ANTI-CANCEROUS AND ANTI-TUMOROUS ACTIVITY OF ALGAE – A REVIEW

1Indira Majumder, 2Subhabrata Paul, 3Rita Kundu *
Centre of Advanced Study, Department of Botany, University of Calcutta, INDIA

Abstract
Cancer is a multigenic disease causing about one fifth of the deaths in each year worldwide. Cancer is caused mainly due to mutation or malfunction of cell cycle controlling machineries. Standard treatment for curing cancer including chemotherapies, coupled with radiation therapies are available but sometime they are associated with severe side effects, as for example, radiation therapies partially disrupts patient’s normal immune systems. Nausea, vomiting, loss of appetite are also common side effects of those standard treatment. Complementary and alternative medicines or CAM treatments opened up a new pathway which relies on active botanicals obtained from various plant sources. CAM obtained from marine flora specially from both micro- and macro algae reported to have active anti- carcinogenic potentiality. Marine algae constitute about 90% of marine organisms diversity, at the same time contain diverse types of biomolecules; such as vitamins, minerals, dietary fibres, sterol, polyphenols, different types of polysaccharides and numerous secondary metabolites. These chemical diversity and huge unused biomass of algae can be explored for drug development. Algal biodiversity was previously used commercially to make neutraceuticals, food supplements, meals, gelling substances. Recent research work revealed their active anticarcinogenic potentiality. Most of the algal extracts induce cancer cell death by inducing apoptosis or pre-apoptosis either by caspase dependent or caspase independent pathways. In this review, we have discussed in brief about the antiproliferative properties of some of these algae and their active anticarcinogenic compounds, belonging to Cyanophyceae, Chlorophyceae, Phaeophyceae and Rhodophyceae.

Keywords: Cancer, Marine algae, anticarcinogenic.

Corresponding Author

Rita Kundu

Department of Botany,
Centre of Advanced Study, Department of Botany,
University of Calcutta, INDIA

Email: kundu_rita@yahoo.co.in

Available online: www.ijipsr.com
INTRODUCTION

Cancer is the leading cause of death in the well-developed as well as developing countries. According to Globocan 14.1 million new cases, and 8.2 million death due to cancer was reported globally in 2012. Lung, liver, stomach, colorectal and breast cancers cause most cancer deaths worldwide. In low and middle income countries, 20% of cancer deaths are caused due to viral infections such as HBV/HCV and HPV infections. It was estimated that annual record of cancer cases will increase from 14 million in 2012 to 22 million in the next two decades. This statistics of cancer cases and mortality rates clearly indicates the great threat of this dreaded disease. Causes of cancer are multiple, it may be familial, may be due to viral infection, or may be related with obesity and life-style patterns. Standard treatments involve many therapies, such as chemotherapy, surgical therapy, radiation therapy, adjuvant therapies etc. which are associated with severe side effects. Those side effects include nausea, vomiting, loss of appetite, loss of hair and impairment of the immune systems by the chemotherapeutic drugs used to stimulate CD34+ cells and migration of bone marrow stem cell in vivo. Chemotherapeutic drugs sometimes coupled with radiation or without radiation can damage blood producing cells, resulting in low blood cell count, increasing the chances of frequent infection, as white blood cell count decreases; severe bleeding may occur due to decreased platelet count, breathing problems may also increase as red blood cells are decreasing. Diarrhoea can also result during radiation therapy. At the same time, cancer treatment by conventional chemotherapy is much expensive and unaffordable for third world countries.

That's why, many are opting for an alternative medicine which has lesser/no side effects, at the same time affordable to all. According to Natural Cancer Institute (NCI), Maryland, USA; ‘Complementary and alternative medicine (CAM) standard treatments are based on scientific evidence from research studies’. This includes treatments by using natural products or “botanicals”. Natural products derived from plants, marine organisms and microorganisms have drawn attention of many scientists. Some important findings have also gained significance for natural biomolecules in the field of cancer research. The general acceptance of CAM is good, with recent reports stating that 34%–38% of the US adult population are using CAM. The effective goodness stored in nature and its natural products are yet to be unfolded and can be explored, most of which till remain in research level.
Algae in both micro and macro form have tremendous scope for exploring bioactive compounds. They have been used traditionally for medicinal purposes in India, China, Japan, Korea, Ireland, Wales and other countries. Brown seaweeds (macro algae) are reported to have anti-inflammatory, antitumoral and immunostimulant activities [1]. *Laminaria, Undaria* and some other members of brown algae are recognized sources of Iodine. Marine algae are sources of pharmacologically active metabolites [2] having antimicrobial, antineoplastic and antiviral properties.

