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Review Article

REVIEW POTENT PHARMACEUTICAL PRODUCTS FROM AQUATIC PLANTS-REVIEW

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ABSTRACT

Several biologically active secondary metabolites from aquatic plants have been extracted and identified using modern instrumental BioTechniques and used in various ways as flavors, food, additives, coloring agents, nutraceuticals, cosmetics, and also as unique source of pharma industries for the discovery or development of new drugs. From algae to aquatic macrophytes belonging to various categories, aquatic plants produce a variety of compounds such as polyketides, peptides, alkaloids, flavonoids, phenolic compounds, terpenes, steroids, quinones, tannins, coumarins, and essential oils commercially involving in antibiotic, antiviral, antioxidant, antifouling, anti-inflammatory, anticancer, cytotoxic, and antimitotic activities; thus making them a rich source of medicinal compounds. Moreover, they are comprehensively used in human therapy, veterinary, agriculture, scientific research, and in countless areas. Importantly these chemicals are exercised for developing new antimicrobial and cancer drugs. Furthermore, antioxidant molecules in aquatic plants and seaweeds have recently been acknowledged. This review contains a consolidated contemporary document consisting of entire knowledge available on pharmaceutical products of aquatic plants and highlights major differences among secondary metabolites found in aquatic (algae) and terrestrial plants.

Keywords: Aquatic plant's secondary metabolites, Antioxidants, Flavonoids, Cancer, Triterpenes.

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INTRODUCTION

The secondary metabolites are specialized biochemical compounds, also called a natural product which plays no apparent role in plant growth, enlargement, and reproduction but helps them in fighting under stress conditions of environment and adaptation [1,2]. They are biologically active taxonomically extremely miscellaneous compounds produced by plants and released by plants to protect them from insects and herbivores [3]. Secondary metabolites demonstrate some kind of biological activity against few or many living organisms [4]. Secondary metabolites do not engage in any precise role in the internal organization of producers but help the plants to compete with the environment [5,6]. They are low molecular weight compounds and have limited phylogenetic distribution [7]. Nevertheless, these natural products are used in traditional and folk medicines [8]. It is an established truth that secondary metabolites play a major role in defense mechanisms and their investigation could result in the identification of new signaling molecules [9,10].

Plant secondary metabolites interact biologically between plants and other organisms. Their noteworthy contribution lies in plants to plant and plant to animal interaction through which they communicate, provide signals, attract pollinators, and protect themselves from enemies. Even endophytes are known to produce beneficial secondary metabolites [11].

They are also remarkable by playing a vital role as antioxidants necessary for human beings to supplement in diet to remove toxic substances from the body [12]. Antioxidant molecules in aquatic plants and seaweeds have attracted the attention of scientists globally recently for searching for new and novel antioxidants from them [13,14].

Aquatic plants produce a variety of compounds such as flavones, flavonoids, flavonols, phenolic polyphenols, quinones, tannins, coumarins, terpenoids, essential oils, alkaloids, lectins, and polypeptides like terrestrial plants [15,16]. Some of them can be utilized as food and feed [17]. These substances are used for developing new antimicrobial [18-20], antiviral anti-angiogenesis [21], and anticancerous drugs [22-24]. Furthermore, secondary metabolites extracted from aquatic plants have become of vital importance after realizing its role as antioxidants [25-27]. The successful *in vitro* production of secondary metabolites has raised the plant cell factory concept [28,29].

Today, thousands of biologically active metabolites from terrestrial plants are available in the form of databases which are being used following modern tool for bioinformatics *in silico* drug discovery [30]. However, aquatic plants were ignored for the detection of natural products so far [31]. Although a large number of published information is available, reviews have not been published on secondary metabolites in aquatic plants to date. However, they have been studied earlier for its general biology, physiology, and adaptations. There have been numerous investigations on ecological productivity and dynamics in aquatic ecosystems [32]. The competition and allelopathy among aquatic plants have also been reviewed [33]. They are also being utilized in the bioremediation of soil and water [34]. This paper presents a review of the secondary metabolites of aquatic plants, their biological activity, and their application.

EXTRACTION, ISOLATION, AND IDENTIFICATION TECHNIQUES

The crude extracts of plants in various organic solvents run through column chromatography for fractional distillation. The isolated fractions were further separated using thin-layer chromatography and purified. The purified compound was tested and identified by various traditional analytical techniques such as nuclear magnetic resonance (NMR) and infrared spectroscopy methods [35]. New methods involved spectrophotometer determination and high-pressure liquid chromatography (HPLC), etc. Modern BioTechniques for the identification of secondary metabolites include HPLC-ultraviolet (UV), HPLC-mass spectrometry (MS), and HPLC-NMR [36].

AQUATIC PLANTS

Aquatic plants live in either aquatic freshwater or marine environment. They may be unicellular algae called phytoplankton or large macroalgae/macrophytes. Aquatic macrophytes in facts encompass a different category of plants, including macroalgae, bryophytes, pteridophytes, and angiosperms that are well acclimatized to the aquatic environment [37]. Sculthorpe [38] classified aquatic angiosperms into the following four life forms, namely, submerged, floating-leaved, emergent, and free-floating.

All aquatic species belonging to angiosperm are called hydrophytes which may be monocot or dicot. These plants have specialized modified structures as an adaptation which helps them to survive in an aquatic environment.

AQUATIC PLANTS CLASSIFICATION

There are many doubts about aquatic plants. The above-mentioned references might be in context with angiosperms, that is, hydrophytes. Further, the term aquatic macrophytes are used in the perspective of angiosperm only. However, members of Phaeophyceae and Rhodophyceae are also large size and hence macrophytes. To avoid any confusion among aquatic plants, the following convenient classification is derived and presented (Fig. 1).

