorophylls and Carotenoids, both water-insoluble with green and yellow/orange/red pigments, and water-soluble Phycobilin or Phycobiliproteins, featuring bluish, blush green, or purple hues (Zahidul Islam, 2020). Three types of Phycobiliprotein are found: Phycocyanin, phycoerythrins, and allophycocyanins (Silva et al., 2020).

3.9.1 Chlorophyll:

Chlorophylls are green, lipid-soluble pigments involved in photosynthesis, featuring a porphyrin ring in their structure. The porphyrin ring contains a free electron, facilitating the easy transport of electrons. This enables the porphyrin ring to readily gain or lose electrons, energizing them and allowing the transfer of solar energy (Humphrey, 2004). Chlorophyll a and chlorophyll b are the most common types of chlorophyll, and red algae also contain chlorophyll c and d (Humphrey, 1980). The main use of chlorophyll is to replace artificial colorings in different industries, particularly in the food manufacturing industry. Demonstrating a multifaceted impact, chlorophyll enhances wound healing by over 25%, promotes tissue growth, and effectively inhibits bacterial growth, as evidenced by its significant antibacterial effects on *B. subtilis*, particularly when derived from *Scenedesmus* and *C. vulgaris* (Smith et al., 2010). The growth of different species of *Staphylococci, Lactobacilli,* and *Streptococci,* as well as oral bacteria like *Fusobacterium nucleatum* and *Porphyromonas gingivalis*, was inhibited by both chlorophyll (a and b). Derived from chlorophyll-a, chlorophyllide-a, and pheophytin-a, isolated from *I. galbana*, demonstrated inhibitory effects on opportunistic pathogens such as *Flavobacterium sp, Brevibacterium sp, Staphylococcus aureus,* and *Micrococcus sp* (Bruce et al., 1967). The treatment of chronic ulcers is often prolonged, but derivatives of chlorophyll exhibit pain elimination within a few days and aid in enhancing the appearance of the infected tissue (Lady and Morgan, 1948), Pheophorbidea,

chlorophyll-a derivatives from *E. prolifera*, actively displayed antiviral effects against SARS-CoV (Alam et al., 2021).

3.9.2 Carotenoids:

Carotenoids, lipid-soluble colored compounds, are tetraterpenoids with a 40-carbon polyene structure derived from 8 isoprene (C5) units, constituting over 1100 naturally occurring variants synthesized by a diverse array of 600 organisms, encompassing plants, bacteria, algae, fungi, and archaea. Carotenoids can be categorized into two groups: oxygen-containing xanthophylls and purely hydrocarbons with no oxygen-containing carotene. Carotenoids play a role in reducing the susceptibility to inflammation, type 2 diabetes, amyotrophic lateral sclerosis, cardiovascular ailments, cancer, Alzheimer's disease, Parkinson's disease, obesity, and chronic eye and macular diseases (Novoveska et al., 2019). Additionally, they are employed in the creation of creams, lotions, and diverse natural herbal and organic beauty formulations.

3.9.2.1 β-Carotene:

β-carotene, a prominent food colorant and a source of vitamin A (provitamin A/retinol), has experienced a significant surge in demand, particularly in multivitamin preparations. *D. salina* is one of the best natural sources of β-carotene to be commercially grown for use in dietary supplements and natural food coloring (Australia, USA, and Israel) (Borowitzka, 1989a). Incorporating β-carotene-1 into the diet is linked to a reduced risk of age-related macular degeneration, suggesting its potential as a proactive measure to protect ocular health and mitigate the onset of this condition. It can also prevent eye diseases like cataracts and night blindness. β-carotene has been used to treat disorders such as asthma, and cardiovascular and erythropoietic protoporphyria. Furthermore, β-carotene has been utilized for mitigating the risk of various cancers, including breast and lung cancer, owing to its antioxidant properties and antitumor effects. Green seaweeds contain β-carotene, neoxanthin, lutein, violaxanthin, and zeaxanthin, while red seaweed is characterized by the presence of α and β-carotene, lutein, and zeaxanthin. Brown algae, on the other hand, are rich in β-carotene, violaxanthin, and fucoxanthin (Perez, 2016). In the context of COVID-19, β-carotene from *C. crispus* and *D. salina* reduces elevated ROS activity, protecting cells from damage caused by SARS-CoV infectivity and mitigating oxidative stress-induced inflammation in the lungs (Alam et al., 2021). *H. pulmosa, G. cornea, and P. lanosa* harbor β-carotene, a compound renowned for its elevated antioxidant and antiviral activities, thereby underscoring the potential health-promoting attributes associated with the presence of this carotenoid in these marine organisms. The antioxidative quality of β-carotene proves efficacious in combating UV radiation, a leading factor in skin damage and premature aging of the skin (Estavinho et al., 2008).

3.9.2.2 **Astaxanthin:**

Occurring naturally in esterified form, astaxanthin serves as a precursor of vitamin A and is intricately linked with processes such as embryo development and cell reproduction, whereas its synthetic counterpart exists in a free form (Blue et al., 2018). In *H. pluvialis*, astaxanthin makes up 90% of the total carotenoids, and other microalgae like *Chlamydomonas sp, Chlorella sp, Dunaliella sp, Scenedesmus sp, Botryococcus sp, Tetracystis sp* also have the ability to accumulate this secondary carotenoid (Borowitzka 2013). This secondary carotenoid presence elevates cellular resistance to oxidative stress induced by light, UV-B irradiation, and nutrient factors (Lemoine and Schoefs, 2010). Within the post-initiation phase of carcinogen-induced colon and oral cancer models, dietary astaxanthin exhibits antitumor effects, while its inclusion in the human diet demonstrates the potential to mitigate inflammation and oxidative stress, thereby enhancing the immune system in patients with cardiovascular diseases (Guedes et al., 2011) (Koyande et al., 2019). It enhances anti-aging, antibody production and shows sunproofing, anti-oxidant even antibacterial potentiality. It inhibits LDL oxidation and increases HDL-C and Adinopectin (Blue et al., 2018). Reports indicate a preferential hepatic absorption of astaxanthin in comparison to β-carotene and lutein, elucidating distinctive patterns in the bioavailability of these carotenoids within the physiological context. The Natural Algae Astaxanthin Association (NA XA) advocates for astaxanthin benefits, endorsing its use from *H. pluvialis* with primary antiviral drugs for enhanced health and reduced recovery time in COVID-19 patients, approved for human consumption by the United States Food and Drug Administration (Talukdar et al., 2020). Inflammation reduction and ROS scavenging during SARS-CoV infectivity are facilitated by astaxanthin derived from *C. vulgaris and H. pluvialis.*

3.9.2.3 Fucoxanthin:

Fucoxanthin, a xanthophyll-like carotenoid predominantly occurring in brown algae, has garnered attention due to its diverse health benefits, encompassing anti-obesity, anticancer, anti-inflammatory, antioxidant properties, and anti-proliferative, its preventive effects against cerebrovascular diseases (Mikami and Hosokawa, 2013). It prompted apoptosis and cell cycle arrest in a colon cancer cell line, and exhibited anti-proliferative activity, inducing apoptosis in a human leukemia cell line (Hosokawa et al., 1999). It has demonstrated the ability to inhibit carcinogenesis in the duodenum and skin as well as tumorigenesis in mice. Numerous studies have elucidated the anticancer properties of fucoxanthin, highlighting its impact on various pathways, including MAPK, caspase-3, caspase-8, caspase-9, and others, with fucoxanthin regulating their expression levels (Mondal et al., 2021). Fucoxanthin, together with its metabolite fucoxanthinol, demonstrated antioxidant activity by operating as effective scavengers of free radicals, showcasing their capability to counteract oxidative stress by neutralizing free radicals in biological systems. (Mikami and Hosokawa, 2013). Prolonged and excessive alcohol consumption results in both direct and indirect damage to liver cells, culminating in alcoholic liver inflammation. The primary pathway instigating the inflammatory response in alcohol-induced liver injury involves TLR 4-induced signaling pathways. Fucoxanthin, however, mitigates this process by inhibiting TLR-4-induced signaling pathways, thereby attenuating the hepatic inflammatory responses triggered by alcohol (Zheng et al., 2019).

3.9.2.4 Zeaxanthin and Lutein:

Zeaxanthin (β, β-carotene-3,3-diol) is a carotenoid alcohol present in many microalgae such as *T. suecica, Nannochloropsis sp, P. cruentum, I. galbana, P. tricornutum,* etc. Recognized as an efficacious strategy, the oral administration of Zeaxanthin-4 has been identified for the management of acute inflammatory responses induced by UVB irradiation (Zhang et al., 2014). Non-toxicity towards human normal colon epithelial cells was demonstrated by Zeaxanthin, while cytotoxic effects against the human colon adenocarcinoma cell line were observed (Grudzinski et al., 2018).

Contrastingly, yellow oxycarotenoid lutein, characterized by two cyclic groups (a β-ionone ring and an ε-ionone ring), is chiefly sourced from organisms like *Haematococcus sp, C. pyrenoidosa, I. galbana, C. protothecosis, Tetraselmis sp, Spirulina sp,* and *D. salina.* Lutein exhibited similar anticancer potentiality as zeaxanthin (Praveen and Nadumane, 2016) Lutein extracted from *C. protothecoides, S. maxima* and *D. salina*, demonstrated anti-inflammatory effects in countering endotoxin-induced uveitis by impeding Ikβ degradation. This led to the suppression of various pro-inflammatory mediators, including NO, TNF-α, PGE-2, IL-6, MCP-1, and MIP-2 (Zhang et al., 2014). *H. pluvialis* and *C. pyrenoidosa* also abundant with lutein, showed antioxidant capacity. Zeaxanthin and lutein, crucial for preserving normal visual function and safeguarding the eyes from oxidation, exhibit a nutrient-health connection in age-related cataract prevention and maculopathy, as evidenced by epidemiological and intervention trials using extracts from *S. almeriensis* (Lorencio et al., 2009). (Sun et al., 2016).

3.9.3 Plycobiliprotein or Phicobilin:

Phycobiliproteins, vibrant and water-soluble antenna-proteins pigment, form phycobilisomes that are arranged on the external surface of thylakoid membranes. The hues of phycobiliproteins primarily arise from covalently attached prosthetic groups, characterized by open-chain tetrapyrrole chromophores containing A, B, C, and D rings, collectively known as phycobilins (Sekar and Chandramohan, 2007). Phycoerythrins predominate among phycobiliproteins in red algae, while cyanobacteria exhibit abundance in phycocyanins. The classification of phycobiliproteins is based on the chromophores present, leading to three groups: Phycocyanin (blue), Phycoerythrin (purple-red), and Allophycocyanin (bluish-green). Another variant, Phycocerythrocyanin, imparts an orange hue and is a different type of phycobiliprotein (Sekar and Chandramohan, 2007). These pigments demonstrate notable hepatoprotective, antioxidant, anti-inflammatory, and free radical scavenging properties, making them safe for application in cosmetics such as face makeup, eye shadow, and lipstick, as well as in food coloring. These pigments are also used in beverage and alcoholic drinks because modified pigments are stable at low pH. Certainly, pure phycobiliproteins sourced from *Spirulina*, *Porphyridium*, and *Rhodella* function as powerful fluorescent labeling agents extensively utilized in clinical and research immunology, serving as dyes, fluorescent markers, and diagnostic tools with broad applications (Arad and Yaron, 1992). Metabolites from *Arthrospira sp*., including phycocyanobilin, phycoerythobilin, and folic acid, exhibit potential antiviral activity against SARS-CoV-2 (Petit et al., 2020).

Allophycocyanin (bluish-green protein) and phycocyanin (blue protein) are readily extractable water-soluble protein pigment complexes. Extensive research, predominantly focused on *Spirulina sp.*, elucidates the composition of phycobilisomes, comprising allophycocyanin cores surrounded

by c-phycocyanin—a predominant phycobiliprotein, comprising up to 20% of its dry weight (Chaiklahan et al., 2012). Phycocyanin finds primary application as a colorant in dairy products, chewing gums, soft drinks, candies, and cosmetics such as lipstick, and serves as a natural dye across various industries, albeit with limited use in food due to its sensitivity to heat treatment (Chaiklahan et al., 2012).