Marine environment covers about 75% of total Earth’s surface. Marine organism diversity is very rich and composed of about half of total biodiversity of world. Microalgal and macroalgal flora comprising 90% of total marine biomass, contain various novel compounds which can be explored for treating diseases. Soft-bodied marine macroweeds need various types of chemicals to protect themselves from various adversities. Besides that, numerous microalgae is reported to contain various essential compounds. These chemical diversity can be explored for potential drug development. Algae provide many vitamins including: A, B₁, B₂, B₆, niacin and vitamin C and are rich in iodine, potassium, iron, magnesium, and calcium. Polysaccharides, also a major compound used for food, fodder and therapeutics are also obtained from marine algae (Rhodophyceae). Poly unsaturated fatty acid (PUFA ) which are precursor of eicosanoids, regulating normal physiology and body homeostasis are found in many macroalgae [3]. Seaweeds have different carotenoid pigments, green seaweed species have β-carotene, lutein, violaxanthin, neoxanthine and zeaxanthine while red seaweeds contain mainly α and β carotene, lutein and zeaxanthin. In brown seaweeds β-carotene, violanxanthin and fucoxanthine are present [4]. Algae contain diverse types of sterols, fucosterol, cholesterol and sitosterol are found in chlorophyceae; brassicasterol, cholesterol, fucosterol are found in phaeophyceae; desmosterol, sitosterol, cholesterol, fucosterol, chlinasterol etc. are found in rhodophyceae. [5,6].

Fibers found in different algal groups are also diverse, cellulose, mannans and xylan are water insoluble whereas agars, alginic acid, porphyran, furonan and laminarin are important water soluble fibers mostly found in sea-weed [7]. These seaweed’s fibers contain some valuable nutrients as well as pharmacologically active substances, and nowadays there is a lot of interest in seaweed meal, functional foods and nutraceutical for human consumption. These phytochemical diversity of macroalgae now a days are being used as alternative food supplement and the algal compounds are reported to have anti viral, anti bacterial and anti fungal activity. There is a huge scope to obtain novel bioactive compounds from these unexplored large bio-mass of sea organisms.
In this present review we have been trying to encompass the beneficial role of marine macro and micro weeds primarily against uncontrolled cell proliferation and subsequent tumor formation.

**Anti-cancerous activity and anti-tumor activity of marine algae:**

In the present days alga is not only used as food but also as medicine, as its medicinal value to treat life-threatening diseases is being explored by researchers worldwide. Biogenic compounds such as plant extracts from lower groups of unicellular alga to higher groups of plants are used as complementary therapeutics which has little/no side effects and are safe. Algal extracts are expected to show anti-cancerous activity and its therapeutic properties can be explored to avoid the side effects of chemotherapeutic drugs and radiation therapy used to treat various types of cancer by conventional ways. Some novel bioactive compounds that serve as anti cancerous compound are derived from algae. Tumor development is associated with escaping normal cellular cell death process or apoptotic pathways leading towards uncontrolled cell proliferation. The tumor development starts when a single cell become mutated and proliferates abnormally. Additional mutation followed by selection of more rapidly growing cells within the population that results in progression of the tumor and malignancy. Destroying normal cellular homeostasis, those kinds of cells show variety of biochemical and physiological changes and become resistant to conventional chemotherapeutics during transformation process.

Many ayurvedic agencies also suggest patients who are suffering from cancer to take neutraceutical medicines made from algal origin. National cancer institute (NCI,USA), approved the use of crude extracts from plant origin and pure fractionate extract with IC$_{50}$ values ≤50µg/ml and ≤4µg/ml.

