

Prolific Anticancer Bioactivity of Algal Species

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Abstract: Algae play major role in global primary productivity and act as excellent sources of lipids, polysaccharides, vitamins and secondary metabolites. Both marine and fresh water micro or macro algae have antibacterial, anticancer, antioxidant, antifungal and antiviral properties due to the presence of secondary metabolites including terpenoids, flavonoids, sterols, sulfated polysaccharides, polyphenols, sargaquinoic acids, sargachromenol etc. The specific phytochemical compounds of multicellular and unicellular algae which are effective against tumour growth and metastasis in turn help to synthesize antiproliferative pharmaceutical drugs in future. Some of the algae that show anticancer activities are *Laurencia*, *Padina*, *Ulva*, *Caulerpa*, *Chaetomorpha*, *Gracilaria*, *Gelidium* etc..

Keywords: Microalgae, cancer therapy, antiproliferative, seaweeds, metastasis

Algae, the photosynthetic organisms, are growing in an aquatic environment and able to grow alone or concurrently with other organisms. The organism can be classified into red algae (Rhodophyta), green algae (Chlorophyta) and brown algae (Phaeophyta). According to the size, it can be classified into macroalgae or microalgae. Macroalgae, seaweeds, are large sized multicellular group that visible by the naked eye; while the microscopic single celled microalgae may be prokaryotic or eukaryotic.

Fresh water and marine microalgae are a great source of several useful byproducts like medicines, cosmetics and pharmaceuticals. Major constituents in this lower group are lipids, proteins, polysaccharides, vitamins and antioxidants. It enhances the defense mechanism by increasing natural killer cell

activity, activation of the immune system and inhibition of the cancer cell growth. The natural potent antimalignant activity of algae derived compounds is very useful in drug industry now. One of the carotenoid, fucoxanthin, present in microalgae like diatom and brown seaweeds, shows potent anticancer properties via growth prevention of malignant cells and stimulation of cancer suppressor genes.

Macroalgae grown in fresh and marine water also contribute to the proapoptotic, antiangiogenic and antiinvasive activities due to their derived compounds. Among them, with less than 3% of world's marine macroalgal species are assessed for anticancer activities. Normally, the macroalgae contain different types of flavonoids which are assumed to have unique chemical structures and bioactivities. These flavonoids are not only good

antioxidants but also have the abilities to kill cancer cells by inducing apoptosis and autophagy.

Chemotherapy is usually the first line treatment to cure cancers such drugs are able to destroy or at least inhibit the growth of cancerous cells. These drugs are allied through noxiousness that ranges from a mild reaction to severe life threatening illness. Many side effects of chemotherapeutic drugs comprised baldness and loss of appetite. To avoid or reduce the side effects, new anticancer agents should be investigated from various natural resources. Plants have been an essential source of conventional and clinically valuable drugs for the treatment of numerous forms of tumours. Investigating plants for their effective anticancer agents with moderately low side effects seem to give an attractive strategy of anticancer drug development. A lot of natural antitumour amalgams or their byproducts are generally produced by algae are very helpful in treating different human cancers.

1. Medicinally significant compounds in algae

The aquatic life is producing various and distinctive chemical components essential for the human survival. Due to the harsh conditions such as high salinity and deficiency of nutrients, light and space, which make the marine environment competitive, organisms adapt to the environment by producing various chemicals and metabolites to help them survive under such conditions. The secondary metabolites produced by algae are the source of fatty acids, fibers, antioxidants, carotenoids, sterols, proteins, phytocolloids, lectins, oils, amino acids, unsaturated fatty acids and

vitamins which could be commercially utilized.