All kinds of aquatic plants have been classified into two, that is, I. Microphytes and II Macrophytes. Microphytes are cyanobacteria and microalgae. The unicellular microalgae, namely, *Spirulina* sp. (cyanobacteria) and unicellular algae (*Chlorella* sp., *Chlamydomonas* sp., etc.), are also called phytoplankton, which are microscopic unicellular photosynthetic organisms that float with water but cannot swim against the water current. Phytoplanktons make important producer components of nearly all freshwater bodies, marine lakes, and oceans.

Macrophytes are further divided into 4, that is, (1) macroalgae, (2) aquatic bryophytes, (3) aquatic pteridophytes, and (4) aquatic angiosperms. Except for unicellular algae, all other filamentous large algae are placed in macroalgae under macrophytes. Aquatic angiosperms are classified into the following four categories, that is, (1) free-floating macrophytes, (2) floating leaves but rooted plants, (3) submerged macrophytes, and (4) emergent macrophytes.

MICROPHYTES (MICROSCOPIC)

Cyanobacteria are blue-green prokaryotes that may be unicellular (*Spirulina* sp.) or multicellular (Genus *Nostoc*, *Anabaena*, and *Oscillatoria*). The microalgae and the phytoplankton include all unicellular organisms.

Cyanobacteria

The Gram-negative Cyanobacteria, the pioneer inhabitants, are highly significant in maintaining a major role in carbon and nitrogen sources in

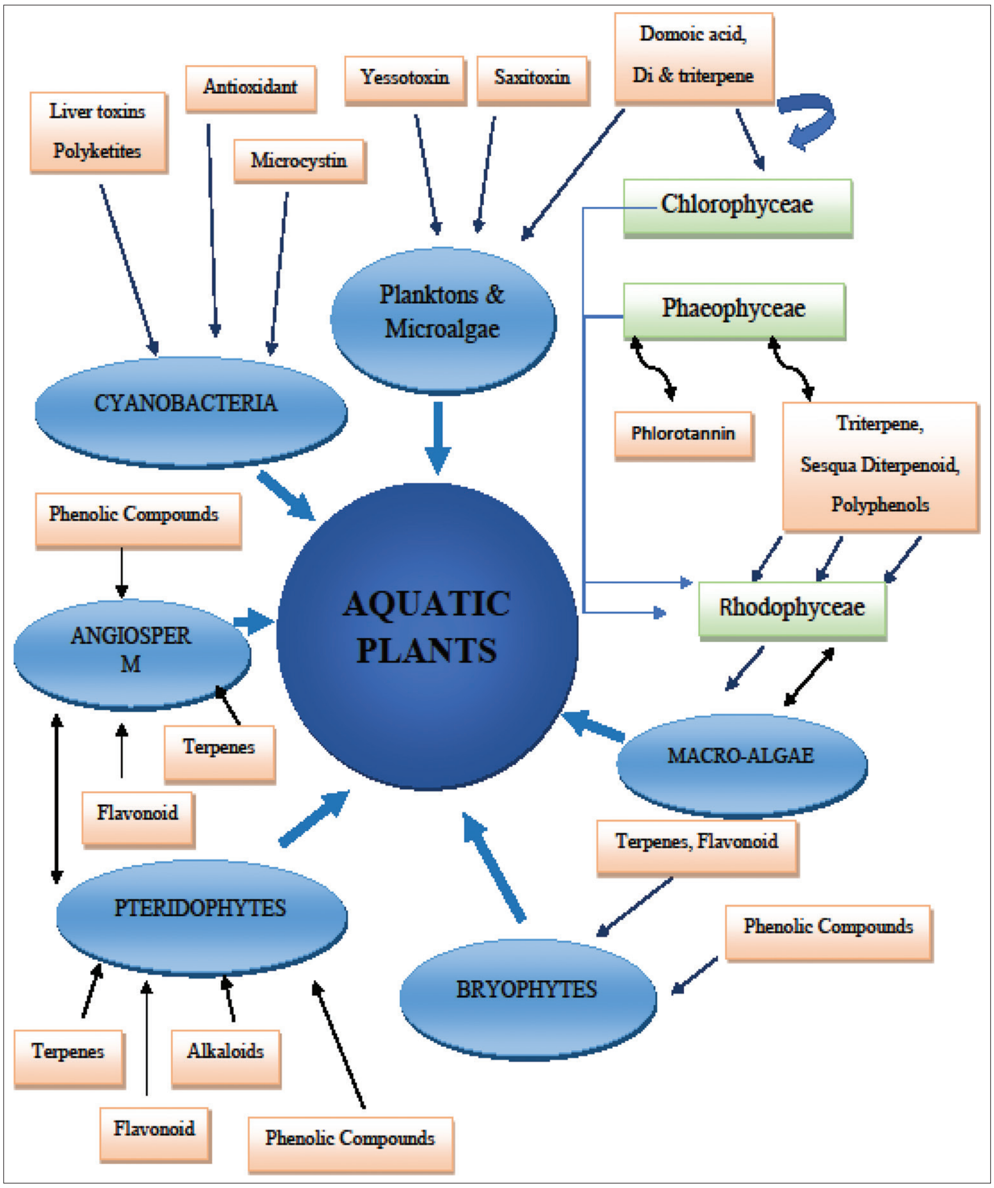

Fig. 1: Important phytochemical present in aquatic macrophytes

the biosphere and the marine ecosystem in particular [39]. Being the oldest, it has huge diversity within the group, which synthesizes a great variety of metabolites of economic importance [40]. These metabolites are employed in innovative pharmacological, biotechnological, industrial, and agricultural applications. Many drugs are designed using cyanobacteria [41].