**Blue-green algae (Cyanophyceae):**

They are known as the source of neurotoxins. Along with them other biologically active molecules are also isolated from them. Cryptophycin 1 isolated from Nostocsp GSV 224 showed cytotoxicity against human tumor cell lines and solid tumors. Cryptophycin strongly suppressed the ability of microtubules to assemble in vitro. A semi-synthetic analogue Cryptophycin-8 was found to be more efficient *in vivo* [8,9]. A boron containing metabolite Borophycin, an acetate derived polyketide compound, isolated from marine Nostoc linckia and *N. spongiaiforme var. tenue* had exhibited potent cytotoxicity against LoVo and KB cell lines [10,11].

Cucarin-A, isolated from *Lyngbya majuscula* (Curacao collections) is a selective inhibitor of various cancer (breast, colon, renal) cell lines. It acts by inhibiting tubulin polymerization by
binding in the Colchicine binding pocket [12]. Brominated fatty acid from extracts of *Anabaena cylindrica* and *A. variabilis* had shown anti-tumour properties [13]. Several strains of marine benthic cyanobacteria, *Anabaena sp.* like M4, 27, 30, 44, 45 have activity against AML cells, but not against non-malignant cells like hepatocytes and cardiomyoblasts [14]. *Yessotoxins* isolated from algal extract *Protoceratium reticulatum*, was able to induce apoptosis in Hela cells with clear morphological changes, DNA fragmentation along with changes in mitochondrial membrane potential [15]. *Calothrixins A and B* isolated from *Calothrix* sp. are indole phenanthridine alkaloids. They have shown cytotoxicity against HeLa cells in nanomolar concentrations [16]. *Scytonemin* isolated from *Stigonema* sp., previously known natural sunscreen is also found to be antiproliferative for some human fibroblast and endothelial cells. It acts as serine-threonine kinase and functions through regulating cell cycle and have role in regulation of mitotic spindle formation [17]. *Leptolyngbya* sp. contain a novel n-methyl – depsipeptide *coibamide*, (synthetic name:N-{(2S)-2-[(N,N-Dimethyl-L-valyl)oxy]-3-methylbutanoyl}-N,O-dimethyl-L-seryl-N-[3S,6S,9S,12S,15S,18S,21S,22R]-15-[(2S)-2-butanoyl]-9-isobutyl-6-(4-methoxybenzyl)-18-(methoxymethyl)-3,4,10,12,16,19,22-heptamethylenyl-N,N2-dimethyl-L-leucinamide, formula: C$_{65}$H$_{110}$N$_{10}$O$_{16}$) that induced autophagosome formation and mTOR independent cell death in human U87-SG and SF-295 glioblastoma cells and mouse embryonic fibroblasts (MEF) cells. This natural compound acted differentially in different cell lines. In case of U87-SG cells, it induced caspase-3 activation while formation of vacuoles was observed in SF-295 cells [18].

**Coibamide-A** also had displayed potent cytotoxicity against NCI-H460 lung cancer cell line in nanomolar range. It showed dose dependent increase of G1 cells without interfering with tubulin and actin. Later this compound was screened against NCI’s panel of 60 cell lines selective for breast, colon, ovarian cancer cells and found to be most cytotoxic against MDA-MB-231 cell line (2.8nM). [19].

**C-Phycocyanin** isolated from *Spirulina platensis* induced morphological changes along with DNA fragmentation, increased Fas expression, ICAM expression, decreased Bcl-2 expression and activation of caspase 2,3,4,6,8,9,10 in HeLa cell line and also showed activity against MCF7 cells [20]. Ethanolic extracts of *Aphanizomenon flos-aquae* had arrested AML cell lines at G0-G1 stage[21]. *Aphanizomenon flos-aquae & Haematococcus pluvialis* were reported to inhibit proliferation of HL-60 and MV-4-11 cell lines [21]. Treatment with *Phormidium molle* extracts or growth media altered mainly the adherent cells (HeLa, Jurkat, U-937, A2058, RD, 3T3,FL)
showing dose-dependent destruction of the monolayer and morphological changes [22]. **LU 103793** (N,N dimethyl-i.-valyl-L-valyl-W-methyl-L-valyl-L-prolyl-L-prolinebenzylamide) novel compound from *Symploca* sp. also act as an anticarcinogenic and anti tumor agent to interfere with microtubule synthesis [23]. **Largazole** isolated from *Symploca* sp. also act as an potent anticancerous agent which decreased the level of type 1 histone deacetylase enzyme (HDAC) [24].