Laurencia claviformis and *L. tasmanica* are the source of pacifenol, terpenoid isolated from seaweeds. *Styopodium* is a rich source of polycyclic meroditerpenoids such as stypodiol, epistypodiol, stypotriol, taondiol, epitaondiol, 2 β ,3 α -epitaondiol, flabellinol, flabellinone, stypotriolaldehyde, stypohydroperoxide, isoeptaondiol and 14-ketostypodiol. Epitaondiol is a terpenoid present in brown algae, *Styopodium flabelliforme* which is the source of derivative of 14-keto-stypodiol diacetate (SDA). *Dunaliella salina* is one of the richest sources of natural β -carotene. The green algae, *Chlorella vulgaris* has produced canthaxanthin and astaxanthin in fairly high yields. *Ecklonia cava*, edible brown algae, has effective antioxidant activity due to the high phenolic content production (Alassali et al., 2016). Many biologically active compounds like terpenoids, flavonoids, sterols, sulfated polysaccharides, polyphenols, sargaquinoic acids, sargachromenol and pheophytine include in different *Sargassum* species. *Spirulina* presents with nutritional benefits including 50 to 70% protein, 5 to 10% lipids, 10 to 20% carbohydrates, 10% vitamins especially vitamin B12 and pro vitamin A (β -carotene) and minerals such as iron and one of the few sources of dietary γ -linolenic acid (GLA). The bioactive compounds in the crude extract of *Caulerpa* are 2-(-3-bromo-1-adamantyl) acetic acid methyl ester and chola-5, 22-dien-3-ol. The marine green alga, *Ulva lactuca*, contains 3-O- β -D glucopyranosyl-stigmasta-5,25-dien. *Padina* is the source of oleic, palmitoleic, 9-cis-hexadecenoic, linoleic, α linolenic, arachidonic and elaidic acid. *Gracilaria bursa-pastoris* contains a high total phenolic content, vitamin E and vitamin C. It

also included *mycosporines* and *mycosporine* like amino acids. Majority of the algae are the rich source of primary and secondary metabolites in turn will become the major source of nutrient supplements in future. The secondary metabolites will ameliorate the opportunities in drug industry and pharmacology.

2. Anticancer algae

2.1. *Caulerpa* J.V. Lamouroux

Caulerpa is a genus of seaweeds in the family Caulerpaceae among the green algae. They are the macroalgae found in a variety of shallow water marine habitats. These are unique in that they are made up of just one cell, but it has several nuclei, making it one of the largest single cells in the world. The *Caulerpa* genus has a variety of growth patterns. They have a stolon with downward growing rhizoids that anchor the plant to the substrate. Assimilators or erect fronds or leaves are supported by the stolons. The assimilator's structure can be ligulate as in the case of *C. prolifera*, or it can have a central axis known as a rachis. The rachis may possess lateral branchlets called ramuli, which can be arranged in a variety of ways and take diverse shapes including terete, turbinate, clavate, peltate, falcate and vesiculate. The distichous ramuli are uniformly spaced out in opposition to one another (*C. taxifolia*), irregular vesiculate ramuli with no distinct arrangement (*C. racemosa*) or verticillate whorled ramuli (*C. cupressoides*). *Caulerpa* species can be eaten in some cases. *C. lentillifera* and *C. racemosa*, both known as 'Sea grapes' are most frequently consumed in Southeast Asia, Oceania and East Asia. They are traditionally gathered from the wild and marketed there. The species have a distinctive

'sea' flavour and a crunchy texture and are used in salads. *Caulerpa* has other uses besides as a food source including bioremediation, fertilizer and health and wellness. Well researched *Caulerpa* antioxidant chemicals are utilized to treat a variety of illnesses and health concerns including cancer and cardiovascular conditions. It has been demonstrated that *Caulerpa* is efficient at filtering the water used to cultivate fish, mollusks and shrimp (*C. lentillifera*). Invasive plants of a different species, *C. taxifolia*, have been found in the Mediterranean Sea, Australia and Southern California where it has since been eradicated.

Anticancer activities: *C. taxifolia* is excellent marine green algae which produces enormous bioactive compounds with more biological activities. The species mediated Ag NPs has superior anticancer activity against A549 lung cancer cells. Moreover, the nanoparticles show increased bioactivities including antibacterial, antiviral, antimalarial, antioxidant, larvicidal and wound healing properties (Zhang et al., 2020). More interestingly, *C. lentillifera* is novel bioresource agents for anticancer drugs especially for hepatoma, leukemia and breast and colorectal cancers (Nurkolis et al., 2023). *C. microphysa* pepsin digested extracts inhibit myelomonocytic leukaemia (WEHI-3) and human promyelocytic leukaemia (HL-60) cell lines (Lin et al., 2012).