Cyanobacterial metabolites are in great demand due to their properties as antioxidants [42], the biodegradable potential of Naphthalene, phenol, [43], bioremediation of dairy waste products [44], production of biofuel [45], production of harmful toxic compounds [46], drug discovery [47] and neuro drug [48,49]. Peptides are used in cancer drug [50]. Many species of Cyanobacteria are used to produce antibacterial drugs [51], namely, malyngolid from *Lyngbya majuscula*, Norharmane from *Nostoc insulare*. *Anabaena* spp., *Scytonema hofmanni*, *Hapalosiphon fontinalis*, *Fischerella* sp., *Nostoc communes*, *Nostoc spongiaeforme*, and *Phormidium* sp. synthesized antimicrobial compounds. An antimicrobial compound noscomin has been isolated from *Nostoc commune* [52] and carbamidocyclophanes, and paracyclophanes from other species of *Nostoc* sp. [53].

Cyanobacteria can synthesize novel biomolecules of therapeutically important (Table 1). In addition, they produce mycotoxins from cyanobacteria (*Macrocystis, Anabaena*), Planktothrix (*Oscillatoria* sp.), *Hapalosiphon*, *Nostoc* sp., etc. It is a potent biotoxin released from cyanobacteria. Although it is persistent toxins in freshwater habitats that have attracted scientists all over the world on global health issues, ultimately enter the marine environment. Freshwater microcystins (biotoxin) entered the food chain through the intake of marine clams, mussels, and oysters of species by marine animals and finally humans. Thus, the passing of toxin from the lowest trophic level to higher in the food chain and through biomagnifications has caused serious environmental hazards. Many hepatotoxic shellfish poisoning has been reported due to Microcystin-cyanotoxins. It also provided evidence of harmful algal bloom in the Pacific coastal environment [54]. On receiving a huge quantity of nitrates and phosphates, water gets eutrophied and accelerates the heavy production of algal mass that floats on the water surface. This condition leads to the depletion of oxygen. The toxins produced by cyanobacteria greatly affect aquatic communities through biological interactions.

Microalgae (Unicellular algae)

It includes the following unicellular algae *Botryococcus*, *Chlamydomonas*, *Chaetoceros*, *Chlorella*, *Crypthecodinium*, *Dunaliella*, *Haematococcus*, *Isochrysis*, *Schizochytrium*, *Spirulina*, *Nannochloris*, *Nitzschia*, *Phaeodactylum*, *Porphyridium*, and *Skeletonema* belonging to various classes of algae. They are mostly used for inclusion in diets for keeping good health and medicines. The main secondary product of microalgae is polyunsaturated fatty acids [55]. They are also being used for nanotechnology applications [56]. Further, red microalgae are also found in acidic hot springs as benthic organisms producing mostly enzymes and hydrocolloids [57].

Table 1: Secondary metabolites extracted from cyanophycean bacteria (1) and algae (2–7)

S. No.	Bacteria/algae	Secondary metabolites/toxins	Reference
1.	Cyanophycean bacteria	Microcystins, Antioxidants	[54]
2.	Bacillariophyceae	Domoic acid, Saxitoxins	[61,64]
3.	Euglenophyceae	Euglenophycin, an alkaloid	[68]
4.	Dinoflagellate	Yessotoxins, polyether with lipophilic Sulphur	[66]
5.	Chlorophyceae	Diterpene chlorodesmin, Halimeda-tetraacetate, Dithiolane, and trithiane, mycosporine-like amino acids	[69]
6.	Rhodophyceae	Sesquiterpenoids, diterpenoids, Phlorotannin, eckol, and tocopherols	[70]
7.	Phaeophyceae	Polyphenols (Phlorotannins) terpenoids	[71,72]

Chlorophyceae

Among unicellular chlorophyll-containing green algae, different species of *Chlorella* are prominent in producing industrial products on large scales, particularly antioxidants, whereas *Dunaliella* (which can tolerate higher salinity) produces vitamins, enzymes, antioxidants, and antibiotics [58]. *Chlamydomonas* synthesizes vitamins [59].

Bacillariophyceae (Diatoms)

Members of Bacillariophyceae, also called diatoms, occupy at the producer level in the food chain and provide food for the next trophic level. Thus, they are playing a vital role in the marine ecosystem. They produce toxic metabolites affecting reproduction potential in copepod [60].

Many diatoms belonging to the genus *Pseudo-nitzschia* produce a strong neurotoxin called domoic acid [61]. This toxin is responsible for causing toxicity in herbivores (Tables 1 and 2). Its toxicity increased in iron-rich waters. It can enter in food chain through contaminated shellfish [62,63]. Domoic acid was also responsible for shellfish poisoning that causes amnesic shellfish poisoning and diarrhetic shellfish poisoning. Saxitoxins are responsible for paralytic shellfish poisoning [64]. It causes nausea, vomiting, headache, dizziness, diarrhea, and coma, sometimes leading to death in humans, whereas mucus released from mouth and disorientation and death in animals [65].

Dinoflagellates

They produce yessotoxins responsible for seafood contamination (Tables 1 and 3). It is lipophilic sulfur-containing polyether toxins secreted by several dinoflagellates, including *Lingulodinium polyedrum* and *Gonyaulax spinifera*. This toxin enters in food chain through mollusks. They are highly toxic and produce gastrointestinal disorders and accelerate cancer in the human body [66]. Polyol compound symbiodinolide isolated from dinoflagellate *Symbiodinium* sp.

Euglenophyceae (Euglenophytes)

Metabolites from marine bioresources have created a center of attention for scientists all over the world from the last few years. The cells of *Euglena*, a unique unicellular microorganism, are nutritious and have anti-cancerous activity. It is also used in the production of trehalose from glucose, arachidonic acid, wax ester, and Vitamin E [67]. A toxin called euglenophycin is an alkaloid herbicidal in nature (Tables 1 and 4) and anticancerous [68].

MACROPHYTES (MACROSCOPIC AND LARGER AQUATIC PLANTS)

The larger aquatic plants, namely, large size algae (filamentous algae, marine giant size kelp, etc.), lower seedless plants (Bryophytes and Pteridophytes), and higher aquatic Angiosperms are referred to as macrophytes.

Macroalgae (Multicellular algae)

Large size filamentous and multicellular algae are also macrophytes but are called macroalgae.