3.10 Vitamins, minerals, and others nutritional value:

"Functional foods" refers to food components that offer specific health benefits beyond essential nutrition. The development of functional foods is closely tied to the idea of preventing diseases and enhancing the overall well-being of consumers, in addition to meeting their basic nutritional requirements (Plaza et al., 2008). In recent times, seaweeds have gained significance as a crucial food source in numerous countries due to their abundance of micronutrients and vitamins. Despite being underutilized in Bangladesh, they have the potential to emerge as a significant food resource in the pursuit of achieving Zero Hunger (Islam et al., 2020). Seaweeds serve as a nutrient-rich reservoir, providing vital elements such as dietary fiber (carbs), proteins, and lipids. Additionally, they offer a varied spectrum of vitamins (A, B, B12, C, D, E) and minerals (calcium, iron, zinc, copper, potassium, phosphorus, sodium, etc.) (Lordan et al., 2011). Marine algae, integral to diets in Korea, Japan, China, Hawaiian islands, and the Far East, have historical significance. East Asian nations, like Japan, Korea, and China, have long embraced macroalgae, linking it to diverse health benefits. The Japanese, with the world's longest life expectancy and reduced cardiovascular disease rates, attribute these outcomes to their unique dietary practices, prominently featuring regular macroalgae consumption (Shimazu et al., 2007).

Known bioactive compounds, including vitamins and fatty acids, are synthesized by many microalgae. Vitamins such as biotin, pro-vitamin A/β-carotene, B12, B6, etc., and polyunsaturated

fatty acids like docosahexaenoic acid, eicosapentaenoic acid, γ-linolenic acid, and arachidonic acid, are produced by these microorganisms (Borowitzka, 1988a) (Borowitzka, 1988b). Soluble fibers, including carrageenan, alginate, agar, fucoidans, and ulvans, make up a substantial portion of seaweed's dried weight, reaching up to half. These fibers show potential in crafting functional foods. Consumption of fiber-enriched products from macroalgae is linked to preventive effects against type II diabetes, colon cancer, obesity, and cardiovascular diseases (Jimenez-Escrig et al., 2000). Although seaweeds constitute only 1% to 5% of their dry weight in lipids, their impact is noteworthy in treating obesity and various diseases. Macroalgae, with a substantial protein content ranging from 10% to 47%, encompass all essential amino acids. Their beneficial effects extend to addressing disorders such as cancer, thrombosis, hypertension, and oxidative stress (Lordan et al., 2011).

Mineral contents may vary from 8%-40% of algae DW. Their high content in essential minerals is Na, Mn, Mg, I, K, P, Zn, and Fe. Most of the algal contain high levels of Na and K, which is important to compensate for the modern diets, typically rich in NaCl. Furthermore, numerous edible macroalgae exhibit higher magnesium content compared to terrestrial plants and animals, for example, *P. tenuins* containing 44.13%. Specific species are notably enriched in calcium, as seen in *H. boergesenii* (756.924 mg) and *S. tenerrimum* (733.538 mg), and iodine content can reach up to 0.5 g per 100g of dry weight (Dewinta et al., 2019) (Haque et al., 2009) (Yeh et al., 2014). Seaweeds contain calcium phosphate, which is more bioavailable than the calcium carbonate present in milk (Meinita et al 2022). A-tocotrienol, classified as vitamin E, prevents neurodegeneration associated with stroke (Khosla et al., 2006). The administration of *G. changii* dried powder to high cholesterol/high-fat rats for eight weeks resulted in a significant reduction of 40.34%, 35.95%, and 30.91% in plasmatic TC, LDL-C, and TG contents, respectively. This effect

is attributed to the substantial dietary fiber content of *G. changii*, amounting to 61.29% (Chan et al., 2014). Supplementing the diet with *U. ohnoi* and *D. tenuissima* has been reported to result in a lowering of systolic blood pressure, a reduction in final body fat mass by 29 mm Hg and 24%, and an improvement in insulin sensitivity and glucose utilization (Kumar et al., 2015). In hypertensive elderly Japanese patients, the daily oral consumption of 5g of dried *U. pinnatifida* powder over eight weeks has demonstrated a significant reduction in both systolic and diastolic blood pressure (Hata et al., 2001). Dietary NaCl increases blood pressure, while potassium intake has the opposite effect. The WHO recommends a minimum daily potassium intake of 3.51g for adults. Algae such as *Laminaia sp, P. umbilicalis, P. palmata, G. changii, I. galbana, E. arborea, H. elongata* and *T. suecica,* serve as sources of vitamin C. *Chlorella sp, Dunaliella sp, T. suecica, Chondrus sp, I. galbana, Laminaria sp,* and *Porphyra sp* contain vitamins B1, B2, and B12. Vitamin E and α-tocopherol are abundant in *H. elongata, P. palmata, E. arborea, T. suecica, I. galbana, Chlorella, M. pyrifera, Gracilaria,* and *C. fragile* (Alam et al., 2021). A novel functional food, derived from the digested extract of *S. muticum* and *Osmundea sp*, has been employed to enhance the gut microbiome, representing a significant strategy for the prevention and treatment of the novel COVID-19 (Zhang et al., 2020)

Chapter 4

Bioactive compounds sourced from algae hold promise for potential therapeutic interventions against various life-threatening ailments:

Seaweeds have been regarded for their therapeutic utility, with documented medicinal value dating back to as early as 3000 B.C. in the Orient. The Chinese and Japanese civilizations historically employed seaweeds in the management of goiter and glandular ailments, while Romanians embraced their healing properties for wounds, burns, and rashes. Furthermore, the British

strategically utilized *Porphyra* to prevent scurvy, mitigating Vitamin C deficiency diseases during extended sea voyages. Seaweeds have been traditionally employed for remedying conditions such as coughs, stomach issues, chest ailments, bladder complications, and kidney disorders, showcasing their versatile therapeutic properties that extend to vermifuge and antiscorbutic functions (Boney, 1965). *Pterocladia sp, Chondrus sp, Gracilaria sp,* and *Gelidium sp,* have been historically applied in the treatment of diverse stomach and intestinal disorders, offering relief from constipation and associated discomfort. Additionally, *Laminaria* is recognized for its analgesic properties, serving as a painkiller and aiding in the correction of a distended uterus. *Sargassum* species are traditionally harnessed for their cooling properties and blood-purifying attributes, while *Gelidiella* demonstrates efficacy in combating the mumps virus and influenza B virus (Kumar et al., 2018) Astaxanthin, the predominant carotenoid in *H. pluvialis,* serves dual roles as a nutraceutical and a medicinal component, documented against degenerative conditions including H. pylori infection, inflammation, and cancer (Rao et al., 2010). Phycobiliproteins derived from red seaweeds exhibit potential benefits in addressing neurodegenerative diseases arising from oxidative stress. Additionally, the pivotal roles played by Ω-3 fatty acids and ω-6 fatty acids are noteworthy in preventing osteoarthritis, diabetes, and cardiovascular diseases. *Porphyra* (Nori) is very rich in vitamins A and C, used as a nutritional and functional food (Rao et al., 2018). Metabolites derived from algae, harnessed across diverse sectors, emerge as pivotal candidates for exploration in the context of combating severe or life-threatening diseases. Elaborating on their potentiality in this regard becomes imperative, emphasizing the indispensable role they may play as a foundational resource for the development of novel pharmaceuticals characterized by a comprehensive range of therapeutic activities.

4.1 Antiviral activities:

In the last decade, there has been a heightened focus on investigating microalgae, macroalgae, and cyanobacteria for bioactive compounds with pharmacological potential. Current limitations in antiviral treatments emphasize the urgent demand for innovative medicines. The exploration of marine-derived antiviral compounds stands out as a promising and viable solution to address this healthcare challenge (Falais et al., 2016). The initial evidence of potential antiviral activity stemming from algal compounds dates back to 1950. Polysaccharides extracted from *G. cartilagenium* were found to provide protective effects for embryonated eggs against both Influenza B and mumps viruses. This early discovery highlights the multifaceted nature of algal compounds in exhibiting antiviral properties, with implications for viral protection across diverse contexts (Gerber et al., 1958).

Viral growth is generally divided into three stages, **stage I:** adsorption and invasion of virus cells, **Stage II:** Eclipse phase or forced to synthesize multiple copies of that virus and **Stage III:** maturity and release of the virus particles. Antiviral action may take place at a single stage (or more). Such as the anti-HSV factor from *Dunaliella sp* inactivates the viral function at stage I (Guedes et al., 2011). Carrageenans achieve a discerning impediment of various enveloped and non-enveloped viruses by hampering the binding or internalization of the viral entity into the host cell. Carrageenans are strong inhibitors for HPV (at early stages of infection) and HSV virus (block the replication of HSV by stiff interaction causing inactivation of virions) (Buck et al., 2006) (Carlucci et al., 2002). Antiviral activities against HSV-1 and HSV-2 were demonstrated with carrageenans extracted from *G. skottsbergii*, particularly targeting the viral attachment stages. Different structural configurations of galactans demonstrate efficacy against a range of enveloped viruses, including but not limited to hepatitis A, HSV-1 and HSV-2, Dengue Virus, HIV-1, and HIV-2,

among others (Estavinho et al., 2008). Fucoidans exert their inhibitory effects by impeding the formation of syncytium induced in the host cell by viruses. The efficacy of fucoidan derived from *L. japonica* has been substantiated in combatting a spectrum of viruses encompassing both DNA and RNA types. Notably, its effectiveness extends to viruses such as adenovirus III, coxsackie B3, poliovirus III, ECHO6 virus, and A16 viruses (Li et al., 2008) (Li et al., 1995). Extracts derived from *C. racemosa* and *P.gymnospora* demonstrated a mitigating effect on dengue virus infection, likely attributed to their intervention at an early stage in the viral life cycle, possibly through binding or internalization processes (Koishi et al., 2012). Antiviral efficacy against human metapneumovirus replication was exhibited by two meroditerpenoids, automaric acid, and epitaondiol, originating from *S. zonale* (Mendes et al., 2011). Lectins have demonstrated antiviral effects against a spectrum of viruses, including SARS-CoV, HIV, and Hepatitis C, primarily by impeding the entry of the virus into the host cell (Cheung et al., 2015)

Table 2: **Various classes of algae-derived compounds showcase antiviral properties, each with unique mechanisms of action:**

Targeted virus	**Extract of seaweed species**	**Antiviral properties**	**Mechanism of action**
HSV (HSV-1 and HSV-2)	*1. E. compressa, U. partusa* *2. Dunaliella sp* *3. D. salina* *4. A. plantensis* *5. A. muscoides, G. birdiae, S. filiformis* *6. A.specifera, H. clathratus*	1. Ulvan 2. pheophorbide α, β-like compound 3. short chair fatty acids, β-ionone, phytol, palmitic acid and α-linolenic acid 4. Calcium spirulan 5. Agarans 6. Carrageenans	1. Preventing viral entry and internalization, hindering viral replication and propagation, inhibition of absorption, penetration, infection, and replication. 2. Preventing cellular damage at both stage I and stage II phases of the cytopathic effect. 3.Hinders the virus's ability to infect the cell. 4. Prevents viral replication by intercepting the virus prior to entering the host cell. 5. Hindering virus adsorption and impeding early-stage viral replication. 6. Prevention of spread.
VHSV, ASFV	*Chlorella* sp	sulfated polysaccharides	Replication suppression
mumps virus, measles virus	*A. plantensis*	Calcium spirulan	Blocks viral replication at the pre-entry stage.
HIV	*1. S. swartzii* *2. E. bicyclis, L. japonica, A. nodosum, Saccharina* sp, *F. vesiculosus* *3. L.digitata, L. japonica, L. hyperborean* *4. G. skottbergii, C. okamuranus*	1. Fucidan 2. Laminarin 3. Alginate 4. Carrageenans, Fucoidan	1. Halt in reverse transcription. 2. Impeding reverse transcription process (stage III) 3. Impeding reverse transcriptase during RNA virus replication (Stage III). 4. Prevent viral attachment to cells, inhibit reverse transcriptase, shield cells through interaction with viral envelope glycoproteins, and impede syncytia formation and cell-to-cell spread.