2.2. *Laurencia* J.V. Lamouroux

Laurencia is a genus of Rhodophyta that can be found at temperate and tropical shorelines, in habitats from the littoral to the sublittoral and at depths up to 65 meters. Thalli of the macroalgae can branch and spread in both

bilateral and omnidirectional patterns. On stoloniferous holdfasts, its appendages might have rhizoidal or discoidal appearances. According to morphology, branches have a flat or cylindrical shape. Branchlets can have a shape that is blunt, truncate or claviform, and they might be slightly stiff. As a genus, *Laurencia* has demonstrated significant diversity, with species having distinctive characteristics that may be quickly identified within the *Laurencia* complex. Using rbcL, the molecular research has identified the genus *Laurenciella*, which has similar morphology to *Laurencia* but differs in several ways. During 2015, 1047 secondary metabolites from *Laurencia* and *Aplysia* species have been collected. *Laurencia's* complex chemical make up is primarily related to both environmental and hereditary causes. Humans have used the genus for many years as food, medicines and fertilizers.

Anticancer activities: *Laurencia* terpenoid extract has negative effects on tumour growth and immune modulation; while positively influence on apoptosis of sarcoma 180 cell lines. The ethanolic extracts of *L. catarinensis* and *L. majuscula* show antimicrobial, anti-oxidant and anticancer activities. The ethanol or chloroform extract of *L. papillosa* exhibits the highest levels of cytotoxicity against Jurkat cancer cell line (acute lymphoblastic leukemia) compared with the ethanol or water extract (Tannoury et al., 2017). The methanol extract of *L. obusta* shows antiproliferative effects and inhibiting the human cancer cell lines, A549, HCT15 and MCF-7 (Dellai et al., 2013). *L. caspica* extract includes dodecane, undecane and dodecane, 2, 6, 11- trimethyl as predominant compounds, in turn inhibit proliferation of

breast cancer T47D and HEK293 cells (Moshfegh et al., 2019). *L. okamurai* extract containing laurinterol induces apoptosis in melanoma cells (B16F1) (Kim et al., 2008).

2.3. *Sargassum* C. Agardh

Sargassum is a genus of brown algae in the class Phaeophyceae, a macroalgae in the order Fucales. The genus is well known for its planktonic species, which are widely distributed throughout the temperate and tropical oceans of the world. The species typically live in shallow water and on coral reefs. *Sargassum* appears to be an exception to the rule that most species in Phaeophyceae are primarily cold water organisms that benefit from nutrients upwelling. Due to the abundance of *Sargassum*, the Sargasso Sea in the Atlantic Ocean was given its name. The algae reach the lengths of several metres. They have a holdfast, stipe and frond and are often brown or dark green in colour. Oogonia and antheridia are found in conceptacles that are integrated into receptacles. Certain species fronds include berry like gas filled bladders that aid in flotation. Many are resistant to strong water currents because of their rough, sticky texture and sturdy flexible bodies.

Anticancer activities: The extract from *S. oligocystum* shows the most effective antitumour activity against Daudi and K562 cell lines (Zandi et al., 2010). Similarly, the deacetylated fucoidans from *S. feldmannii* inhibit colony formation of human colon cancer cells, DLD-1, HT-29 and HCT-116 (Usoltseva et al., 2019). Fucoidan isolated from *S. hornery* plays an inhibitory role in colony formation in human melanoma and colon cancer cells in turn act as effective antitumour agents

(Ermakova et al., 2011). The cytotoxicity effect of fucoidan from *S. polycystum* shows a higher percentage of inhibition against the MCF-7 cell line (Palanisamy et al., 2017). *S. mcclurei* includes SmF1, SmF2 and SmF3 fucoidans which are sulfated heteropolysaccharides that contain fucose, galactose, mannose, xylose and glucose and act as anticancer agents. The isolated fucoidan SdF from *S. duplicatum* also exhibit anticarcinogenic activity in colon cancer cells (Usoltseva et al., 2017). However, fucoidan from *S. cinereum* expresses the anticancer activity against Caco-2 cell line. Moreover, the silver nanoparticles from *S. incisifolium* display cytotoxic activity against cancerous cell lines, HT-29 and MCF-7.