Chlorophyceae

The green filamentous macroalga *Chlorodesmis fastigiata* produces diterpene chlorodesmin, a toxin that played an important role in deterring fishes, whereas the same metabolite is utilized by specialist crab to live and feed on this alga. This toxin also kills corals on contacting alga [69]. The genus *Halimeda*, a calcareous macroalga contains less toxic diterpene compound Halimeda-tetraacetate acetate which immediately converted to more active compound halimedatrial upon injury [70-74]. Diterpenes are antimicrobial and anti-inflammatory compounds (Tables 1 and 5). They also possess anti-Chikungunya virus and anti-HIV potential [75].

Three fatty acids 9,12- Octadecadienoic, Tetradecanoic, and hexadecanoic acids have been identified from *Chara vulgaris* which decreased the growth of major bloom-forming cyanobacteria in eutrophic freshwater. Dithiolane and trithiane were reported from the other species, *Chara globularis*. *Nitella* sp. was found to have dithiolane toxic to alga *Nitzschia palea.* An antitumor alkaloid, caulerpin isolated from *Caulerpa racemosa* [76]. They also indicated its nutraceuticals properties.

Phaeophyceae

Marine algae provide valuable complex industrial products, namely, alginate, carrageenan, and agar as phycocolloids [77]. Secondary metabolites obtained from marine brown algae have been extensively used as a traditional herbal medicine for a long time [78]. Furthermore, they show strong antibacterial activity. *Fucales* sp. and *Dictyotales* sp. produce the maximum content of phenolic compounds (Tables 1 and 7) like Phlorotannins. Later is also a significant source of terpenoids [79]. Besides, they also protect plants from UV radiation and defense against grazing (Table 1). Volatile compounds have also been reported from marine brown algae. Among them, b-ionone exhibited antibacterial and antifungal activity and are detrimental to some arthropods [80].

Phaeophyceae are rich sources of polyphenols. Polyphenols, particularly polyphloroglucinol phenolics, possessed peculiar antioxidant properties. Phlorotannins have been isolated from *Ascophyllum nodosum*, *Eisenia bicyclis*, *Sargassum kjellmanianum*, *Sargassum ringgoldianum*, *Ficus vesiculosus,* and *Fucus serratus* in the purified form [81]. These phlorotannins are present in brown algae as chief polyphenol [82]. They are used in medicine as antidiabetics, anti-Alzheimer disease, antimicrobial, antioxidants anti-HIV, antiproliferative activity, anti-inflammatory, radioprotective, and anti-hypertensive activity [83,84].

Phlorotannins possessed therapeutic properties [85-87]. Phlorotannins are specifically present as the only group of phenolic compounds in brown algae. They are just like terrestrial tannins but unlike as phlorotannins consist of oligomers of phloroglucinol [88]; hence, in fact, scavengers in comparison to polyphenols found in terrestrial higher plants. Green tea has only 3–4 rings [89]. They are used in therapeutic medicine as a strong antioxidant.

This compound has been isolated from some brown algae, namely, *Ecklonia stolonifera*, *Ecklonia cava*, *E. bicyclis,* and *S. kjellmanianum*. Polyphenol production by Phaeophyceae has made this group very important because these are very potent antioxidants. Many brown algae are described to show, namely, *A. nodosum*, *E. bicyclis*, and *S. kjellmanianum, S. ringgoldianum*, *F. vesiculosus*, and *F. serratus*. Other polyphenolic compounds are catechins and flavonol glycosides. In Japan, people eat *E. stolonifera* and *Ecklonia kurome* algae in their food. These traditional edible brown algal species improve the property of blood. It has been reported that *Laminaria religiosa* is safe to eat as it produces fucoidan an antitumor compound [90,91].

Rhodophyceae

The red marine algal genus *Laurencia* contains 350 diverge natural halogenated secondary metabolites. It produces sesquiterpenoids [92] as a major compound (Tables 1 and 6). Diterpenoids have been recorded in lesser numbers but not terpenoids. C15 acetogenins are also in larger number mostly halogenated [93]. Sesquiterpenoids are significant for human health. It is being used for its potent role. Sesquiterpenes are also extracted from higher aquatic plants similar to family Asteraceae.

Two new Sesquiterpene, a halogenated C15 acetogenin compounds out of six, have been reported in *Laurencia obtuse* spectroscopically. Out of 34, only four genera (*Plocamium costatum*, *Ballia callitricha*, *Phacelocarpus labillardieri,* and *Osmundaria colensoi*) possessed 20 important secondary metabolites along with five known bromophenols [94]. Eleven novel oxylipins, labillarides are reported from alga *P. labillardieri* and named them A to K. Most of them are macrocyclic compounds significant in therapeutic uses, particularly as antibiotics, antitumor, and antifungal compounds [95].

Different groups of compounds have been isolated and identified, such as hydrocarbons, terpenes, acids, phenols, sulfur-containing compounds, aldehydes, naphthalene skeleton, and alcohol from a diverging group of algae. Marine algae are a great choice for having huge preventive and therapeutic importance due to anticancerous compounds.

Bryophytes

They are pioneer land plants. They comprise the second largest group after angiosperms. The main plant body is haploid and called gametophyte which produces male and female gametes for sexual reproduction. They lack true roots. They also do not have true mechanical tissues such as xylem and phloem but have simple water and food conducting tissues such as leptoids and hadroid. Furthermore, their walls are not lignified.

Freshwater Bryophytes

Out of 15,000 plants [96], only a few are aquatic mosses (*Ricciocarpus natans*, *Riccia fluitans*, and *Riella* sp.) found in freshwaters. Several secondary metabolites have been extracted from liverworts (Tables 1 and 2). The synthesis of biologically active terpenoids was against cancer cells [97]. The paste made from *Riccia* sp. was used to cure ringworm skin disease [98]. Flavonoids Apigenin 7-o-glucuronide, lucenin, luteolin 7-o-glucuronide, and lucenin 2,7-O-rhamnoside have been identified from *R. fluitans* [99]. The latter is also present in tea, coffee, fats, and oils.