Influenza virus (Influenza A and, B, Parainfluenza-2)	*1. C. vulgaris* *2. E. arborea, S. filiformis* *3.Chondrus, Gigartina, Hypnea* and *Euchema* *4. L.digitata, L. japonica, L. hyperborean*	1. Agar 2. Polyphenolic extracts 3. Carrageenans 4. Alginate	1. Hindering cytopathic effects in Stage II, restraining PMN migration towards chemoattractants, and partially blocking adhesion to endothelial cells. 2. Blocking the viral entity. 3. Intercepting host cell penetration, impeding viral replication, and obstructing the attachment of the virus to the host cell 4. Halting reverse transcriptase activity in RNA virus (Stage III).
RSV-A and B,	*C. vulgaris*	Agar	Hindering cytopathic effects in Stage II, restraining PMN migration towards chemoattractants, and partially blocking adhesion to endothelial cells.
Dengue	*1.Chondrus,Gigartina, Hypnea* and *Euchema* *2. G. skottbergii, C. okamuranus*	1. Carrageenans 2. sulfted polysaccharides (Carrageenans, Fucoidan)	1. Intercepting host cell penetration, impeding viral replication, and obstructing the attachment of the virus to the host cell 2. Prevent viral attachment to cells, inhibit reverse transcriptase, shield cells through interaction with viral envelope glycoproteins, and impede syncytia formation and cell-to-cell spread.
Hepatitis B Virus	*L.digitata, L. japonica, L. hyperborean*	1. Polygluronate sulfate 2. Alginate	1. Interference with protein production and transcription. 2. Halting reverse transcriptase activity in RNA virus (Stage III).
Vaccina	*P. cruentum, P. purpureum*	Suloheted exopolysacchaide	Impedes penetration, disrupts replication, and engages with free viral particles.
Human rhinovirus (HRV)	Red microalgae	Iota-carregeenan	Impeding virus adhesion, ingress, and replication.

4.1.1 COVID-19 / SARS-CoV-2/Corona Virus: The COVID-19 pandemic, stemming from SARS-CoV-2 infection, manifests as an acute respiratory ailment marked by prominent clinical manifestations including parched cough, pharyngeal discomfort, fever, headache, breathlessness and fatigue (Liu et al., 2020). Nevertheless, specific individuals displayed an absence of certain symptoms, indicating the presence of an asymptomatic facet to the virus's clinical profile. As the patient deteriorates, they may experience, respiratory tract infection, escalating organ dysfunction, septic shock, and aggravated pneumonia culminating in fatality (Millet and Whittaker, 2014). It holds the distinction of being the most extensive RNA virus documented to date, boasting a genome size ranging from 26 to 32 kilobases. On March 11, 2020, the World Health Organization officially declared the COVID-19 outbreak a pandemic, recognizing the severity of the situation and the lack of alternative preventive measures to mitigate fatalities (*Coronavirus disease (COVID-19) – World Health Organization*. (2023, March 22)) In the absence of vaccines, an imperative arose to urgently formulate antiviral medications, anti-inflammatory agents, and antibodies to combat the disease in the near term. After the SARS-CoV-2 genetic sequence publication, vaccine research led to the development of advanced candidates like Pfizer-BioNTech, Moderna, and Johnson & Johnson/Janssen (Thanh et al., 2020). Phase three trials have been reached by AstraZeneca and Novavax. in the clinical testing of COVID-19 vaccines. Despite the availability of SARS-CoV-2 vaccines, the importance of continuing research on algae-based edible vaccines should not be overlooked. Creating an oral vaccine involves freeze-drying and encapsulating algae, leveraging their cell wall to shield antigens and bioactive compounds from harsh stomach conditions, guaranteeing their safe passage to the intestinal immune system. Marine algal metabolites, encompassing compounds like ulvans, Carrageenan, fucoidans, polyphenolic compounds, lectins, fatty acids, proteins, pigments, etc., have demonstrated expansive antiviral

efficacy against a spectrum of human and animal viruses such as HMPV, HIV, Influenza A and B, HPV, DENV, HSV, etc., suggesting their potential utilization in combatting COVID (Andrew and Jayaraman, 2021). Numerous nations are actively formulating algal-derived products for SARS-CoV-2, with a U.S. research team concentrating on utilizing Heparin as an early intervention. Heparin demonstrates heightened antiviral effectiveness surpassing various antiviral medications, including Remdesivir. Remarkably, the application of Heparin spray alleviates pulmonary coagulopathy and inflammation without triggering systemic bleeding (Kwon et al., 2020). A nasal spray formulation featuring iota carrageenan not only showcases effectiveness and safety against the common cold virus, presently accessible in the market but also proves efficacious against the coronavirus. This is evidenced by its ability to inhibit SARS-CoV-2 infection in Vero cell culture at a concentration of 6μg/mL (Bansal, et al., 2021). Caulerpin from *Caularpa sp* shows promise as a combined therapeutic agent, potentially enhancing its effectiveness alongside other drugs in destabilizing the coronavirus spike protein. In in-silico studies, Caulerpin and its derivatives, investigated as monotherapy against SARS-CoV-2 proteases, demonstrate superior binding energies to the virus's protein receptors compared to predicted drugs like simeprevir, chloroquine, hydrochloroquine, and Liponavir (Ahmed et al., 2020). The viral spike protein exhibits an enhanced affinity for binding with ACE2, a pivotal interaction that facilitates virus entry into host cells. Specifically, in the context of the COVID virus, surface glycosylated proteins play a crucial role by binding to the ACE2 host cell receptor, thereby orchestrating the initiation of viral entry into the cell.

The antiviral activity of marine algal polysaccharides encompasses various processes, including (1) impeding Viral attachment. (2) hindering uncoating and internalization of the virus, (3) thwarting virus transcription and replication, and (4) enhancing immune responses. While

polysaccharides possess the capability to intervene at various stages of the viral life cycle prior to infection, both carrageenan and chitosan stand out by directly exerting virucidal action on enveloped viruses, effectively obstructing the viral infection process (Wang et al., 2012). Fucoidan and sulfated rhamnan exhibit the ability to impede the epidermal growth factor receptors pathway, indicating a potential suppression of coronavirus, while ulvans are also contemplated as promising therapeutic agents against COVID-19. Antiviral activity against murine coronavirus A59 was demonstrated by the novel diterpene aldehyde, halitual, extracted from *H. tuna*. Phycocyanobilin, phycoerythrobilin, and astaxanthin demonstrate an active capacity for binding with SARS-CoV-2 (Alam et al., 2021). An Indian research group explored sulfated polysaccharides from Porphyridium sp for developing antiviral drugs, unveiling their capacity to hinder the binding of the virus to host cells and display immunomodulatory characteristics. Additionally, these compounds show promise as a coating material on sanitary items, aiding in COVID-19 prevention (Mahadev et al., 2000). The potential of glycoprotein-based antiviral therapy for SARS-CoV-2 entails a strategic process where, before the coronavirus spike protein attaches to a host cell, the glycans on the host cell's surface undergo glycosylation, masking them with glycosylation epitopes. This transformation results in a substantial glycoprotein, containing 23-38 N-linked glycan sites per promoter, rendering the spike protein non-infective. Lectins, as distinctive carbohydrate-binding glycoproteins, actively inhibit the infectivity of SARS-CoV-2 due to their specificity for the glycan moieties present on the spike glycoproteins of the coronavirus (Alam et al., 2021). Natural astaxanthin plays a protective role against acute lung injury, acute respiratory distress syndrome, and, cytokine storm, presenting potential as a complementary supplement when combined with primary antiviral compounds (Cai et al., 2019). Fucosterol emerges as an effective therapeutic agent for diverse health issues and stands as a promising candidate for treating COVID-

19, such as, fucoidans derived from *U. pinnatifida*, *A. nodosum*, *M. pyrifera*, and *F. vesiculosus* were identified for their capacity to enhance immune function through the activation of DCs, NK cells, and T cells (Rosales- Mendoza et al., 2020). Furthermore, an optimally functioning gut microbiome actively reinforces antiviral immunity, and a well-balanced nutritional diet enhances the resilience of the gut microbiota, thereby mitigating the impact of the novel SARS-CoV-2. This is achieved through the stimulation of augmentation of NK cytotoxicity, reduction of immunopathology, and interferon production (He et al., 2020). In addition to severe damage to the lungs and blood vessels, atypical blood clots in the pulmonary region lead to diminished oxygen levels, potentially resulting in fatalities among COVID-19 patients. This ultimately gives rise to clot-related complications such as renal failure, venous thrombosis, and stroke. Notable antithrombotic and antiplatelet effects have been demonstrated in rats through the influence of polysaccharide derived from *G. acerosa*, with its interaction involving the blood coagulation system and hemostasis (Chagas et al., 2020). Biotech company "TransAlgae" in Israel is actively exploring genetically modifying algae to develop a COVID-19 vaccine. They insert a segment of the spike protein into algae to stimulate antibody production and elicit an immune response. They assert that the addition of the spike protein in minute quantities does not alter the safety profile of the algae for humans. Furthermore, the encapsulation of the algae guarantees the delivery of the vaccine to the intestinal immune system. Oxidative stress plays a central role in SARS-CoV infection, with increased levels of ROS associated with cellular damage due to heightened inflammation at the viral infection site. This disruption in the balance of oxidative-antioxidant status induces oxidative stress, contributing to cellular damage. Considering this inflammatory response, incorporating antioxidants is advised as a potential strategy against COVID-19 (Alam et al., 2021)

4.1.2 Influenza Virus: Influenza, an acute infectious ailment, results from an enveloped ribonucleic acid-containing virus (Orthomyxoviridae family) characterized by virions (80-100nm) enclosed in lipoprotein membranes, consisting of lipids and three types of glycoproteins: hemagglutinin, neuraminidase (NA), and the viral ion channel (M2) (Norkin, 2010). Influenza encompasses three virus types (A, B, C), with Types B and C exclusively afflicting humans; the antigenic determinants carried by hemagglutinin and neuraminidase (HA and NA) delineate influenza subtypes, such as H1N1, H3N2, and H5N1 (Mei et al., 2013). Influenza primarily targets the single-layer multi-row cylindrical ciliated epithelium in the respiratory tract, employing hemagglutinin to adhere to cell receptors, enabling penetration and initiation of the replication cycle. Influenza treatments include Rimantadine and Amantadine for early-stage infection, Umifenovir boosts innate immunity through interferon modulation, and Riamylovir, Zanamivir, and Oseltamivir target viral replication with neuraminidase inhibition (Besednova et al., 2019). Established medications effectively combat certain virus strains, yet the potential emergence of drug-resistant viral strains poses a challenge that these drugs may not effectively address. To address this challenge, there is a pressing need for innovative therapeutic approaches, where seaweed metabolites stand out as uniquely capable candidates. These compounds intricately target specific genes or proteins essential for the influenza virus's replication and reproduction (Besednova et al., 2019). The reported hindrance of Influenza A (H1N1) adsorption and prevention of fusion events by fucans extracted from *F. vesiculosus and A. nodosum* underscores their capacity to impede critical stages in the virus's interaction with host cells (Jiao et al., 2012). Assessment against Influenza virus groups 1 (A/Bervig-Mission/1/18 [H1N1], A/PR/8/34 [H1N1]) and group 2 (A/Hong Kong/8/68 [H3N2], A/chicken/Korea/MS96 [H9N2]) was conducted for phlorotannin derivatives ecol, diecol, fluorofucofuroecol, 7-phloracol, and phloroglucinol.