**Green algae (chlorophyceae):**

Marine filamentous algae *Galaxaura marginata* was reported to be an anti cancerous alga which contain a novel desmosterol compound: 25-hydroperoxy-6β-hydroxycholesta-4,23(E)-dien-3-one, extracted in Ethylacetate; showed cytotoxicity against P338 (Lymphocytic leukemia cells), A549 (human lung adenocarcinoma epithelial cell line), KB (KERATIN-forming tumor cell line HeLa) cell lines with effective doses of 0.28µg/mL, 1.00µg/mL and 0.40µg/mL respectively [25]. Hot water soluble polysaccharide compound derived from marine chlorophycean algae *Capsosiphon fulvescens*, induced apoptotic caspase-3 cascade activation, increased concentration of Bcl-2 regulatory protein and induced cell death in AGS gastric cancer cells via IGF-IR mediated PI3K/AKT pathway [26]. Dichloromethane: methanol extract from two chlorophycean alga *Udotea flabellum* and *U. conglutinate* with effective concentrations of 22.5 µg/ml and 22.2 µg/ml showed anti cancerous activities on human cancer cell line HeLa [27]. Extracts of *Udotea flabellum* was reported to have antiproliferative activity on HeLa, SiHa and KB cell lines [27]. Methanolic extracts obtained from two green algae *Enteromorpha intestinales* and *Rhizoclonium riparium* actively showed antiproliferative potentials against cervical cancer cell line HeLa with IC50 values 309.048 ± 3.083 µg/ml and 506.081 ± 0.714 µg/ml respectively [28]. One green algal genera *Enteromopa prolifera* had suppressive activity to Erhlich’s carcinoma with 51.7% inhibition [29].

**Caulerpenyne** a sesquiterpene, with a bisenol acetate functional group ( synthetic name: 1E,3Z,4S,6E)-3-(Acetoxyethylene)-7,11-dimethyl-1,6,10-dodecatrien-8-yne-1,4-diyl diacetate; chemical formula: C_{21}H_{26}O_{6}) isolated from *Caulerpa taxifolia* is a toxic compound induces cell death by interfering tubulin polymerization. X ray diffraction study shown that it induces aggregation of tubulin units on cell periphery and disables microtubule network forming. It was tested positive against neuroblastoma SK-N-SH cell lines [30]. **Caulerpenyne**, was also found to be antiproliferative against KB cells and colorectal cancer cells in µM ranges [31]. Aqueous extracts of *Chlorella* increased cell death in DMBA induced breast cancer in rats inducing pro-
apoptotic pathway[32]. Green algae Cladophoropsis vaucheriaeformis also have effective anti-tumorogenic properties against murine lymphoid leukemia L1210 cells and for low cytotoxic activity against NIH-3T3 normal cells [33].

**Red algae (Rhodophyceae):**

Dichloromethane: methanol fraction from rhodophycean species Bryothamnion triquetrum with active concentration of 8.2 ± 1.3 µg/ml was evaluated against HEp-2 human cancer cell line[27]. Red algae Porphyra yezonensis and Eucheuma gelatinae showed significant inhibition to cancer cells. Rhodophycean genera Amphiroa zonata contains palmetic acid, which target tumor cell’s DNA topoisomerase I; shows in vivo antitumor activity in mice which also induces apoptosis in MOLT4(acute lymphoblastic leukemia) cancer cell line with an IC₅₀ dose of 50µg/ml [34]. Cold water sea weed Porphyra sp. a Rhodophycean algae was effectively shown to control proliferation of Breast cancer cells. Various sterols like, campesterol, cholesterol, 22-dehydrocholesterol, desmosterol, fucosterol, β sitosterol and stigmasteral are found in this algae [35]. Methanolic extract of red algae Gracilaria tenuistipitata was found to induce sub G1 accumulation in Ca9-12 (Oral cancer cell line) and it shown increased ROS generation, GSH depletion, caspase activation and subsequent cell death. In the treated cells Annexin positive and γ H2AX positive cells increased significantly indicating induction of cell death due to DNA damage. MTS based cell viability assay was found to be effective with an IC₅₀ dose of 326µg/ml [36]. Another red algae Lithothamnion calcarium’s extract was found to be effective against colon cancer [37]. MTT assay showed that best cytotoxic effect obtained from dichloromethane extract and chloroform fraction of Hypnea musciformis on K562 (chronic myelolytic leukemia) cell line with an effective concentration of 3.8 ± 0.2 µg/ml and 6.4 ± 0.4 µg/ml [38]. Chloroform fraction of Hypnea musciformis showed anticancerous activity on HEP-2 (laryngeal epidermal carcinoma) cell line and the effective concentration was 6.0 ± 0.03 µg/ml [38]. Chloroform fraction of H. musciformis showed cytotoxic properties against NCI- H292 cell line (human lung mucoepidermal carcinoma), with an effective dose of 15.0 ± 1.3 µg/ml [38]. Methanolic extraction of Plocamium telfairiae was reported to induce caspase independent cell death in HT-29 human colon carcinoma cells. [39]. Plocamium corallorhiza and Plocamium cornutum contain polyhalogenated monoterpenic compound sargaquinoic acid (SQA) and (RU015); SQA was able
to induce apoptosis in breast cancer cell line MDA-MB-231, with 50% inhibition occurred at 6 μM range. RU015, induces necrosis [40]