2.4. *Chaetomorpha* Kutzing

Chaetomorpha is a macroalgae belongs to the genus of green algae in Cladophoraceae family. Common name of this genus is 'Sea emerald'. The genus is composed of microscopic filaments of cylindrical cells. It is distinguished by its unbranched filaments which give it a characteristic appearance. Thallus is bright to dark green, filamentous, rigid and gregarious. Filaments are unbranched, rough, twisted, loosely knotted with 10-40 cm long. Cells are cylinder shaped in the lower half and with mild constrictions at joints. Basal cell has a lobed attachment. It grows epiphytically on big algae in the middle intertidal to subtidal zones on rocky, sandy-muddy bottoms with stones and shells, and producing floating and free lying interwoven masses in calm shallow pools.

Anticancer activities: The silver nanoparticles from *C. linum* show anticancer effectiveness against colorectal carcinoma cells (HCT-116) by

an increase in the expression of apoptotic caspase 3, caspase 9, BH3 and Bax, along with a decrease in the antiapoptotic protein like Bcl-2 and Bcl-xl (Acharya et al., 2021). *C. ligustica* exhibits antiproliferative effect against colon cancer cell lines, HT29 and HCT116. The bio-synthesized AgNPs from *C. ligustica* extract also shows anticancer potential. Many of the bioactive compounds identified from *C. brachygona* are well known for significant anticancer activities against cervical cancer cells (Bcl-2) by the enhanced expression of Beclin 1 and LC3BII (Majumder et al., 2020). Docking studies in *C. antennina* confirms the occurrence of carpesterol dehydrate and triazines as an anticancer component; hence it can serve as a promising antioxidant and anticancer agent (Dubey et al., 2022).

2.5. *Turbinaria* J.V. Lamouroux

Turbinaria is a macroalgae belongs to brown algae (Phaeophyceae) found in tropical marine waters. It is generally seen in rocky substrate. The genus has an upright thallus with blade bearing radially branching axes having rough texture. The blades might be stipitate, turbinate, crowned or obpyramidal, among other shapes. It's shape is similar to a long pinecone. A holdfast made up of widely spaced branches sprouting from the major axis holds the thallus erect. Receptacles, the mature thalli's reproductive organs, protrude from the tips of the stalks on the blades. *Turbinaria* is used for its alginate extracts which is used in food and drink, cosmetics, and pharmaceutical goods as thickening, gelling and stabilizing agents. In Indonesia, the young thalli of *T. ornata* are eaten fresh, salted or with curry sauce. Due to their ability to enhance growth and serve as nutritional supplements, brown

algae are frequently utilized in animal feed. Prawn feeds with supplements of *T. ornata* boost growth, survival and digestion. In many Asian nations, *Turbinaria* is also applying as a pesticide and fertilizer.

Anticancer activities: The fucoidan isolated from *T. conoides* shows the anticancer activity. The extracted fucoidan contains $53 \pm 0.69\%$ of fucose and $38 \pm 0.42\%$ of sulphate in turn causes antiproliferative effect on A549 cell line (Marudhupandi et al., 2015). The ZnO nanoparticles from the hydroethanolic extract of *T. conoides* are effective against a murine model of Dalton's lymphoma ascites. Treatment with ZnO-NPs and hydroethanolic extract decrease the tumour volume, in turn increasing the lifespan of DLA-bearing mice. The anticancer activity of polysaccharides and modified derivatives of fucoidan ToF2 in *T. ornata* against several cancer cell lines are prominent in pharmacology. Usually, the fucoidan ToF2 and its derivative obtained by enzymatic hydrolysis inhibit colony formation of human colorectal, breast adenocarcinoma and malignant melanoma cell lines (Ermakova et al., 2016). Hexadecanoic acid (HA) of *T. ornata* also shows inhibitory effect on HT-29 human colon cancer cells. The α -amylase inhibitory activity of native fucoidan from *T. ornata* is the basic of NIDDM therapy. The synthesized AuNPs using hydromethanolic extract of *T. decurrens* show anticancer effect and cytotoxicity against human cancer cell lines.