Inhibition of the neuraminidase (NA) was notably strong for Fluorofucofuroecol against group 1 Influenza viruses, while Diecol demonstrated potent inhibition of the NA for group 2 Influenza viruses (Besednova et al., 2019). The highly vulnerable variant, H1N1, and the antiviral process may involve impeding viral entry, suppressing the initiation of the epidermal growth factor receptor. Fucoidan has the potential to suppress the secretion of cytokines from human primary bronchial epithelial cells by acting on TLR3, thereby alleviating bronchial inflammation induced by viral infection (Rosales-Mendoza et al., 2020). When evaluated against H3N2 and H1N1 strains, I-Carrageenan demonstrated superior effectiveness over κ-Carrageenan. It hindered the formation of syncytia and interfered with the interaction between the virus and host cells. Remarkably, I-Carrageenan notably decreased viral replication by 2-4 log units within 96 hours after infection (Leibbrandt et al., 2010). Furthermore, Carrageenan, identified in *Eucheuma, Gigartina, Hypnea, and, Chondrus*, demonstrated notable inhibitory impacts on the Influenza virus. In Europe, a carrageenan-based nasal spray has found success in alleviating respiratory viral infections. This product effectively reduces symptoms like cough, runny nose, sneezing and nasal congestion, related to common colds and inflammation. Importantly, the nasal spray, enhanced with Zanamivir, demonstrates efficacy when used within the first 48 hours after symptom exposure (Kumar et al., 2011) (Ludwig et al., 2013). Oligosaccharide CO-1 and its derivatives bound to viral mRNA post-cell internalization, curtailing viral protein expression and H1N1 influenza virus replication. A similar hindering of virus adsorption and internalization was observed with galactan (Wang et al., 2017) (Wang et al., 2011). In vitro antiviral activity was demonstrated by the aqueous extract of *L. obtusa,* with the suppression of replication observed in both Influenza A (H3N2, H1N1) and Influenza B (Pérez-Riverol et al., 2014). Inhibitory effects on Influenza A, Influenza B, and Parainfluenza-2 viruses are exerted by agar, derived from *C. vulgaris* and *Porphyridium*

sp., through the impediment of their adhesion to endothelial cells (Alam et al., 2021). Administering Fucoidan from *U. pinnatifida's* sporophylls orally to mice infected with H5N3 and H7N2 strains reduced virus replication and enhanced specific antibody production in vivo. This polysaccharide actively targeted the inhibition of virus release from cells, resulting in increased titers of virus-neutralizing antibodies and IgA (Besesnova et al., 2019). Extracted from *L. japonica*, Fucoidan displayed no cytotoxicity or morphological changes in SPEV culture cells, yet actively and selectively suppressed the infectious properties of H5N1 strain, demonstrating antiviral activity within the first 24 hours of infection (Besednova et al., 2019). Recognizing HM-glucans in virus spikes, lectins, particularly KAA-2 from *K. alvarezii*, directly associate with Influenza virus Hemagglutinin (HA), robustly preventing viral entry into host cells (Hori et al.,1990). Optimal inhibition of influenza infection was achieved with the HM-binding lectin ESA-2 from *E. serrai*, exerting its effects through a direct interaction with the viral envelope glycoprotein HA and effectively suppressing the virus (Sato, 2015). Various lectins, including BCA from *B. coacta*, HRL40 from *H. renschii*, BSL from *Bryothamnion sp*, HML from *H. musciformis*, and Sfl from *S. filiformis*, exhibit effectiveness against diverse strains of the Influenza virus (Alam et al., 2021). Algal biopolymers have recently been scrutinized as promising contenders for adjuvant technologies in vaccine formulation. Particularly, sulfated polysaccharides sourced from brown algae showcase advantageous adjuvant properties such as non-toxicity, safety, and exceptional biocompatibility. These attributes play a pivotal role in shaping innate and adaptive immunity and modulating associated signaling pathways (Petrovsky and Cooper, 2011). TLRs serve as primary targets for innovative adjuvant development, with TLR agonists being the preferred adjuvants for vaccines, particularly as polysaccharides interact specifically with human TLRs. Fucoidan isolated from S. cichorioides, F. evanescens, and S. japonica, interacts with TLR2 and TLR4, initiating the

activation of the adaptive NF-κB pathway, fostering the generation of a Th1-type adaptive immune response to unrelated antigens. That means, Fucoidan exhibits dual functionality by acting as an adjuvant, enhancing immunogenicity, while concurrently inactivating influenza virus A. Henceforth, Fucoidan emerges as a secure and efficacious adjuvant, given its elevated biocompatibility, absence of toxicity, and favorable tolerability within the human body, positioning it as a valuable component in the formulation of advanced influenza vaccines (Besednova et al., 2019).

4.1.3 Dengue / DENV: Dengue, an enveloped virus in the Flavivirus genus with four known serotypes (DENV1-4) capable of causing the disease, has been reported in Malaysia with a newly identified gene branch, indicating a potential fifth genotype, DENV5 (Freile-Pelegrin et al., 2019) (Normile, 2013). Mature virions exhibit a positive single-stranded RNA genome encased in a nucleocapsid, while the envelope and membrane proteins extend from the lipid bilayer membrane of the host. The clinical presentations of DENV infection range from a non-specific fever (dengue fever, DF) to more critical conditions such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), with the potential for fatal outcomes (Koishi et al.,2012). The transmission of the dengue virus, characterized by diverse genotypes, occurs through the bites of female mosquitoes belonging to the species *Aedes albopictus* and *Aedes aegypti* (Ahmad, et al., 2016). Approximately 3.5 billion people worldwide are at risk of contracting dengue fever, with 1.3 billion residing in endemic areas, primarily transmitted by the predominant vector species *Ae. aegypti* WHO, 2023 (https://www.who.int/publications/i/item/sea-cd-334). Continuous use of synthetic organic insecticides in vector control since their discovery in the 1940s has led to mosquito resistance due to prolonged exposure. Marine algae harbor a diverse array of chemical compounds exhibiting antiviral effects against DENV, as well as larvicidal and adulticidal activities against *Aedes* species.

Enveloped RNA viruses typically initiate their replicative cycle by attaching to the host cell's surface, making the prevention of virus binding to the host cell a valuable strategy to establish an initial barrier and suppress infection (Freile-Pelegrin et al., 2019). Ulvan, derived from *Caulerpa sp.,* demonstrated potent in vitro activity against DENV-1 in the Vero cell line by masking viral structures and interfering with the virion envelope, thereby impeding virus adsorption to cells and preventing infection (Rodrigues et al., 2017). Fucoidan isolated from *C. okamuranus* demonstrated

pronounced inhibition of DENV-2 infection, displaying a moderate effect against DENV-3 and DENV-4. The interaction of DENV-2's glycoprotein involves both glucuronic acid and sulfated fucose residues, disrupting the binding of the surface envelope glycoprotein with cell receptors and thereby exhibiting antiviral activities (Hidari et al., 2008). A dose-dependent response was observed in the effective suppression of viral replication by the organic extracts from *O. obtusiloba, C. racemosa, and K. alvarezii* (Freile-Pelegrin et al., 2019). A proposed target-agnostic approach for dengue drug discovery involves in-situ ELISA (enzyme-linked immunosorbent assay) and screening marine weed extracts, with standardized and validated in-situ ELISA for human hepatoma cell lines infected with all DENV serotypes. In this study, scientists noted that the antiviral effectiveness against dengue showed dependence on both host-cell type and viral serotype. Examples include *Gymnogongrus* and *C. crenulata*, which demonstrated efficacy against DENV-2 by impeding multiplication in Vero cells. *P. gymnospora* and *C. racemosa* inhibited DENV-1 and DENV-3, exerting their influence at the early stages of viral infection. Extracts from *Plocamium, Gigantina, and Undaria*, demonstrated notable activity when introduced within the initial hour of DENV-4 viral infection. Various chemical compositions were identified as antiviral components; for instance, *P. gymnospora* encompasses fatty acids and sulfated polysaccharides, *while C. racemosa* yields sterols, terpenes, fatty acids, and alkaloids (Koishi et al., 2012). Seaweeds exhibit promising larvicidal activity, underscoring the importance of alternative methods beyond vaccination. The chloroform fraction derived from *C. edule* stands out as a potent alternative larvicidal agent to synthetic counterparts, demonstrating substantial efficacy with an LC50 value of 19.54 ppm. Significantly, the fraction includes myristic acid (12.4%), β-sitosterol (22.45%), and palmitic acid (25.75%), against *A. aegypti*. Additionally, these naturally-occurring metabolites are inherently safe for human application (Alkuriji et al., 2020). *S. ilicifolium, S.*

wightii, and *G. acerosa* extracts displayed larvicidal activity against *A. aegypti*, with LC90 values of 423.012, 52.00, and 354.903, respectively, featuring notable phytochemical constituents such as octadecanoic acid, n-Hexadecanoic acid, and phytol (Pachiappan, et al., 2022).

The *C. parvula* extract displayed bifunctional impacts on digestive enzyme activity in the mosquito vector, leading to growth impairment, metabolic imbalance, and eventual mortality. Significantly, this extract showed no toxicity towards other species and demonstrated eco-friendliness in contrast to alternative synthetic chemicals. Besides its strong enzyme inhibition targeting essential components of the digestive system in the dengue mosquito, the *C. parvula* extract demonstrated prospective larvicidal effects, a repellent influence, and showcased detoxification enzyme activity, encompassing CYP450, Carboxylesterase (α and β), and GST, against the vector. Considering these attributes, the *C. parvula* extract holds potential for commercialization as an eco-friendly, natural mosquitocidal agent, capitalizing on its green-based properties (Yogarajalakshmi et al., 2020).

4.2 Antibacterial activities:

Antibiotic resistance is a global concern due to the escalating use and improper administration of antibacterial drugs by humans and animals, threatening the effectiveness of essential medicines. The emergence of drug resistance not only prolongs hospitalization, elevates healthcare expenditures, and contributes to mortality but also amplifies the incidence of nosocomial bacterial infections, compounding the multifaceted challenges associated with antibiotic resistance. Marine algae, regarded as a natural and alluring biotechnological reservoir, present a promising source for the discovery of innovative antibiotics.