Marine Bryophytes

Sphagnum a peat moss marine bryophyte *Sphagnum magellanicuml* produced hydroxyl hydroxybenzoic acid [100]. Polysaccharides extracted from this species possessed antibacterial and antifungal properties [101]. It produces sterols, terpenoids, and polyphenols [102].

Pteridophyte

The common aquatic pteridophytes are referred to as aquatic ferns. The common genus is represented by genus *Equisetum*, *Marsilea*, *Salvinia*, and *Azolla*. Few compounds have been isolated from pteridophytes (Table 2).

Two compounds isoquercetin and flavonoid have been ascribed from *Equisetum arvense*. The total phenolic content of N-butanol was 96.4 mg/g of dry extract of *E. arvense*. It showed antibacterial activity against the growth of test bacteria [105]. Flavan4-ol glucosides identified in *Equisetum arvense* [106].

Table 2: Secondary metabolites extracted from bryophytes and pteridophytes

S. No.	Bryo/ Pteridophytes	Secondary metabolites	References
1.	Bryophytes	Polyphenols, sterols, terpenoids	[103,104]
2.	Pteridophytes	Alkaloids, steroids, tannins, flavonoids, terpenoids, cardiac glycosides, phenolic compounds, and terpenoids	[105-110]

Alkaloids, phenolic compounds, flavonoids, saponins, and tannins have been extracted from ferns *Azolla pinnata*, *Marsilea minuta*, and *Salvinia molesta* [107,108]. The former exhibited antibacterial [109] and anti-diabetes properties [110]. Alkaloids, steroids, tannins, flavonoids, terpenoids, cardiac glycosides, phenolic compounds, and terpenoids have been reported from the crude extract of *Cyclosorous interruptus* [111]. Alkaloids, arbutin, and tannin are identified from this fern [112]. A paste of aquatic fern *Ceratopteris thalictroides* is used as a poultice for a skin disorder and to stop bleeding.

Gymnosperm

A conifer species *Retrophyllum minus* is the only obligate inhabitant of aquatic habitats [113], but this is an endemic species to New Caledonia and not much is known about their chemical profiling. This category of plants is not included in the classification of aquatic plants in this paper.

Angiosperms

These are higher plants and the highest evolved. Macrophytes (Angiosperms) are aquatic vascular plants also known as hydrophytes. These specialized plants are adapted to live in the presence of an excess of water in aquatic communities.

Free-floating aquatic plants

These plants float on the water surface. They are also called amphibians because they can also survive on moist soil. Their leaves are exposed to air. *Pistia stratiotes* and *Eichhornia crassipes* are medicinal plants known from the ancient system of Indian medicine and used in Ayurveda [114]. Alkaloids, phytosterols, Phenols, flavonoids, and tannin are detected in *P. stratiotes* [115-117]. Phenolic compounds exhibited antiapoptotic. Antibacterial and anticancer activity was found in this plant [118-120].

Linolenic acid, β-sitosterol, 24-Ethyl-cholest-4-ene-3,6-dione, sterols (24-Methylenlophenol), and flavanol glycosides (Isorhamnetin-3-o-glucoside, Quercetin-3-o-neohesperidoside, and Isorhamnetin-3-o-neohesperidoside) have been identified from *P. stratiotes* [121,122]. All these allelochemicals possessed antialgal properties. A compound isolated from Pistia altered the physiology and ultrastructure of *Selenastrum capricornutum* [123-129]. *Stratiotes aloides* were found to have lipophilic compounds active against some algae (Table 3).

Tannin, phlobatannin, saponin, steroids, terpenoids, alkaloids, flavonoids, quinines, anthraquinones, cardiac glycosides, sterols, anthocyanins, phenols, carotenoids, polyphenols, carbohydrates, resins, etc., have been recently reported from *E. crassipes*. Moreover, studies on exudation from the roots in freshwater plants are few. Bioactive sterols have been reported from this plant [130]. He identified five allelochemicals as 24-Methy cholesta, 24-Ethyl cholesta, 22, 24 – diene, and Methyl–22, -diene- β, 6 α -diol. These allelochemicals were bioactive against *Chlorella emersonii* of Chlorophyta. The first two compounds also exhibited toxicity against *Synechococcus leopoliensis*, *Muriella aurantiaca*, and *Chlorella vulgaris,* whereas 3rd and 4th compounds against *Navicula pelliculo* and *C. vulgaris* and last one against *N. pelliculo*. The following four bioactive sterols have been identified from *E. crassipes* as alpha-asarone, y-linolenic 12 hydroxy 9, 13, 15-octadecatrienoic, and 9 hydroxy 10, 12, 15 octadecatrienoic. They were toxic to microalgae belonging to the group Cyanochloronta, Rhodophycophyta, Chrysophycophyta, and Chlorophycophyta. Further, most of them inhibited the growth of another green alga *Selenastrum capricornutum*. Flavonoids are involved in pharmaceutical activities, namely, anti-allergic, anti-inflammatory, antimicrobial, and anticancer activity. Terpenoids are especially used as therapeutic agents in Alzheimer's disease and liver cancer [131,132].