2.6. *Padina* Adanson

Padina is a macroalgae belongs to the brown algae in the family Dictyotaceae. The genus is seen in tropical regions, although they are seen in cooler temperate waters from South

America to South East Asia. They have a characteristic shape resembling a peacock tail structure and are attached to hard substrate or growing as epiphytes on larger seaweeds. With a brownish off-white colouring, the thalli have a flabellate look. The thallus is made up of cells that are fan shaped, 2-8 layers thick and have hairs covering the edges. It has a stipe attached to its rhizoidal holdfast, and the blades of the stipe prominently resemble several layers of cells thick. The thalli appear to have apparent zonations that produce coextensive rows of rigid segments of hair. The number of cell layers, the placement of sporangial sori in relation to hair bands and the presence or absence of hair bands on the lower thallus surface is used to distinguish between different species of *Padina*. The group is ecologically significant macroalgae which function as excellent bioindicators of aquatic pollution and remediation in marine ecosystems.

Anticancer activities: The sulfated and acetylated fucoidan fraction of *P. boryana* contains fucose, galactose, mannose, glucose and uronic acid. The native and modified fucoidan fractions show anticancer effect against the colorectal carcinoma cells, DLD-1 and HCT-116 (Usoltseva et al., 2018). Pd-NPs induce antiproliferation of breast cancer MCF-7 cells and enhance mRNA expression of apoptotic marker genes in the order of p53 > bax > caspase 3 > caspase 9 at 125 $\mu\text{g/mL}$. Hence, the PB extract capped Pd-NPs can be used for successful clinical management of MDR pathogens and breast cancer cells. The polysaccharide, fucoidan, isolated from *P. tetrastromatica* acts as capping and reducing agent which exhibits antiproliferative activity on HepG2 and A549 cell lines. The methanolic

extract of *P. pavonica* shows anticancer activity against lung carcinoma. Extract includes phenols, terpenes, amino acids, alkaloids, flavones, alcohols and fatty acids, induces antibiofilm, antibacterial, antioxidant and anticancer activities (Makhlof et al., 2023). The methanol extract of *P. pavonica* possesses cytotoxic activity against human cervix (HeLa) and breast cancer (MDA-MB-453) cell lines; while the extracts did not exert any significant cytotoxicity toward normal human fetal lung fibroblast cells (MRC-5). Often, the extract reduces the number of cells with distorted shapes and condensed cytoplasm. Similarly, fucoidan from *P. distromatica* shows inhibitory effect against A-431, A-549, HL-60, HT-29 and MCF-7 cell lines (Stanojkovic et al., 2013).

2.7. *Gracilaria* Greville

Gracilaria is a macroalgae belong to Rhodophyta. It is notable for its economic importance as an agarophyte and food for humans and various species of Jellyfish. They are found in warm waters throughout the world and occur seasonally in temperate waters. It has been traditionally cultivated as a source of agar. A little discoid holdfast gives rise to an erect thallus. The thalli typically have lateral, alternating or subdichotomous branches which are cylindrical, depressed or blade shaped. Occasionally a single plant will have a variety of branches. Many species have varied branch apex and base styles. The thalli of some species like *G. eucheumoides*, grow horizontally along the substrate and develop secondary holdfasts from the margin of branches.