A total of 39 algal specimens underwent screening for antibacterial efficacy against *E. coli and S. epidermidis*. Among Chlorophyta species, *C. gracilis* exhibited the most substantial inhibition zone for both bacterial strains. Notably, *F. spiralis* from Phaeophyta demonstrated complete clearance of *S. epidermidis*. The antimicrobial effects were attributed to terpenes and acrylic acid produced by these algae (Lustigman and Brown, 1991). n-hexane, methanol, and dichloromethane extracts from 12 marine macroalgae displayed significant antibacterial activity against *B. subtilis* but had no effect on *E. coli*. Notably, *S. coronopifolius* exhibited the strongest inhibition of *B. subtilis*, with isolated metabolites including fatty acids, acetogenins, hydrocarbons, and terpenes. This positions *S. coronopifolius* as a promising candidate for the development of antibacterial drugs (Pinteus et al., 2015). Bangladeshi marine algae, tested against various pathogens, showed superior antibacterial activity in ethanol extracts compared to methanol and chloroform. *Chlorella sp, A. specifera, E. prolifera, Nostoc sp,* and *U. lactuca,* inhibited all strains, with *A. specifera* notably effective against *B. subtilis* (17 mm). Noteworthy efficacy was observed in *Nostoc sp, E. prolifera, Chlorella sp, D. membranacea, U. lactuca,* and *S. vulgare,* against *B. subtilis (17.9 mm), P. aeruginosa (16.1 mm), K. pneumoniae (20.3 mm), E. coli (26.0 mm), S. aureus (12.7 mm),* and *K. pneumoniae (14 mm),* respectively. Antibacterial compounds identified included phenols, brominated phenols, hydroquinones, polyphenols, and sesquiterpenoids (Mehadi et al., 2015). Screening encompassed 44 macroalgae species across three major divisions, and exclusive antibacterial activity against all targeted microorganisms, including *B. subtilis, A. fumigatus, E. faecium, S. cerevisiae, S. marcescens, M. smegmatis, P. aeruginosa and S. aureus,* was demonstrated by only one species, *A. taxiformis,* exhibiting the highest inhibition zone of 15mm among the 28 species with antimicrobial activity (González et al., 2001). Moderate activity against various nosocomial bacteria (*P. aeruginosa, E. coli, K. pneumoniae, B. cereus, S. aureus,* and *B.*

subtilis) was exhibited by ethanol crude extracts from *U. lactuca*, *L. optusa,* and *T. triquatra,* along with their fractions containing oleic acid, palmitic acid, fucoxanthin, and fucestercol. Oleic acid, a monounsaturated fatty acid, hinders the activity of the protein kinase KinA, impacting sporulation initiation in *B. subtilis*, while also inducing membrane depolarization, leading to a significant decrease in bacterial viability. Inhibitory effects on *B. cereus* spore formation were observed with palmitic acid. The inhibition of these bacteria may be attributed to the cytotoxicity effects of fucosterol and fucoxanthin. Plasmolysis and a reduction in the cell size of *E. coli* were induced by a combination of oleic and palmitic acid (Deyab, 2013). Eicosapentaenoic acid sourced from *P. tricornutum,* in addition to butanoic acid and methyl lactate extracted from *H. pluvialis*, demonstrated cell lysis capabilities against a diverse range of bacteria, spanning both Gram-positive and Gram-negative strains, inclusive of MRSA. Unsaturated and saturated long-chain fatty acids from *S. costatum* exhibited antibacterial effects against *Vibrio spp and L. monocytogenes* by impeding cellular respiration, inducing cell membrane damage, causing cell leakage, and reducing nutrient uptake Lysis of bacterial protoplasts, disrupting the growth and survival of bacterial strains, was induced by compounds derived from the organic extract of *S. costatum*. Potent antibacterial activity was demonstrated by the extract, with MIC values of 7.8 µg/mL and 1.9 µg/mL against *S. aureus* and *H. influenza*, respectively, as well as against *E. coli, P. aeruginosa, S. epidermidis, M. luteus, P. phosphoreum, A. hydrophila*, among others (Amaro et al., 2011).

Table 3: **Extracted compounds from marine algae with antibacterial activities**

Compounds	**Biological source**	**Targeted bacteria**		**Activity IC50 or MIC**	**Ref**
		Gram +	**Gram -**		
Elatol, deschloroetatol, allolaurinterol, debromolaurinterol (terpenes)	*L. rigida*, *L. obtusa*, *L. flexilis*	-	*M. tuberculosis*, *M. avium*	32 µg mL^{-1}, 16 µg mL^{-1}, 64 µg mL^{-1}	Konig et al., 2000
Elatol, ISO-obtusol, laurinterol, allolaurinterol, isolaurinterol, cupalaurenol (Sesquiterpenes)	*L. spp*, *L. majuscula* *L. okamurae*	- - *S. epidermidis*, *S. aureus*, *S. pneumoniae*, *Enterococcus sp*, - *S. faecalis*	*Salmonella sp*, *K. pneumoniae*, - - - *Escherichia coli* -	25-30 mm, 19-24 mm 7-12 mm 19-24 mm 1.6 µg mL -1 12-18 mm 6.3 µgmL-1	Vairappan, 2003 Vairappan et al., 2004
Bromoditerpens	*S. coronopifolius*	*S. aureus EMRSA- 16*, *S. aureus (ATCC 25923)* -	- - *P. aeruginosa*	0.3 µg mL^{-1}, 0.5 µg mL^{-1}, 6.35 µM	Smyrniotopoulos et al., 2008 Smyrniotopoulos et al., 2010
Sargafuran, Sargaquinoic acid, Sargachomenol	*S. macrocarpum*	*S. pyogenes*	*P. acnes ATCC 11827*	15 µg mL^{-1},	Kamei et al., 2009

Fucoidan (52.7% fucose and 29.3% sulfate)	*S. wightii*	-	*V. cholerae*, *P. aeruginosa*	31 µg mL^{-1}, 62.5 µg mL^{-1}	Maradhupandi and Kumar, 2013
Fucoidan	*L. japonica*	*S. aureus*	*E. coli*	10 mg mL^{-1},	Liu et al., 2017
Polyphenol	*P. tetrastromatica*, *P. gymnospora*	*S. aureus*	-	7.7-26.5 mm	Jegan et al., 2019
Phlorotannins	*A. nodosum*	-	*E. coli (Serotypes O113: H21 and O154: H10)*	6.4 $\log^{10}$ CFU/cm^2	Bumunang et al., 2019
Fucoxanthin (carotenoid)	*L. obtusa*, *T. triquetra*, *U. lactuca*	*S. aureus*, *B. subtilis*, *B. cereus*	*K. pneumoniae*, *E. coli*, *P. aeruginosa*	4 mm- 7 mm	Deyab, 2013
Saringosterol	*Lessonia sp*	-	*M. tuberculosis*	0.125 µg/mL-1.00 µg/mL	Wächter et al., 2001
Phlorofucofuro-eckol A (PFF-A) Eckol, Phloroglucinol (six derivatives)	*E. bicyclis*	MRSA	*P. acnes*	32-64 µg/mL	Eom et al., 2013 Eom et al., 2017
Diphlorethohy-droxycarmalol	*I. okamurae*	*S. aureus*	*P. aeruginosa*	128 µg/mL	Kim et al., 2020
Cladophorols A – I	*C. socialis*	MDR strain of VRE/ *E. faecium*	*P. aeruginosa*, *E. coli*, *K. pneumonia*, *A. baumanni*	1.4 µg/mL	Bhowmick et al., 2020
Bromophycolids J-Q	*C. serratus*	*E. faecium*, *S. aureus* -	- M. tuberculosis	5.8 µM 1.4 µM	Lane et al., 2009

Tuberculosis poses challenges with prolonged treatments and severe side effects, effective therapy for *Mycobacterium species (M. tuberculosis, M. bovis)* requires direct delivery of antitubercular agents to the lungs due to their intracellular survival in host alveolar macrophages. Several natural polymers present an important advantage, being composed of basic units that directly recognize the macrophage's lectin type and seven transmembrane receptors which are reported as macrophage activators. These macrophages might recognize several moieties on the infecting organisms or bacterial cell wall surfaces. Fucoidan extracted from *L. japonica*, comprising sulfated fucose and additional sugar residues, demonstrates an affinity for alveolar macrophage surface receptors, promoting microparticle internalization and enabling drug delivery at the injection site. Inhalable fucoidan, combined with isoniazid (92%) and rifabutin (95%), and directly administered to the respiratory zone with suitable aerodynamic characteristics, demonstrated effective inhibition of mycobacterial growth in vitro. These drug-loaded microparticles exhibited no cytotoxicity on lung epithelial cells (A549) but showed mild toxicity on THP-1 cells at the minimum inhibitory concentration (MIC) of 1mg/mL which presents a promising prospect as a potential treatment for tuberculosis (Cunha et al., 2018). Derived from red edible seaweed, Carrageenan, a sulfated polysaccharide, directly targets alveolar macrophages. The successful production of an inhalable microparticle formulation, containing Carrageenan, isoniazid (96%), and rifabutin (74%), demonstrated no toxicity to lung epithelial cells. Carrageenan, acknowledged by macrophage lectins, acts as a platform for precise drug delivery (Rodrigues et al., 2020).

4.3 Anti-parasitic/Anti Protozoal activity:

Neglected communicable protozoa parasite diseases (such as Malaria, Leishmaniasis, and trypanosomiasis), prevalent in tropical regions, pose a severe threat to human health, particularly impacting impoverished populations in developing countries. As per the WHO, the neglected tropical diseases (NTDs), encompassing 20 conditions, are endemic in 149 nations, impacting over one billion individuals globally. (WHO, 2023 https://www.who.int/news-room/questions-and-answers/item/neglected-tropical-disease)

Chemotherapy, the primary approach for tackling these diseases, is marked by potential toxicity, pain, lengthy procedures, and restricted access, posing challenges for impoverished individuals affected by these conditions (Falkenberg et al., 2019). *Malaria, leishmaniasis, and trypanosomiasis* emanate from parasitic protozoa belonging to the genera *Plasmodium, Leishmania, and Trypanosoma* species. Trypanosomiasis, a vector-borne NTD, is caused by the kinetoplastide parasite genus Trypanosoma, and it is transmitted to humans through bites from *Glossina sp* (tsetse fly) or triatomine bugs. Existing therapeutic options for these diseases include Nifurtimox, Suramin, Pentamidine, Denznidazole, Eflornithine. Leishmaniasis, resulting from diverse species such as *L. donovani, L. chagasi, L. infantum, L. major, L. tropica, L. braziliensis, L. mexicana, L. amanzonensis,* and others, is transmitted via female phlebotomine sandfly bites, with available therapeutic options in the market encompassing Liposomal amphotericin B, Miltefosine, AmBisome, Paramomycin, Deoxycholate, and more (Freile-Pelegrin et al., 2019). Malaria, the most perilous and infectious ailment induced by Plasmodium species (including *P. falciparum, P. ovale, P. vivax, P. malariae,* etc.), formerly depended on medications like Chloroquine, Quinine, and Quinidine until 2006. Artemisinin derivatives, specifically artemether and artesunate, along with amodiaquine, mefloquine, sulfadoxime-pyrimethamine, etc., constitute the current pharmacotherapeutic arsenal against malaria (Álvarez-Bardón et al., 2020). The primary transmitter of the malaria parasite P. falciparum is the female Anopheles stephensi mosquito. However, among the approximately 400 extant species of Anopheles mosquitoes, about 30 species are recognized as formidable vectors capable of causing malaria (WHO, World Malaria Report (2022)). Marine macroalgae harbor various natural products known for their reported antiparasitic effects. A selection of these includes.

Table 4: **Antiparasitic effect of marine algae and their mechanisms of actionl**

Active compounds of marine algae	**Target**	**Mechanism of Action**
L. drendoidea (elatol, obtusol, a triquinane derivative (silphiperfol-5-en-3-ol))	*L.amazonensis* *T. cruzi*	Triggering mitochondrial membrane depolarization and boosting reactive oxygen species levels without harming the host cell.
D. pfaffi (dolabelladienetriol)	*L. amazonensis*	Depolarization and lipid peroxidation of the mitochondrial and target membranes.
C. serratus (bromophycolide A and its derivatives)	*P. falciparum*	Efflux pumps confer chloroquine resistance in parasites, while bromophycolide A acts through acylation in the p-hydroxybenzoate group, inhibiting heme crystallization and artemisinin.
L. viridis (Dehydrothysiferol, 28-iodosaiyacenols A and B)	*T. cruzi* *L. amazonensis*	Adding an iodine atom showed notable antileishmanial effectiveness.
L. japonica (Sulfated Polysaccharide fucoidan)	*L. donovani*	Clearing 90% of parasite burden in liver and spleen involves a potent Th-1 response, triggering NO production and increased free radical generation in infected macrophages.
L. vadossa (Fucosterol)	*L.infantum,* *L. amazonensis*	Effectively targeting intracellular amastigotes and extracellular promastigotes, no toxicity to the host cell.
Sargassum sp (Quinone)	*L. amazonensis*	Balanced macrophage activity by inhibiting NO and stimulating ROS production.