Rooted aquatic plants with free-floating leaves

These plants are rooted, but their leaves float on the water surface. Genus *Nuphar*, *Nymphaea*, and *Nelumbo* are common plants of the water lily family Nymphaeaceae. All these three species are potent medicinal herbs. They are used to cure, particularly diabetics, liver disorders, etc. Antimicrobial activity of the Members of Nymphaeaceae has been documented. High antibacterial activity of root exudation of *Nuphar luteum* has been reported [133]. *Nymphaea tuberosa* exhibited high antibacterial activity against *Mycobacterium smegmatis* and *Staphylococcus aureus*. It also possessed anti-fungal properties and inhibited fungi *Alternaria* sp. and *Fusarium roseum* [134]. They have reported tannic acid, gallic acid, and ethyl gallate from other species *N. tuberosa*. Alkaloids such as nupharidine, 7-epideoxynupharidine, and nupharolutine and sesquiterpenes like nupharidines have been identified from *N. luteum.* All these compounds exhibited anticancer, antidiabetics anti-inflammatory potential [135]. The former plant possessed antitumor and anti-diabetic properties [136]. *Lotus pedunculatus* (Fabaceae) contained nitro toxin compounds [137]. These nitro compounds identified as a mixture of 3 nitro propanoyl-D-glucopyranoses, karatatin, coronation, and cibarian present in the roots. *N. stellata* declined the growth of water hyacinth; both aboveground and underground parts of the former plant harmed the later [138].

Nymphaea caerulea is used in traditional medicine to treat diabetics, cardiotonic for palpitation of heart, and liver disorders [139,140]. Many compounds were isolated from four *Nymphaea species*. Further, triterpenes have been reported in all [141-145]. They recommended 5-glycosyl isoflavones as a taxonomic character to identify plants of this group (Table 4).

Total phenolic contents were observed 7.61% (w/w) in *Nelumbo nucifera*. The seeds contain alkaloids, saponins, phenolics, and carbohydrates. Significant antioxidant activity is reported in this plant [146]. Secondary metabolites alkaloids, flavonoids, phenols, and sesquiterpenes, 2, 3, 4, 5- tetrafalloyal-D-glucose have been identified from *Nuphar* sp. [147]. Phenols [148] and flavonoids have been reported from *Limnophila geoffrayi* [149].

Submerged macrophytes

These aquatic plants remain inside water under submerged conditions [150]. *Ceratophyllum* sp., *Hydrilla* sp., *Vallisneria* sp., and *Potamogeton* sp. are commonly found in freshwater lakes. Most of them produce phenols and flavonoids*. Ceratophyllum demersum* synthesized

Table 3: Secondary metabolites present in free-floating macrophytes

S No.	Aquatic macrophytes	Secondary metabolites	References
1.	*Pistia stratiotes*	Fatty acids – α-linolenic acid, linolenic acid, β-sitosterol, 24-Ethyl-cholest-4-ene-3,6-dione, sterols (24-Methylenlophenol), flavanoglycosides Isorhamnetin-3-o-glucoside, Quercetin-3-o-neohesperidoside, Isorhamnetin-3-o-neohesperidoside, Alkaloids, phytosterols, Phenols, flavonoids, and tannin	[124]
2.	*Stratiotes aloides*	Lipophilic compounds	[125]
3.	*Eichhornia crassipes*	24 –Methylcholest 4 ene-3,6-dione, 24-Ethylcholesta –4, 22-diene-3,6, dione, 24-Methyl cholesta-5, 22-dien-3β -ol, 24 –Ethyl-Cholesta –5, 22 –diene –3 β - ol, and 24- Methyl Cholesta –22,-diene-3 β, 6 α -diol. Sterols- alpha-asarone, y-linolenic, 12 hydroxy 9, 13,15-octadecatrienoic, 9 hydroxy 10,12,15 octadecatrienoic.	[126-129]
4.	*Azolla pinnata*	Flavonoids	[107]

a huge amount of total phenols (76.55 μg/mg) under *in vitro* conditions [151]. It also inhibited cyanobacteria. Two flavonoids have been isolated from this plant in Table 5 [152-163]. Besides, antioxidant contents were identified as β-carotene, flavonoid, and lycopene.

Polyphenolic-like compounds have been obtained from many species of *Myriophyllum*, *Myriophyllum spicatum* [164], *Myriophyllum alterniflorum*, *Myriophyllum heterophyllum,* and *Myriophyllum brasiliense*. Environmental factors may influence the production of secondary metabolites. The amount of this phenolic content increased in *M. spicatum* in limited nitrogen. *Myriophyllum* can suppress the growth of cyanobacteria. Besides, phenylpropanoid glucosides (α-asarone, β-asarone, 1-o-coumaroyl-6-o-galloyl- β -D-glucopyranose) were identified from *Myriophyllum verticillatum* (N-hexadecanoic Acid). These biomolecules have the potential to clean water in shallow lakes.

Micranthemum umbrosum an attractive fast-growing aquarium plant contained four compounds: 3,4,5-trimethoxyallylbenzene [1] and three lignoids [158]. These compounds played an important role in herbivores against Asian grass carp (*Ctenopharyngodon idella*).

Oxygenated fatty acids have been reported in submerged plants, namely, *Potamogeton* [165], *Najas*, and *Ruppia* species. *Ruppia maritima* consisted of ent-labdane diterpenes active against algae *Chlorella vulgaris* and *Selenastrum carpricornutum*. The latter indicated antialgal diterpenes. *Potamogeton natans* contained antifungal potential [166]. Two new furanoid diterpenes, effective antiviral potamogetonyde and potamogetonol have been isolated from *P. malaianus* [167]. *Elodia* sp. shows allelopathy against phytoplankton and epiphytes [168]. Later, flavonoids have been isolated from this plant [169].

Antialgal alkaloids with the highest degree of toxicity 2-ethyl-3-methylmaldeimide have been isolated and identified from *Vallisneria spiralis* belonging to the family Hydrocharitaceae, which inhibited the growth of *Microcystis aeruginosa* [170]. *Hydrilla verticillata*, the other member of the same family, produced many secondary metabolites just like higher terrestrial plants for defense purposes [171] and causing the allelopathic effect. It also exhibited toxicity against the growth of *M. aeruginosa* due to the presence of n-butyl phthalate. They also identified antifungal phenolic compounds from this plant. This plant inhibited the distribution of *Ceratophyllum* sp. and reduced the growth of *S. molesta*. Although allelopathy in *H. verticillata* is known since 1983, biochemical compounds, namely, Sesquiterpene, diterpenes, terpenoids saponins, steroids, linoleic acid, phytol, steric acid, phenolic acids, alkaloids, and flavonoids, have been documented recently. It is also rich in Vit. A, C, E, B6, B5, B12, and calcium [172].