Anti-cancerous and anti tumorous efficiencies of edible marine seaweed *Palmaria palmate* were reported [41].

**Condriamide-A** isolated from *Chondria sp* shown to be active against human KB and colorectal cancer cell lines LOVO; with an active concentrations of 0.5 μg/ml and 5μg/ml respectively [42]. Alcoholic extracts of some marine sea-weed *Acanthaphora spicifera* exhibited high cytotoxicity in *Ehrilch’s ascites* carcinoma cells [43]. **Halomon** isolated from red algae *Portieria hornemannii* is a *polyhalogeneted monoterpen*e ((3S,6R)-6-Bromo-(bromomethyl)- 2,3,7-trichloro-7-methyl-1-octene) C₁₀H₁₅Br₂Cl₃ is found to be toxic against many marine fauna but its active anti cancerous properties was approved by NCI against brain, colon and renal cancer cell lines (Hl 60TB, MOLT-4, K562, HCT 116, Ht 29, OVCAR, A498 etc.) but showed selectively lesser cytotoxicity against melanoma and leukemia cell lines[44]. Laurenmarianol and (21A) 21 – hydroxythrysiferol were isolated and identified from *Laurencia mariannensis* showed cytotoxicity against p388 tumor cell with an IC 50 doses of 0.6 and 6.6 mg/ml respectively. 16-hydroxy dehydrothysiferol, thyresenol A and thyresenol B isolated from *Laurence viridis* also showed cytotoxicity in p388 cells. From another species of *Laurencia, (L. obtuse )* five more cytotoxic triterpenoids were also isolated. Four bromophenols isolated from *Rhodomela confervoides* showed antitumor activities against human epithelial tumor cell (KB), human hepatocellular carcinoma (Bel 7402) and lung cancer cell (A549). Among these compounds, compound 1(3bromo-4, 5dihydroxy benzoic acid methyl ester) showed most efficacy against all the three tumor cells with an IC50 dose of 3.09 μg/ml.[45]. **Champia feldmannii** contain novel sulfeted polysaccarides showed anti-tumor activity against sarcoma 180 tumor cells [46].

**Brown Algae:**

Brown algae *Himantothallus grandifolius* ethanolic extract was reported to have suppressed cell proliferation and promote apoptosis-mediated cell death with induction of initial stages of apoptosis in different epithelial tumour cell lines (A375, A549, Hep-2,HeLa) compared to non-malignant cell line (Hek-293) [47]. Dichloromethane: methanol fraction from *Pheophycean genera Lobophora vairegata* and *Dictyota caribaea*, with an effective concentrations of 26.2 ± 1.3 μg/ml and 27.9 μg/ml were evaluated and result showed positive anti cancerous activity on human cancer cell line KB [27]. Edible sea weed *Undaria pinnatifida* extracts was effectively shown to control proliferation of breast cancer cells[48]. Methanolic extract of *Padina pavonia*