Anticancer activities: *Gracillaria* extracts with different solvents include bioactive components as anticancer agents and antiplatelet

aggregations. The n-hexane, ethyl acetate, chloroform and ethanol extracts of *G. verrucosa* act as anticorectal cancer agent that inhibits the proliferation of HCT-116 cells (Kurniasari et al., 2018). *G. corticata* normally shows cytotoxicity against HeLa, K-562 and MDA-MB cell lines. Butanolic extract of *G. corticata* shows greater anticancer activity than hexane and methanolic extracts. The species exhibit anticancer activity against different cancer cell lines including human promyelocytic leukemia (HL-60), a human lung carcinoma (A549) and a mouse melanoma (B16F10). The alcoholic extract shows antiproliferative activity against five important human cancer cell lines (MCF-7, MDA-MB-231, HeLa, HepG2 and HT-29) proliferation, apoptosis and cell cycle arrest. The methanol extract of *G. edulis* exhibits antiproliferative and apoptotic activities against human rhabdomyosarcoma (RD) and breast adenocarcinoma (MCF-7) cells by activating the caspase 3/7 pathway (Gunathilaka et al., 2020).

2.8. *Gelidium* J.V. Lamouroux

Gelidium is a genus of Rhodophyta in the family Gelidiaceae. It is a macroalgae found in tropical to temperate regions but lacking in polar region. In the ocean they are seen in intertidal to subtidal zone. Thalli branching are irregular and producing tertaspores. Irregular branching occurs in rows on either side of the main stem. Thalli are cartilaginous, blackish-red color when slightly dry and forming turf. Many of the algae in this genus are harvested for agar.

Anticancer activities: Matrix metalloproteinase-9 (MMP-9) from *G. crinale* is a proteolytic metalloenzyme that degrades the central part of the extracellular matrix (ECM)

and promotes tumour metastasis. Sulfated polysaccharide from *G. crinale* influences on tumour metastasis and MMP-9 expression of human fibrosarcoma (HT1080) cells in turn influence excellent activity in inhibition on migration and invasion (Zheng et al., 2022). The compounds of *G. latifolium* inhibit the growth of human cancer cells by causing cytotoxicity in HeLa and Caco2 in turn cause apoptosis and boost the immune system (Prasedya et al., 2018).

2.9. *Ulva* Linnaeus

Ulva is an edible macroalgae belongs to Chlorophyta and the family Ulvaceae which are widely distributed along the coasts of the world's oceans. They are commonly called as 'Sea lettuce'. It has light to dark green in colour and thallus attached by disc holdfast. They have a leaf like flattened structure and eaten by different sea animals like manatees and sea hares. Many species of *Ulva* are food source for humans in China, Japan and Ireland. Humans use sea lettuce raw in salads or use to prepare soups. It is high in proteins, dietary fibres, vitamins and minerals like iron. *Ulva* also causes a major public health scare as it decomposed. The rotting leaves of this produce a toxic gas hydrogen sulphide.

Anticancer activities: *U. rigida* exhibits the most potent antiproliferative effect on EAC cell line in a dose dependent manner. Treatment with methanol or chloroform extract of *U. rigida* results in significant reductions in the level of lipid peroxidation (salem & Ibrahim, 2011). Sulfated polysaccharides isolated from *U. fasciata* show in vitro antioxidant and antitumour activities. The concentrated extract of *U. lactuca* exhibits anticancer activity against

breast MCF-7 and colorectal HCT-116 cells with IC₅₀ ranging from 21 µg/mL to 99 µg/mL due to the presence of metabolites including steroids, glycosides, flavonoids and tannins. Biogenic silver nanoparticles (U-AgNPs) using marine green macroalga, *U. lactuca* extract exhibits the mechanism behind its anticancer activity against the human colon cancer (HCT-116). The cytotoxicity reveals the dose dependent cell death in colon cancer cells with no loss of viability in normal human colon epithelial cells. AgNPs treated cancer cells show the rise in proapoptotic markers (P53, Bax, and P21) and decline in antiapoptotic markers (Bcl-2), thus confirming the p53 dependent apoptosis mediated cell death in HCT-116 (Acharya et al., 2022).