Comparable anti-*L.amazonensis* amastigote activity was demonstrated by meroditerpenoid atomaric acid and its methyl ester derivatives from *S. zonale* (Soares et al., 2016). Antiplasmodium efficacy against the *P. falciparum* parasite was demonstrated by fucoxanthin, saragaqunoic acid, Saragaquinoic acid, sargahydroquinoic acid, and tetraprenylated toluquinols, all derived from *S. heterophyllum* (Afolayan et al., 2008). Geranylgeraniol, steroids, and phenols within a range of phytochemical classes exhibited promising molecular targets against *Leishmania*, *Trypanosoma*, and *Plasmodium* spp parasites; notably, 2´,4´-dihydroxychalcone was recognized as a selective inhibitor acting on the glycolytic enzyme glycerol-3-phosphate dehydrogenase in these parasites (Falkenberg et al., 2018). Spiralyde A and 3,4-epoxy-7,18-dola–belladiene, derived from the crude extract of *D. spiralis* and possessing antikinetoplastidal activity, demonstrated moderate inhibition against *L. amazonensis* (Chiboub et al., 2019). Among the fractions isolated from *B. tenella*, including fatty acids, esters, steroids, low molecular hydrocarbons, and neophytadien, certain fractions exhibited superior antiprotozoal activity compared to gentian violet and amphotericin B against *T. cruzi and L. amazonensis* (de Felício et al., 2010). The dichloromethane

extract of *D. menstrualis* yielded bicyclic diterpenes, namely pachydictyol and isopachydictyol, which exhibited noteworthy anti-leishmanial activities against *L. amazonensis* promastigotes. Notably, these compounds effectively impeded parasite growth, all while demonstrating toxicity levels equivalent to those observed in macrophages (Freile-Pelegrin et al., 2019). Derived from *C. cervicornis*, the 4-acetoxydolastane diterpene demonstrated noteworthy antileishmanial effects against diverse forms of *L. amazonensis*—promastigotes, intracellular amastigotes, and axenic amastigotes. Moreover, it induced heightened lipid peroxidation, substantial ultrastructural changes, and mitochondrial depolarization (Santos et al., 2011). Derived from *B. bifurcata,* elenganolone, an acyclic diterpene, showed strong antitrypanosomal activity against *T. brucei* trypomastigotes and notable growth inhibition against both *T. brucei and T. cruzi.* Furthermore, it exhibited potent antiprotozoal activity against *P. falciparum.* Derived from the same species, Bifurcatriol has exhibited inhibitory effects against both *Trypanosoma sp and Plasmodium sp,* underscoring its potential as an antiparasitic compound (Freile-Pelegrin et al., 2019) (Smyrniotopoulos et al., 2017)

4.3.1 Malaria:

Malaria occurs due to infection by an apicomplexan endoparasites species of *Plasmodium* genus, which are transmitted by *Anopheles* sp. mosquitoes, and is a major problem in developing countries. *P. falciparum* is responsible for 99% of malaria cases in African and Asian regions, while *P. vivax* approximately 9% of cases world wide (Álvarez-Bardón et al.,2020). According to WHO (2022) (https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2022), 99% of estimated malaria cases were in Africa, followed by Western Pacific (71.9%), the Eastern Mediterranean (69%) Southeast Asia (62.8%) were caused by P. falciparum parasite (Hikmawan et al., 2020). Over 70% of malaria-related fatalities in the region are ascribed to P. falciparum, frequently resulting from delayed treatment (World Malaria Day, WHO 2023). Quinine and quinidine, the initial compounds isolated from the cinchona tree bark in the early 19th century, functioned as antimalarial drugs until 2006. Serving as the foundational scaffold, artemisinins, as sesquiterpene lactones, are utilized in the synthesis of semisynthetic derivatives such as artemether and artesunate. These derivatives are currently employed in the management of both complicated and uncomplicated cases of falciparum malaria (Álvarez-Bardón et al.,2020).

Combining artesunate with mefloquine serves in managing uncomplicated malaria, addressing chloroquine resistance, and providing prophylaxis for travelers. Additionally, introducing sulfadoxine and pyrimethamine in combination therapy, along with artesunate, is part of the treatment strategy for uncomplicated falciparum malaria resistant to chloroquine (Álvarez-Bardón et al., 2020).

Chloroquine-resistant *P. falciparum* displayed high susceptibility to a mono-hydroxy acetylated sterol derivative, Helymeniaol, produced by *Halymenia sp*, demonstrating antimalarial potency without inducing cytotoxicity (Meesala et al., 2018). Potency against the *P. falciparum* strain has been demonstrated by several valuable antimalarial compounds from marine cyanobacteria, including Hoshinoamides A and B, gallinamide A-18, Ulongamide A, Palstimolide A, Lyngbyabellin A, symplostatin 4-19, and Ikomide (Nweze et al., 2021) (Abdollahi et al., 2018). Intriguing insights into the impact on the plasmodium vector *A. stephensi* were provided by the toxicity assessment of diverse solvent extracts from *S. wightii, S. ilicifolium,* and *G. acerosa*. Lethal effects on *A. stephensi* were manifested by *S. wightii* ethyl acetate extract, with a mortality rate recorded at a concentration of 3.98 µg/mL as LC50 and 12.17 µg/mL as LC90 value. Subsequently, a fatality rate on A. stephensi was demonstrated by *G. acerosa* ethyl acetate extract, with concentrations of 4.59 µg/mL as LC50 and 15.91 µg/mL as LC90 value. Lastly, the highest mortality was showcased by *S. ilicifolium* ethyl acetate extract, with a concentration of 18.934 µg/mL as LC50 and 371.753 µg/mL as LC90 value. These findings indicate that the ethyl acetate extracts of all seaweeds may contain significant metabolites responsible for inducing the highest larval mortality (Pachiappan et al., 2022). The mass spectral analysis of ethyl acetate crude extracts from *S. wightii* unveiled 15 compounds, featuring Phytol acetate at 11.93% and Hexadecanoic acid at 21.07%, potentially linked to mosquito larvae mortality. Likewise, *S. ilicifolium* extracts comprised 11 compounds, including 3-Tetradecene (12.66%) and 5-Octadecene (7.19%), suggesting potential contributions to larvicidal effects. *G. acerosa*, with 20 identified compounds, showcased Cholest-5-en-3-ol (23.70%) and hexadecanoic acid (46.76%) as potential agents implicated in the recorded mortality of mosquito larvae (Pachiappan et al., 2022).

Superior efficacy against malaria has been demonstrated by various marine algae when compared to standard drugs. The anti-plasmodial potential of terpenoids extracted from *B. bifurcata and L. vadosa* was found to be

equivalent to that of well-known drugs artemisinin and chloroquine. Additionally, the effectiveness of metabolites from *S. heterophyllum* surpassed that of chloroquine against *P. falciparum*. Notably, the most potent compounds, sargaquinoic acid, sargahydroquinoic acid, and sargaquinol, were found to exceed the activity of chloroquine against the parasite (Afolayan et al., 2008). *In vivo* analysis revealed that a dose of 100 mg kg-1 day-1 of *U. pinnatifida* containing fucoidan resulted in a 37% reduction in parasitic burden in *P. berghei*-infected BALB/c mice (Chen et al., 2009). The most active compounds against chloroquine-resistant parasites, *P. falciparum*, were found to be Bromophycolide A and its derivatives, which were isolated from *C. serratus.* Additionally, these compounds were characterized by their potential as they were not substrates for efflux pumps, displayed low toxicity to mammalian cells, and acted as inhibitors of heme crystallization (Stout et al, 2011).

4.4 Preventive and Protective agents for cardiovascular diseases (CVDs):

Cardiovascular diseases encompass a spectrum of disorders affecting the heart and blood vessels, constituting a multifaceted array such as Ischemic heart disease, Stroke, and Peripheral vascular disease. Within this realm, Valvular heart disease, congenital heart defects, and Elevated cholesterol levels further contribute to the intricate tapestry of cardiovascular anomalies. Deep vein thrombosis and pulmonary embolism, both intricately woven into this complex fabric, underline the diverse challenges within this group. Comprising a spectrum of risk factors, CVDs are influenced by a myriad of elements, including intrinsic factors such as family ethnicity, history, and age, alongside modifiable aspects like physical inactivity, unhealthy diet, harmful alcohol consumption, and tobacco use. Hypertensive disorder, lipid metabolism disorder, elevated blood pressure, overweight, and obesity are conditions wherein these behaviors and risk factors are typically reflected (Cardoso et al., 2015). Comprising a staggering 31% of global mortality, cardiovascular diseases (CVDs) cast a formidable shadow on public health. Projections ominously predict that approximately 23.6 million lives will succumb to the grasp of CVDs by the year 2030 (Aronow, 2008). Numerous studies show that lipid-lowering drugs effectively reduce cardiovascular events; however, the prevalent side effects (hepatic and rhabdomyolysis) have spurred a shift towards exploring traditional and alternative treatments. Soluble dietary fibers, lipids, phlorotannins, minerals, peptides, and an array

of valuable compounds derived from macroalgae intricately participate in fostering cardiovascular well-being. Additionally, seaweeds are acknowledged as a natural repository of liposoluble vitamins, embracing tocopherols, β-carotene, and polyunsaturated essential fatty acids, such as those from the omega-3 family, potentially acting to alleviate the susceptibility to cardiovascular diseases.

Positive impacts have been noted in adult mice subjected to a cholesterol-rich diet, about plasma lipid levels, cardiac oxidative stress, and the expression of genes related to inflammatory cytokines, as a result of the administration of the ethanolic extract from *U. lactuca*. Oxidative stress induced by hypercholesterolemia was alleviated, the expression of pro-inflammatory cytokines was reduced, the inflammation process was inhibited, and myocardial injury was prevented by the free radical scavenging activity of *U. lactuca*. Phytochemical investigation substantiated that five principal flavonoids from *U. lactuca* (quercetin-3-0-glucoside, isorhamnetin, vanillic acid, isorhamnetin derivative, and luteolin derivative) actively contributed hydrogen to neutralize free radicals, thereby suppressing lipid peroxidation and averting the onset of hypercholesterolemia (Kammoun et al., 2018). A significant reduction in the serum lipid profile, including lowered plasmatic levels of TC, TG, and LDL-C, was induced by ulvans derived from *U. fasciata* in hypercholesterolemic rats. (Borai, et al., 2015). The supplementation of diets with 21% of *H. elongata* or 23% of *G. pistillata* or 5% of dried *D. tenuissima* in hypercholesterolemic Wistar rats demonstrated notable effects. Specifically, in *Himanthalia*-treated rats, plasmatic TG levels decreased by 28%, while HDL-C increased by 20%. *Gigartina* diet-supplied rats exhibited a significant decrease of 31% in TG, 18% in TC, and 16% in LDL-C. Moreover, *D. tenuissima* supplementation resulted in a substantial reduction in plasmatic TG levels by 38% and TC by 17% (Villanueva et al., 2014) (Kumar et al., 2015)

Table 5: **The effects of some seaweed extracts on CVDs**

Seaweeds species	**Induced Model**	**Effects/Activity**	**Ref**
G. changii	high-cholesterol/ high-fat sprague-Dawley rats	lipid-lowering therapy , influence plasma TC, TG, HDL-C, and LDL-C levels	Chan et al., 2015
E. cava	normal and STZ-diabetic mice	Reduced concentrations of TG, TC, and LDL-C	Kim, M. and Kim, H. S. 2012
S. benderi, M. alfaqhusainii	Hyperlipidemic rats	reductions of LDL-C, TC, and TG	Ruqqia et al., 2015
K. alvarezii, S. polycystum	high-cholesterol diet fed rats	Hypolipidemic impacts, *S. polycystum* and *K. alvarezii* decreased plasma cholesterol by 37.52% and 16.66% and TG level decreased by 40.11%, HDL-C level increased by 56.71%	Dousip, 2014
S. horneri, Cystoseira sp, U. pinnatifida	K K- Ay mouse	Lipid fraction increased DHA, AA, TC and HDL-C levels, while decreased hepatic cholesterol and TG levels	Airanthi et al., 2011
U. ohnoi, D. tenuissima	high carbohydrate, High-fat diet fed rats	Decrease total body fat by 24%, TG by 38%, TC by 17%, and blood pressure by 29 mm Hg. Increase Glucose utilization.	Kumar et al., 2015
S. subrepandum	atherosclerosis-related model	Phlorotannin and fucoxanthin lower oxidative stress markers serum malonaldialdehyde, decrease pro-inflammatory factors like leptin and TNF-α, and boost anti-atherogenic adiponectin	Lihn et al., 2005
Algal oil with DHA/Docosahexaenoic Acid	11 controlled trials with 485 healthy participants without coronary heart disease	reduction of TG, increased HDL-C and LDL-C	Bernstein et al., 2012
U. intestinalis	Single factor analysis and RSM Method	trypsin hydrolysates along with 4 other hydrolysates exhibited ACE inhibitory activity.	Sun et al., 2019
P. yezoensis	human liver cultured cells	Porphyrin reduced apolipoprotein- B 100 decreased synthesis of lipids	Inoue et al., 2009
U. linza, L. trabeculata	High-sucrose, high-fat diet-fed rats.	decreased the levels of intra-abdominal fat, TC, TG, SOD	Ramirez-Higuera, (2014).