Available online: www.ijipsr.com  February Issue
showed cytotoxic activity with an IC50 values of 86.45 μg/ml and 74.59 μg/ml in HeLa (cervical cancer cell line), and MDA-MB-453 (breast cancer cell line) respectively [49]. Dichloromethane extract of *Dictyota dichotoma* and *Padina gymnospora* showed anti cancerous activity on HEP-2 (laryngeal epidermal carcinoma) cell line and the effective concentrations were 16.3 ± 0.3 μg/ml and 8.2 ± 0.4 μg/ml respectively [38]. Whereas ethanolic extraction of *Padina gymnospora* at an effective dose of 15.0 ± 2.8 μg/ml, showed cytotoxicity against NCI-H292 (human lung mucop epithelial carcinoma) cell line [38]. Brown algae *Stypodium* sp., has active compound Stylopoldione that interferes with spindle formation and can be used in alternative therapeutics [50]. Crude extracts of *Scytosiphon lomentaria*, *Cystoseira mediterranea*, *Padina pavonica*, *Hypnea musciformis*, *Spyridia filamentosa* showed potent cytotoxicity in the concentration range of 100-200 μg ml⁻¹ with 24 hours incubation time tested on three cell lines MCF-7, DU145, LNCaP, PC3 [51].

**Heterofucan SF-1.5V**: A form of sulphated L-fucose isolated from *Sargassum filipendula* characterized as a very useful anti carcinogenic drug examined on cervical cancer cell line HeLa. It was found to be very effective inducing cell death as this drug releases mitochondrial Apoptosis inducing factor (Apaf) into cytosol and at the same time decreases anti apoptotic factor Bcl-2 and increases the level of apoptosis inducing factor Bax [52]. Due to presence of sulfated polysaccharide fucoidan, extract of *Sargassum mcclurei* showed anti cancerous activity against DLD-1 colon cancer cell line with the concentrations ranging from 1 to 200 μg/ml [53]. Ethanolic extract of *Sargassum wightii* containing novel polysaccharide exibited anti proliferative properties against AGS, HeLa, MCF-7, PC12 cell lines by inducing apoptotic cascade with an IC₅₀ doses of 43.61 ± 4.1, 46.92 ± 3.6, 99.38 ± 2.9, 158.8 ± 5 lg/mL for each cell lines respectively [54]. Polysaccharide extracted from the brown alga, *Sargassum latifolium* (ethanolic extract derivative) have been proved to have antiproliferative potential against human lymphoblastic leukemia and the IC₅₀ dose was found to be significantly lower(17.18 μg/ml), the extract not only induced apoptosis but also able to induce the carcinogen detoxification enzyme glutathione-S-transferases [55]. *Sargassum heterophyllum* contain novel compound *sargaquinoic acid*, that induced apoptotic pathway by activating caspase -3, -6, -8, -9 -13 and down regulating Bcl-2 protin level in metastatic MDA-MB-231 breast cancer cells with an IC50 dose of 67μM.[40]. Anti-cancer activity of aqueous extract of brown algae *Sargassum oligocystum* proved its effectiveness for treating cancer cell lines Daudi and K562 with an effective IC50 doses of 500μg/ml and 400μg/ml [56]. *Leathesia nana* extract, rich in BromoPhenol, containing
one or several benzene rings, a varying degree of bromine and hydroxyl-substituents, could inhibit the growth of Sarcoma 180 tumors \textit{in vivo} and improve the immune system remarkably [57].

Brown algae \textit{Stypopodium flabelliforme} contain a novel stypodiol compound 14-keto-stypodiol diacetate (SDA) which was tested against human prostate cancer cell line (DU-145), found to be an effective anti-microtubule polymerization compound by inhibiting cell growth at about 61\% with purified SDA at 45\micro M concentration. [58].

Epitaondiol and stypotriol two meroditrpenoid extracted from \textit{Stypopodium flabelliforme} exhibit 50\% inhibition in human neuroblastoma (SH-SY5Y) cell line at the concentration of 12.2 \micro M and 14 \micro M respectively. Varying concentrations of three compounds stypotriol triacetate, epitaondiol monoacetate and epitaondiol also inhibit adenocarcinoma (Caco-2) and rat basophilic leukemia (RBL-2H3) cell lines [59].