Table 4: Secondary metabolites extracted from free-floating rooted macrophytes

S. No.	Aquatic macrophytes	Secondary metabolites	References
1.	*N. ampla* and *N. pulchella*	2 5-glycosyl isoflavones, 7,3', 4' –trihydroxy-5-O-β-D-[2"-acetyl]-xylopyranosylisoflavone, 7,3', 4'-trihydroxy-5-O-α-L-rhamnopyranosylisoflavone, 3-glycosyl flavones	[141]
2.	*N. ampla, N. pulchella, N. gracilis,* and *N. elegans*	Triterpenes, saponins	[141]
3.	*Myriophyllum spicatum*	Tannins, ellagic acid, polyphenols eugenin, phenolic acid, nonanoic acid, tetradecanoic acid, palmitic acid, octadecanoic acid, octadecenoic acid, cis-6-octadecenoic acid, cis-9-octadecenoic acid, gallic acid, pyrogallic acid, [+]-catechin, polyphenolic compound	[142,143]
4.	*Myriophyllum alterniflorum*	α-asarone, phenylpropane glycoside	[144]
5.	*Nuphar* sp.	3 nitro propanoyl-D-glucopyranoses, karatatin, coronarian, and cibarian	[145]
6.	*Nelumbo nucifera*	Alkaloids, saponins, phenolics, and carbohydrates	[146]
7.	*Nuphar lutea*	Gallic acid, myricitrin, myricetin, 1,2,3,4,6- pentagalloyl-D-glucose 2,3,4,5- tetrafalloyal-D-glucose, 6,6'- dihydroxythiobinupharidine	[147]

Table 5: Secondary metabolites present in submerged aquatic macrophytes

S. No.	Aquatic macrophytes	Secondary metabolites	References
1.	*Vallisneria spiralis*	4-oxo-β-ionone, dihydroactinidiolide,2 ethyl 1-3-methylmaldeimide	[152]
2.	*Bacopa monnieri*	Antioxidants	[153]
3.	*Ceratophyllum demersum*	flavonoid glycosides, apigenin-7-O-glucoside, sterols-sitosterol, Volatile- paraffins, benzyl acetate and a sesquiterpene	[154]
4.	*Hydrilla verticillata*	Sesquiterpene- Coryan-17-ol, 18,19-di dehydro-10-methoxy-acetate, Steroids- Ergost -5-en-ol, 22, 23-dimethyl acetate, 1,2-benzene dicarboxylic acid butyl octyester, Linoleic acid-10- Octadecenoic acid, methyl ester, stearic acid- Pentadecanoic acid, 1,4-methyl, methyl ester, Diterpene compound, Phthalic acid-1,2-benzenedicarboxylic acid diisooctyl ester, Dibutyl phthalate, 12-hydroxylauric acid-1,2- 12- hydroxydodecanoic acid, 11,14- eicosadienoic acid, β-sitosterol acetate, β-sitosterol, ethyl palmitate, 1,14-tetradecanedioic acid, 12-hydroxydodecanoie acid,6,10,14-trimethyl-2-pentadecanone, 1-[5'-Hydroxy-4'-hydroxymethyl-1'-methyl-1*H*-pyrrol-2'-yl]-henicosa-2,12,15-trien-1-one, dicarboxylic acid-Octadecanedioic acid, phenolic acid- Ferulic acid, Chlorogenic acid, Caffeic acid	[155-157]
5.	*Micranthemum umbrosum*	3,4,5-trimethoxyallylbenzene [1] and three lignoids: β-apopicropodophyllin [2]; [−] -[3*S*,4*R*,6*S*]-3-[3′,4′-methylenedioxy-α-hydroxybenzyl]-4-[3″,4″-dimethoxybenzyl] butyrolactone [3]; and [−]-hibalactone [4]	[158]
6.	*Myriophyllum verticillatum*	Phenylpropanoid glucosides [α-asarone, β-asarone, 1-o-coumaroyl-6-o-galloyl- β -D-glucopyranose]	[159]
7.	*Potamogeton natans*	Diterpenes	[160]
8.	*Elodia sp.*	Phenolics and flavonoids	[161]
9.	*Ruppia maritima*	Ent-labdane diterpene	[162,163]

Most of the herbivore does not eat aquatic plants due to the presence of flavonoids. Submerged plants are rich in antioxidants, which provide them antibacterial, antifungal, antialgal, and antitumor properties [173].

Emergent aquatic plants

The Emergent macrophytes are mostly C4 plants and known to produce huge biomass in wetlands. Phenols are the most known secondary metabolites in emergent aquatic plants than any other substance. These phenolic compounds released from aquatic plants help in carbon sequestration by delaying their decay [16]. Further, they have recorded wetland emergent grasses such as *Scirpus* sp., *Typha* sp., and *Phragmites* sp. produced very high phenolic contents of more than 10 g/kg DW (10 g/kg, 15 mg/kg, and 27 g/kg DW, respectively). However, in *Phragmites karka* and *Arundo donax*, the phenolic contents in the dry leaves were measured as 4.45 mg/g and 3.95 mg/g, respectively [110].

An emergent grass *A. donax* was found toxic to the growth of duckweed and *S. molesta*. Both plants died within 7 days due to the presence of phenolic compounds [174]. They proved that phenolic extract was toxic to the growth of duckweeds. Thus, emergent plants also possess a high potential for biocontrol due to the presence of phenolic compounds. Many phytotoxic compounds produced by higher plants are phenolic compounds in Table 6 [175-191]. Flavonoids, the phenolic compounds, are the chief ingredients of this plant.