The established strategy for hypertension treatment involves the inhibition of ACE-I. Remarkable ACE-I inhibitory activity has been demonstrated in various seaweeds, including *U. pinnatifida, E. cava, P. tenera, C. crassicaulis, G. amansii, G. tenella, H. fusiforme, E. stolonifera, S. japonica,* and *S. horneri.* This effect is

attributed to the presence of phlorotannins such as eckol, phlorofucofuroeckel A, and dieckol, along with the pigment Fucoxanthin (Cardoso et al., 2015). Peptides derived from *P. yezoensis*, along with papain and trypsin from *P. palmata*, as well as pepsin from *U. pinnatifida* and *C. microphysa*, demonstrate proficient abilities in targeting ACE-I. Inhibitory activity on blood pressure induced by ACE-I in spontaneously hypertensive rats was demonstrated by the peptide fraction obtained from *U. pinnatifida* (Suetsuna et al., 2004). Ingesting edible *G. amansii* augmented lipolysis, leading to diminished adipose tissue, thereby mitigating TNF-α, IL-6, and PAI-1 levels and mitigating the susceptibility to cardiovascular diseases in rats with diabetes. (Aziz, et al., 2020). Reports indicate that alginic acid extracted from *S. wightii* exhibits hypocholesterolemic effects and manifests anti-hypertensive potential (Sarithakumari et al., 2013). The antioxidative potential of *U. pertusa (*Ulvan derivative) in the livers of hyperlipidemic rats was underscored, emphasizing its role in protecting hepatic tissue against the influence of a cholesterol-rich diet and showcasing its anti-hyperlipidemic capabilities (Shah, et al., 2020). Exgtracgt from *P. palmata* decreased blood pressure by 34 mm Hg and showed renin inhibitor activities by 58.97%, investigtated with spontaneously hypertensive rats (Beaulieu, 2019). Potential effects on hypercholesterolemic rats were exhibited by fucoidan from *S. wightii* and *F. vesiculosus,* with elevated serum levels of TNF-α and C-reactive protein, NO concentrations in plasma and cardiac tissues, as well as the levels of iNOS, COX-2 and cardiac mRNA being reduced by a dose of 5 mg/kg bwt/day for 7 days (Preetha and Devaraj, 2010). Sulfated polysaccharides from unicellular algae, as illustrated by *P. cruentum and R. reticulata*, demonstrate significant promise as agents with hypolipidemic and hypoglycemic properties, providing a potential avenue to alleviate coronary heart diseases due to their cholesterol-lowering effects. Ulvan not only enhances bile acid excretion and facilitates the removal of excess cholesterol from the bloodstream but also contributes to a reduction in serum cholesterol, functioning as dietary fibers with the capacity to lower cholesterol (Raposo et al., 2015). The development of beverages with seaweed or their extracts can prevent distinct diseases, including cardiovascular disorders. A beverage comprising water-insoluble algal dietary fiber (ranging from 0.01% to 20%), along with fruit juice, citric acid, sugar, water, and, plant thickeners, has been patented by **Fu and colleagues,** with the intention of averting cardiovascular diseases. A fortified drink with antihypertensive effects, containing

H. fusiforme, has been patented by **Kim. Korea Bio. Polymer Co. Ltd** obtained a patent for a functional beverage aimed at improving cardiovascular health, incorporating Polymann, a refined variant of polymannuronic acid derived from *Undaria* kelp. **Nagai and colleagues** reported that beverages formulated with *E. cava* could derive benefits from their proficiency in targeting ACE-I, coupled with their abundance in minerals and phenolics (Cardoso et al., 2015). Incorporated within select marine crops used as food, including Nori (*P. yezoensis* in Japan), are essential components such as PUFA, soluble fiber, and sterols. Pivotal roles in human health are served by these constituents, actively contributing to the reduction of cholesterol levels and the promotion of cardiovascular well-being (Aziz et al., 2020).

4.5 Antidiabetic potentiality:

Diabetes mellitus, characterized by a chronic metabolic imbalance, manifests through either inadequate insulin production in Type 1 or diminished insulin sensitivity in Type 2, culminating in elevated blood glucose levels. Insufficient insulin secretion or the emergence of insulin resistance in peripheral tissue results in heightened blood glucose levels, rendering diabetes mellitus among the most prevalent chronic conditions globally. Type 2 diabetes, comprising 90% of all diabetes cases, presents more significant health challenges compared to Type 1. Damage to pancreatic β-cells halts insulin production, and the sole remedy is insulin replacement therapy (Bermano et al., 2020). Addressing diabetes mellitus involves a range of approaches, including adjusting the activities of α-glucosidase or α-amylase, modulating the AMPK signaling pathway, managing obesity, curtailing ROS, focusing on DPP-4, GIP, and GLP-1. Moreover, impeding carbohydrate hydrolyzing enzymes and PTP1B enzymes, amplifying glucose uptake effects, and imparting additional protective measures collectively contribute beneficially to regulating sugar levels and alleviating complications linked to diabetes (Chin et al., 2019).

The polysaccharide present in *G. amansii* demonstrates a blood sugar-lowering effect in rats with diabetes. Continuous use of *G. amansii* significantly improves the deterioration of glucose tolerance in a rat model exposed to a high-fructose diet. Adding *G. amansii* hot water extract to the diet lowers both plasma and liver cholesterol levels, concurrently boosting the excretion of fecal cholesterol bile acids and triacylglycerol (Aziz, et al., 2020),

(Yang et al., 2017). In an animal study, diabetes mellitus was effectively prevented by the inhibition of α-glucosidases, intestinal sucrase, and maltase through the use of 2,4,6-tribromophenol and 2,4-dibromophenol purified from *G. elliptica* (Kim et al., 2008). Therapeutically, PTP1B is considered one of the prime targets for treating obese patients and those with non-insulin-dependent diabetes. Caulerpin, Caulerpic acid, Bisindole alkaloids, and racemesin C, in *C. racemosa*, along with caulersin from *C. serrulata*, exhibit potent PTP1B inhibitory activities, while diterpenes 4,5-dehydrodiodictyonema A, α-toxylenoxy and α-tocopheroid, from *C. racemosa*, along with (23E)-3b-hydroxystigmasta-5,23dien-28-one, act as effective preventive agents against PTP1B, with the latter having a notable IC50 value of 3.80 μM (Shah et al., 2020) (Yang et al., 2015). Water extracts from *Padina, Halimeda, Sargassum, and Kappaphycus,* demonstrated efficacy in ameliorating insulin resistance, lowering hyperglycemia, and safeguarding the liver and pancreatic tissue against damage induced by a high-fat diet in mice. The analysis revealed that punctuate, identified as the most potent bioactive compound, not only inhibited both α-glucosidase and DPP-4 but also significantly reduced the body weights of the obese mice. *Sargassum* normalized glycogen levels, *Padina* partially increased muscle glycogen, and punicate, α-linolenate, arachidonate, and Phytol exhibited substantial inhibition of α-glucosidase and DPP-4 (Chin et al., 2019). The flavonoid fraction 5-hydroxy-6,7-dimethoxy-2[4-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-y1]oxyphenyl]chromen-4-one exhibited lipid-reducing activity in zebrafish, and the polyphenol 2,4-dihydroxyheptadec-16-ynyl acetate not only showed lipid-reducing effects but also inhibited acetyl-CoA carboxylase, offering a promising approach for obesity treatment (Bel Mabrouk et al., 2020). At low concentrations of 12.5 mg/mL, *A. nodosum* demonstrated potent inhibition of α-glucosidase activity. Extracts from *F. vesiculosus* exhibited close to complete inhibition (approximately 100%) of α-glucosidase, while the extraction from *P. palmata* demonstrated a substantial 81% inhibition of DPP-4. Porphyrin derived from *Porphyra* extract demonstrated efficacy in diminishing postprandial blood glucose levels and ameliorating glucose intolerance, whereas phenolic compounds found in *L. digitata* were identified as contributors to the reduction of the baseline GLP-1 level (Calderwood et al., 2021).

Extracts from *U. pinnatifida, Sargassum sp, L. japonica, L. digitata, and F. distichus* showed α-glucosidase and α-amylase inhibitory activities like acarbose, attributed to chemical groups like polysaccharides, plastoquinones, phlorotannins, and phenolic compounds. Fucoidan from *T. ornate, T. conoides, and S. wightii,* also inhibited both enzymes (Bermano et al., 2019). Plasma glucose levels were significantly reduced by more than 50%, and both intestinal and plasma α-amylase were inhibited in diabetic rats by *C. fragile,* effectively preventing cellular damage induced by alloxan (Bermano et al., 2019). The ethanol or water extracts of *S. polycystum,* in conjunction with polyphenolic fractions, demonstrated significant decreases in glycated hemoglobin, blood glucose, blood triglycerides, the plasma atherogenic index, and total cholesterol in diabetic rats (Motshakeri et al., 2013). Flavonoid-rich extracts derived from *E. prolifera* enhanced glucose tolerance by modulating the expression of insulin signal transduction genes. The increased expression of IRSI, PI3K, and AKT was observed, concomitant with a reduction in JNK gene expression (Yan et al., 2019). Administering a 12-week treatment of 400 mg/d E. cava polyphenol extract to Korean adults with elevated cholesterol significantly lowered total cholesterol, LDL-C, and CRP levels. Inhibition of adipogenesis is potentially attributed to the downregulation of AMP-activated protein kinase signaling by the phloratannin dieckol in 3T3-L1 preadipocytes (Cherry et al., 2019). Another mechanism to reduce blood cholesterol in humans by sulphated polysaccharides is associated with their high capacity to inhibit pancreatic cholesterol esterase which is responsible for the absorption of cholesterol and fatty acids in the intestine. Sulphated polysaccharides, indeed, regulated the activities of superoxide dismutase and catalase, elevated levels of vitamins E and C, and decreased glutathione levels, as well as the levels of aspartate and alanine transaminases in the liver of rats (Raposo et al., 2015).