Fucoxanthin extracted from various brown algae such as hijikin (\textit{Sargassum fusiforme}), kombu (\textit{Laminaria japonica}), and wakame (\textit{Undaria pinnatifida}); found to be an effective apoptosis inducing compound tested against prostate cancer cell line PC-3, DU 145 and LNCaP; with a concentration of 20 \micro mol/L which exhibited significant inhibition of cell proliferation of about 86\%, 95\% and 90\% in these three cell lines respectively [60]. \textit{Undaria pinnatifida} contains fucoidan, which were screened for antitumor activity and appreciable inhibition of Ehrlich carcinoma tumor cells was found [61]. Fucoxanthinol now been established as a potent anti-carcinogenic compound and a study was done to evaluate the efficacy of the pure fractioned fucoxanthin and its metabolites produced into the gastrointestinal tract against human prostate cancer cells (PC-3). Fucoxanthin metabolized into fucoxanthinol and finally amarouciaxanthin A. Fucoxanthin, fucoxanthinol, and amarouciaxanthin A exhibited 50\% cell growth inhibition of PC-3 cells at 3.0, 2.0, and 4.6 \micro M concentrations respectively [62]. \textit{In vivo} studies with seaweed \textit{Acanthaphora spicifera} extract was found to be more effective to treat Ehrlich’s ascites carcinoma cells than conventional chemotherapeutic drug 5-flourouracil and showed better tumoricidal capability in mice model by decreasing tumor size and increasing viable cell count [63]. Brown algae \textit{Ascophyllum nodosum} has anti-tumor activity tested against sigmoid colon adenocarcinoma cells and its isolated fucoidin proved to be a potent anti-cancerous and anti-tumorous agent [64]. Phaeophycean algae \textit{Sargassum thunbergii} contains novel fucoidin, GIV-A, a L-fucan sulfate; in vivo studies in mice also suggest its effectiveness as well, it showed enhancement of phagocytic macrophages, resulting enhancement of immune response [65].
Meroterpenes, usneoidone E and usneoidone Z, isolated from the chloroform extract of *Cystoseira usneoides* showed antitumor properties against L-1210 cell line (lymphocytic leukemia [66]. Brown algae *Fucus evanescens* contains sulfated polysaccharides which showed anti-tumor activity in mice, transplanted with Lewis lung adenocarcinoma [67]. Evidence of anti-cancerous activities of brown alga like *Scytosiphon lomentaria, Laminaria japonica, Sargassum ringgoldianum, Lessonia nigrescens* against Ehrlich carcinoma [29] has also been found. The percentage of inhibition was 69.8% for *Scytosiphon lomentaria* extract, 60% for *Lessonia nigrescense* extract, 57.6% inhibition for *Laminaria japonica*, 45.6% inhibition for *Sargassum ringgoldianum* extract.

**CONCLUSION**

Diverse types of chemicals isolated and characterized from algal origin (from unicellular cyanophyceae to green, brown and red algae) have been proved to be efficient as anti-proliferative and anti-tumorogenic compound. Many of these chemicals obtained from algal extract contain active compounds such as, diverse types of water soluble or alcohol soluble polysaccharides or fucoidan or sulfated polysaccharides, metal containing polyketides, various types of alkalioids, sterol, depsipeptides, halogenated or sesquiterpenes, phenol derivatives, carotenoids, diverse forms of stypodiols etc. Most of them induce cell death either by inducing apoptotic pathway by activating caspases; or by interfering with cellular microtubule nucleation or by forming inter cellular caspase independent auto-phagosome. Anti cancerous and anti tumorogenic compounds derived from algal origin needs clinical trials and advance molecular characteriziton to support the efficacy of these compounds. Future biological research along with detailed chemical characterization are needed to establish alga derived anti cancerous activity more firmly.

**ACKNOWLEDGEMENT**

The authors wish to thank WB-DST (Sanc. No- 778/(sanc.)/ ST/P/S&T/9G-14/2012) for the financial assistance. We also thank Department Of Botany, Centre Of Advanced Study, University Of Calcutta; Kolkata-700019.

**REFERENCES**

Available online: [www.ijipsr.com](http://www.ijipsr.com) \hspace{1cm} February Issue


Daunorubicin to Kill Leukemia Cells, but not Cardiomyocytes. Mar. Drugs. 2010 8:2659-2672.


Available online: www.ijipsr.com February Issue 84


41. Yuan YV, Carrington MF, Walsh NA: Extracts from dulse (Palmaria palmata) are effective antioxidants and inhibitors of cell proliferation in vitro. Food and Chemical Toxicology 2005 43:1073–1081.