2.10. *Chara* Linnaeus

Chara is a macroalgae belongs to Chlorophyta in the family Characeae. Because of their stem like and leaf like structures, it resembles to land plants. They are found in fresh water where they grow submerged or attached to the muddy bottom. The genus prefers less oxygenated and hard water and not found in waters where mosquito larvae present. They are also known as 'Stoneworts' because of the covering with calcium carbonates. Nitrogen fixing cyanobacteria found growing as epiphytes on surface of *Chara*. The plant is a gametophyte which consists of the main axis that differentiated into nodes and internodes. The branches are dimorphic, long branch of unlimited growth and short branches of limited growth. The rhizoids are multicellular with oblique septa and stipuloides form needle shaped structures at the base of secondary laterals.

Anticancer activities: About 89 chemical

constituents identified in ethanol extract of *C. baltica*. The extract shows anticancer activity against cancer cell lines MCF-7, DLD-1, HeLa, FADU, A549 and SKOV3 (Tatipamula et al., 2019). The cytotoxicity of the aqueous extract and crude alcohol extract of *C. elegans* clearly visible on the cancer cells line, HeLa. Hence, it is a promising alga in treatment of cancer through its inhibition of the proliferation on cancer cells (Mohammed et al., 2018).

2.11. *Spirulina* Turpin ex Gomont

Spirulina is symbiotic, multicellular and filamentous blue green microalgae. The aquatic organisms inhabit in fresh water alkaline lakes. However some species are found in marine ecosystem. They are mesophilic and are able to survive over a wide range of temperatures. They are filamentous, undifferentiated and rod or disc shaped. The main photosynthetic pigment is blue coloured phycocyanin, also contain chlorophyll a and carotenes. Gas vesicles give them buoyancy in the aquatic environment. They reproduce by fission. *Spirulina* is consumed by humans and animals. They have significantly high macro and micronutrient value; hence used as food supplement in the dietary or whole food, aquaculture, poultry and aquarium.

Anticancer activities: *S. neglecta* exhibits the anticarcinogenicity. The cytotoxic effects of *S. platensis* hot methanolic extracts on L20B and MCF-7 human cancer cell lines are prominent. The phytochemical compounds from extracts including alkaloids, phenols, terpenes, steroids, flavones, resins, saponines, proteins, amino acids and tannins cause the cytotoxicity (Fayyad et al., 2019). Polysaccharides from *S. platensis* with the highest degree of sulfation

demonstrate maximum anticancer activity against MCF-7 breast cancer cell line. The anticancer activity of the commercial *Spirulina* product against lung cancer cells strongly supports the knowledge of the chemopreventive properties of *Spirulina* species. *Spirulina* product reduces the phosphorylation of Akt and Rb proteins and the expression of cyclin D1 and CDK4, while increasing the Bax to Bcl-2 ratio in the A549 cells (Czerwonka et al., 2018).

2.12. *Spirogyra* Link

Spirogyra is a macroalgae belongs to filamentous Chlorophyta of order Zygnematales. They have helical or spiral arrangement of chloroplasts, characteristics of the genus. It is commonly known as 'Sare water silk', 'Mermaids tresses' and 'Blanket weed'. The vegetative structure of *Spirogyra* is filamentous that is branched or unbranched. Multicellular thallus with each cylindrical cell attached end to end to form a ring structure. It has a cell wall, nucleus, pyrenoid and spiral chloroplast. The freshwater genus found as green slimy patches on the ground near ponds and other water bodies having stagnant water.

Anticancer activities: The galloyl glucose derivatives in methanol extract of *Spirogyra* varians could be used as antimicrobial and anticancer agents. *S. porticalis* methanol extract provides protection from hypoxia-induced oxidative stress. The extract shows cytotoxic activity on human hepatocellular carcinoma HepG2 and colon carcinoma RKO cell lines due to the presence of fatty acid esters, sterols, unsaturated alcohols and alkynes having substantial phyto pharmaceutical importance (Kumar et al., 2015).

Methanolic extract of *S. triplicata* exhibits anticancer proliferative activity against MCF-7, A549, HEPG2, REH and MOLT4 cell lines. In the extract, GC-MS clearly indicates the presence of nineteen major components and twenty three minor components which have more or less bioactivity and would help in therapeutics in future (Mridha et al., 2020).