4.6 Anticancer activities:

According to WHO, an estimated 21 million new cancer cases and 13 million deaths are projected to occur by 2030, highlighting the significant global impact of this lethal disease (WHO Report on Cancer: Setting Priorities, Investing Wisely, and providing Care for All. 2020). Lung and breast cancer, with 2.21 million and 2.26 million cases respectively, are the leading causes of cancer-related deaths, while colon, stomach, bladder cancer, liver, prostate, non-melanoma, non-Hodgkin lymphoma, and leukemia are also prevalent types of cancers worldwide

(World Health Organization, WHO,2022). Surgical removal, radiation therapy, and cytotoxic drug-based chemotherapy represent the principal treatment approaches for diverse medical conditions, including cancer; however, they are fraught with the inherent difficulty of inducing adverse side effects. Bioactive compounds from nature, especially metabolites derived from marine sources, manifest cytotoxic effects by selectively impacting macromolecules within cancer cells. These compounds showcase robust antitumor efficacy, demonstrating significant growth inhibition in human tumor cells both in laboratory settings/in vitro, animal models/in vivo, and clinical trials for cancer treatment, like Taxol from the western Yew tree bark (*Taxus brevifolia),* have demonstrated effectiveness in preventing and treating cancer, particularly showing utility in breast cancer treatment (Khalifa et al., 2019). Algal metabolites safeguard normal cells from genetic harm and exhibit properties that deter cancer growth, causing cell death and preventing proliferation. In contrast, standard anticancer treatments like ionizing radiation, hyperthermia, alkylating agents, DNA topoisomerase inhibitors, and platinum compounds inflict non-specific DNA damage, impacting both healthy and rapidly dividing cancer cells (Abdollahi et al., 2018).

Anticancer activities of eight algal meroterpeneoids, including usneoidone Z, cystomexicone B, cystomexicone A, cystodione A, and cystodione B, 11-hydroxy-1-0-methylamentadione, 6-cis-amentadione-1–methylether, amentadione-1'-methylether, from *C. usneoides,* were investigated. The growth of human colon cancer cells HT-29 was inhibited by all the meroterpenoids, with cell cycle arrest in G2/M phase induced by most of them and apoptosis triggered by some. These meroterpenoids elicited a decline in the phosphorylation status of extracellular signal-regulated kinase, suppressed phosphorylation of protein kinase B, and attenuated the phosphorylation levels of C-JUN N-terminal kinase (Zbakh et al., 2020). Antiproliferative activity against cervical cancer cells (IC50: 309.048 µg/mL) was exhibited by methanol extracts from *E. intestinalis,* while Erhlich's carcinoma cell line was suppressed by *E. prolifera* with 51.7% inhibition (Paul and Kundu, 2013) (Noda et al., 1990). The scrutinized isolated compound caulerpin from *Caulerpa* was found to impede HIF-1 and hinder the induction of HIF-1α protein, a crucial oxygen-regulated subunit, in specific cancer cell lines (LOVO, MDA-MB-231, SW480, T47-D, HMEC, DU145, MCF-7, PC3) under hypoxic conditions. α-tocopherol quinone from *Caulerpa sp*

exhibited cytotoxicity against human carcinoma and promyelocytic leukemia cells, while glycoprotein from *C. decorticatum*, and algal extract from *C. compressa* demonstrated superior anticancer activity against human breast carcinoma cells; additionally, Caulerpenyne from *C. taxifolia* is employed in colorectal cancer (Shah et al., 2020). The consumption of seaweeds has yielded divergent effects; specifically, the intake of *Porphyra spp* is inversely associated with breast cancer risk in premenopausal women, whereas *U. pinnatifida* consumption has been implicated in inducing thyroid cancer among postmenopausal women (Cherry et al., 2019). Antitumor functions, antiproliferative activities, and the capacity to prevent colony development, showcasing antimetastatic effects, have been documented for fucoidans extracted from *F. evanescens, E. cava, U. pinnatifida, S. japonica, S. hornery, and C. costata.* Induction of apoptosis in the human breast cancer cell line by low molecular weight fucoidan was facilitated through the modification of mitochondrial membrane integrity. This process included the release of cytochrome c and the suppression of antiapoptotic proteins such as Bcl-2, Bcl-xl, and Mcl-1. Furthermore, it triggered the activation of apoptosis-inducing factors, encompassing caspase-3, caspase-7, and caspase-9 (Zhang et al., 2013). Derived from *E. bicyclis,* laminarin displayed anti-proliferative effects in ovarian carcinoma and papillary serous adenocarcinoma cell lines through the PI3K/MAPK intracellular signaling pathway. It triggered apoptosis by enhancing the release of cytochrome C, leading to heightened DNA fragmentation and increased expression of apoptosis-related proteins. Moreover, laminarin induced cell cycle arrest at the Sub G1 phase. Laminarin induced MMP loss and triggered autophagy, involving the deactivation of ULK1 and phosphorylation of P62, in both the carcinoma cells (Bae et al., 2020). Anticancer effects were demonstrated on human leukemia cell lines by siphonoxanthin, a keto-carotenoid isolated from Caulerpa sp and C. fragile. It activated caspase-3, induced apoptosis, reduced Bcl-2 expression, promoted chromatin condensation, and led to the upregulation of the expression of GADD45α and DR5 (Ganesan et al., 2011). Inhibitory effects on the activation of NF-κB in the HeLa carcinoma cell line were identified for various phaeophytins, including porphyrinolactone, 20-chlorinated (13²-S)-hydroxy-phaeophytin A, (13²-S)-hydroxy phaeophytin A and B, and (13²-R) hydroxyphaeophytin A and B, isolated from *C. fascicularis.* These compounds demonstrated the inhibition of TNF-α-induced NF-κB translocation from the cytoplasm into the nucleus (Huang et al., 2007).

Antitumor effects, including apoptosis induction in various tumor cell lines such as lung and skin, are exhibited by sulphated polysaccharides from *E. bicyclis.* Stimulation of immune-activated macrophages by sulphated polysaccharides from *E. bicyclis* leads to the production of pro-inflammatory IL-2 and IL-12 and IFN-γ, collectively enhancing natural killer cell activity and inducing apoptosis. Upregulation of IFN-γ secretion is also facilitated by natural killer cells. Antitumor activity is demonstrated by algal sulphated polysaccharides through their anti-adhesive properties, hindering the attachment of tumor cells to the basal membrane and thwarting the initiation of metastatic activity initiated by the implantation of a tumor cell into the extracellular matrix (Reposo et al., 2015). There are some other anticancer agents from marine algae are shown in the below table

Table 6: **Anticancer effect of different metabolites from different seaweeds**

Metabolites from marine algae	**Used cell lines**	**Effect/Mechanisms**	**IC50-Values**	**Ref:**
Sargachromanol J and R (Terpenoids)- *S. siliquastrum*	Human colon cancer cell HT-29	Suppressed cancer cell proliferation.	29.3 µg/mL and 3.4µg/mL	Lee et al., 2014
Zonaquinone acetate (Terpenoids)- *S. zonale*	Human colon cancer cell HT-29	Suppressed cancer cell proliferation.	17.3 µM or 7.08 µg/ml	Penicooke et al., 2013
Nonyl 8-acetoxy-6 methyloctanoate (Fatty alcohol ester)- *P. tricornutum*	Human Promyelocytic leukemia cell (HL-60), Human lung carcinoma cell line (A549)	Caused Sub G1-phase cell cycle arrest, suppressed antiapoptotic Bcl-XL, and activated Bax. Elevated the expression levels of caspase-3 and p53 proteins.	50µg/ml	Samarakoon, 2014
Laminarin (Polysaccharide)- *E. bicyclis*	Papillary serouse adenocarinoma cell line (OV90)	Suppression of proliferation, Caused Sub G1-phase cell cycle arrest, Enhanced apoptosis..	2 µg/ml	Menshova et al., 2014
Cryptophycinl (Macrolide peptide)- *Nostoc sp*	Breast cancer MDA-MB-435 mammary adenocercinoma	Suppression of proliferation, Caused Sub G2/M Phase cell cycle arrest	50pM	Mooberry et al., 1997

Biselyngbyasid B (Macrolide glycoside)- *Lyngbya sp,*	Hela S3 cells, HL 60 cells	Inhibition of the proliferative activity of cancer cells induced Cytotoxicity	3.5 µM and 0.82 µM	Morita et al., 2012.
Tasipeptins A and B (Cyclic depsipeptide)- *Symploca sp*	kB oral epidermoid cancer	Showcased anticancer efficacy with cytotoxicity.	0.93 µM, 0.82 µM	Williams et al., 2003
Carraginaans and Polyphenol contents- *P. palamata*	Epithelial adenocarcinoma Hela cell lines	Inhibited cancer cell proliferation, antitumor potential	0.5-5mg/mL	Yuan et al., 2005
Alcoholic extract- *A. spicifera*	Ehrlich's ascites carcinoma cell	Antitumor activity via oral dose	100 and 200 mg/kg	Lavakumar et al., 2016
Fucoidan (Polysaccharides) - *A.nodosum*	colon cancer cell lines (Colo 320 DM)	Suppress arterial smooth muscle cell proliferation.	80 to 100 µg/mL	Vischer and Buddecke,1991
Heparin (Polysaccharides)- *D. delicatula*	colon cancer cell lines (Colo 320 DM)	Suppress arterial smooth muscle cell proliferation.	80 to 100 µg/mL	Vischer and Buddecke,1991
Calothrixin A and B (Phenanthridine alkaloids)- *Calothrix sp*	human HeLa cancer cell lines, CEM leukemia cells	Suppressed proliferation and boosted cytotoxicity, cell cycle arrest at G1 and G2/M Phase	40 and 350 nM. 0.20 to 5.13 µM	Rickards et al., 1999
Curacin A (Ketopeptide) – *L. majuscule*	Lung cancer (A549) cell lines	Suppressed proliferation, Elevated apoptotic processes. Induced G2/M phase arrest. Binds to tubulin at colchicines binding site	0.72 ± 0.02 µM	Mondal et al., 2020
Scytophycin B (Macrolides) - *S. pseudohofmanni*	human nasopharyngeal carinoma cell line	Demonstrated anticancer potency with cytotoxicity.	1 µg/mL	Borowitzka, 1994

Red algal flavon-3-ols with catechin demonstrate efficacy against HT29 cells and monoblastoid leukemia (Yoshie et al, 2000). Extract from *B. triquetrum,* comprising lectin interacting with glycans and glyco-conjugates, displays robust anti-cancer defense like metastasis, exhibiting peak activity against Hep-2 cell

lines (Moo-Puc et al., 2009). Noteworthy biological effects against MCF-7 human breast cancer cell lines were demonstrated by *L. papillosa* and *H. musciformis.* The observed cytotoxicity was attributed to sulfated polysaccharides carrageenan K (LP-W1), t (LP-W2), and λ (LP-W3), resulting in the inhibition of MCF-7 cell viability. The exposure to LP-W2 and LP-W3 underscored their potential for breast cancer treatment (Aziz et al., 2019). Numerous in vitro studies have highlighted the potential of NPs as potent anticancer agents, demonstrating apoptotic-induced robust anticancer effects on various cancer cells, including those associated with human breast, cervical or lung cancer. Algae have been extensively employed for the synthesis of NPs, particularly AgNPs, utilizing species such as *T. conoides, S. tenerrimum, U. fasciata, J. rubins, C. sinusa, G. acerosa, G. corticata, P. tetrastromatica, P. pavonica, P. gymnospora, C. vulgaris,* and others. The investigation into the anticancer activity of AgNPs, synthesized using extracts from *E. cava,* against human cervical cancer cells (Hela cells) revealed a significant induction of apoptosis, underscoring the subsequent anticancer effects (Venkatesan et al., 2016). Similarly biosynthesized AgNPs from *C. serrulata* exhibit potent anticancer efficacy, demonstrating significant activity against HeLa cells with an IC50 value of 34.5 µg/mL (Jeyaraj et al., 2013) (Chanthini et al., 2015)

Chapter 5 Conclusion:

Bangladesh is abundant with so many commercially, and economically important seaweeds as well as medicinally. This review paper showed many examples of different natural metabolites extracted from different marine algae that are very effective as antiviral, antibacterial, antiplasmodial, anticancer, antidiabetic, and many more. Much more detailed research should be done on these, only then it will be easy to get cures for many diseases in the near future. Simply seaweed cultivation and mass production must be determined first, therefore, easy methods of cultivation should be found. After that, bulk extraction of metabolites should also be considered. Only then it is possible to find out the cure against the deadly diseases. The chances of getting rid of these diseases will increase in the People of other countries of the world including Bangladesh.

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