2.13. *Chlorella* Beyerinck (Beijerinck)

Chlorella is a green unicellular microalga belongs to Chlorophyta in the family Chlorellaceae. It is the single celled genus. The cells are spherical in shape and are without flagella. Their chloroplast has green photosynthetic pigments, chlorophyll a and chlorophyll b. *Chlorella* is a best food source due to its high protein content and essential nutrients. The dried form contains 45% protein, 20% fat, 20% carbohydrates, 5% fibre, and 10% minerals and vitamins; hence, they are considered as super foods.

Anticancer activities: Au/cellulose nanocomposite synthesized from *Chlorella* species shows anticancer activity against A549 cancer lung cells and HEL299 normal lung fibroblasts by increasing the relative expression of tumour suppressor 53 (p53) (Hamouda et al., 2021). *C. vulgaris* showed marked cytotoxicity against breast cancer, MCF-7 cell lines due to the presence of phenol and flavonoid contents. *C. vulgaris* exhibits antioxidant and anticancer activity against Hela cancer cell lines by the activity of (2E,7R,11R)-3,7,11,15-tetramethyl-2-hexadecanol (Jayshree et al., 2016). The silver nanoparticles (AgNPs) synthesized from the chloroform extract have anticancer activity against MCF-7 and 4T1 cells by the presence of hexanedioic acid, bis (2-ethylhexyl) ester, neophytadiene,

eicosane, hexatriacontane and 13-Docosenamamide, (Z). The formulation could lead to the development of potent therapeutic agents against breast cancer with reduced or no side effect (Hussein et al., 2020).

2.14. *Nostoc* Vaucher ex Bornet & Flahault

Nostoc is the most common species of cyanobacteria that may form colonies made up of filaments of moniliform cells encased in a gelatinous sheath of polysaccharides and found in a various environments. It is a genus of gram negative, photosynthetic cyanobacteria that can be found in both aquatic and terrestrial settings. The algae develop symbiotically within the tissues of plants, supplying its host with nitrogen via the activity of terminally differentiated cells known as heterocysts. *Nostoc* is occasionally found in aquatic environments, on moist rocks, in soil, and at the bottom of lakes and springs. Many species have an outer layer and a thick inner matrix of polysaccharides that give them their "jelly-like" or gelatinous appearance. These polysaccharides also serve as a layer of defense against their surroundings and can aid in the absorption of moisture. This enables them to endure challenging circumstances like erratic temperatures, drought, salt stress, desiccation, UV radiation and pathogen invasion. Depending on the species, the colonies can be found as mats or gelatinous masses that range in colour from brown to yellow to green and are made up of aggregated trichomes. Certain *Nostoc* species can also go into quiescent states that help them to survive harsh environments and enables them to start their metabolism again when rehydrated.

Anticancer activities: Phycobiliprotein, phenolic compounds, flavonoids, tannins etc.

are present in *Nostoc* species. *N. linckia* extract shows anticancer activity against the cell lines like A549, Hela, HCT 116, and MCF-7. Moreover, the species can resist under heavy metal stress and it can act as the strategy to reduce the water pollution (Ramadan et al., 1972). Methanolic extract of *Nostoc* sp. N42 shows cytotoxicity against liver and lung cancer cells. The polysaccharides isolated from *N. commune* exhibit strong antimicrobial and antioxidant activities against growth and proliferation of MCF-7 and DLD1 cells. Similarly, *N. entophyllum* has effective anticancer properties against tumour cells (Guo et al., 2015).

3. Outlook

Algae are rich in phytochemicals and

show diversity depends to species. They are a promising source of secondary metabolites that useful in drug industry in future to prevent different diseases due to their antioxidant, antibacterial, anticancer, antifungal and antiviral properties. Moreover, in medical and pharmaceutical biotechnology, algae are used for the synthesis of growth factors, hormones, antibiotics, vaccines and immune regulators that promote the human health. Similarly, algae can speed up the decomposition of plastics and promote the biofilm formation. It can also act as the important blue carbon sink in turn save the world.

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