The medicinal values of reed, *Phragmites* sp., have been explored from the ancient days for herbal medicine. Long-chain fatty acids, flavonoids such as luteolin and apigenin-7-0-glucoside, cyanidin-3,5-diglucoside, delphinidin-3, 5-glucoside, and quercetin from flowers of *Polygonum orientale* have been reported. Anthocyanins, delphinidin-3-*O*-glucoside, and cyanidin-3-*O*-glucoside possessed anti-cancer property and induced cancer cell death in human (maze). In addition to these polyphenols and flavonoids, alkaloids have also been isolated from *Phragmites vallatoria* [192]. They have detected the highest radical scavenging activity (IC 50=735 μg/ML) in this plant. Further, *Phragmites* plants are an abundant natural source of flavonoids. Their Gas chromatography–mass spectrometry (GC-MS) analysis emphasized the presence of fatty acids and antioxidants. Out of seven, the main compound was Hexadecanoic acid (30.88%). Others were 9, 12, 15-Octadecatrienoic acid (alpha-Linolenic acid) and 9, 12-Octadecadienoic acid, two unsaturated methyl esters, and two fatty acids, diisooctyl ester, 3, 7,11, 15-Tetramethyl-2-hexadecen-1-ol, and phytol. It tends to reduce wound, fever, vomiting, and sickness after chemotherapy. Furthermore, treat arthritis, rheumatoid arthritis, diabetes, diuretic and diaphoretic problems, etc. Its antiviral properties have also been well described [188].

The plant is rich in proteins and edible. The *Phragmites* sp. contained phenol and gallic acid as a prominent compound. Gallic acid and the organic acid ethyl 2-methyl acetoacetate (EMA) methyl acetoacetate were isolated from root exudates, whereas taraxerol and taraxeron from the leaves [193]. High cellulose and lignin were also reported in the aqueous solution of *Phragmites australis* [194]. Naturally occurring glucosides have been isolated from *P. australis* flower [195]. A compound EMA was discovered from *P. communis*, which was found allelopathic to green algae [196].

It has been used for the treatment of diabetes and other diseases such as arthritis and rheumatism in various preparations of different plant parts. Its paste is also used to heal any external injury. Ethanolic extract of *P. vallatoria* has been reported efficient antidiabetic potential in rats [197]. *Phragmites* plants are an abundant natural source of flavonoids. A flavone Apigenin-7-O-glucoside and luteolin present in this plant have much therapeutic importance as antioxidants, anti-inflammatory, antioxidant, Alzheimer's disease, and various types of cancers [198]. These compounds have been reported both from *Phragmites* sp. and *P. orientale*. Lutein is a very good source of eye tonic. Flavone, luteolin can inhibit cell proliferation by inducing apoptosis [199]. This could be a good natural anti-cancer agent. Similarly, it may inhibit breast cancer invasion and ameliorate the conditions [200]. Crude water extract of *P. australis* decreased multiplication of bovine herpesvirus type 1 in Madin-Darby bovine kidney cells demonstrated an anti-inflammatory effect [201].

Elsharkawy [202] strongly emphasized the importance of alkaloids as seed germination inhibitors. Many aquatic plants are reported to inhibit seed germinations. *P. karka* and *A. donax* inhibited seed germination due

Table 6: Secondary metabolites extracted from emergent macrophytes

S. No.	Aquatic macrophytes	Secondary metabolites	References
1.	*Arundo donax*	Alkaloids, N- [4'- Bromophenyl]-2,2- Diphenylacetanilide, Curarimimetic indoles	[175,176]
2.	*Bacopa monnieri*	Alkaloids, saponins, sterols, betulinic acid, stigmasterol, beta-sitosterol, and bacopa saponins.	[177]
3.	*Cyperus rotundus*	α-cyperone, β- selinene, cyperene, cyperotundone, patchoulenone, sugeonol, kobusone and isokobusone, sesquiterpene-rotundone, flavonol glycoside, saponin, vitamin-C, sesquiterpenoids and essential oils, polyphenol, cyperine	[178,179]
4.	*Eclipta alba*	Resin, alkaloid eclitine, wedelolactone, triterpenoid	[180,181]
5.	*Eleocharis microcarpa*	Fatty acid- trihydroxy cyclopentenyl, phenolic acids, linoleic acid, α linolenic acid	[182]
6.	*Juncus* sp.	*p*- coumaric and vanillic acids, cycloartane triterpenes cycloartane glucosides, and 9,10-dihydrophenanthrene glucosides	[183-185]
7.	*Phragmites australis*	3'-O-glucosides and 3'-O-gentiobioside, ethyl 2-methylacetoacetate, ferulic acid, p-coumaric acid, syringic acid, vanillic acid, p-hydroxy benzoic acid, p-hydroxybenzaldehyde, aurantiamide acetate, 2,3-dihydroxy-1-[4-hydroxy-3,5-dimethoxyphenyl]-1-propanone, palmitic acid, heptadecanoic acid, β-sitosterol, stigmasterol methyl gallate, [+]-lyoniresinol, and [+]-lyoniresinol-3α-O-β-D-glucopyranoside	[186,187]
8.	*Polygonum* sp.	Alkaloids, flavonoid quercetin	[188]
9.	*Polygonum orientale*	Flavonoid- luteolin and apigenin-7-0-glucoside, cyanidin-3,5-diglucoside, delphinidin-3, 5-diglucoside, quercetin	[189]
10.	*Schoenoplectus sp.*	11 free and glycosylated low-molecular polyphenols, 17 cinnamic acid and Hydrocinnamic acid derivatives, flavonoids, and 10 C13 nor-isoprenoids,1-benzoyl-glycerol-2-α-l-arabinopyranoside, [−]-catechin	[190]
11.	*Typha domingensis*	Alkaloids, sterols, and flavonoids (nonacosanol, lupeol acetate)	[191]

to the presence of alkaloids. About 12 different alkaloids were identified from *A. donax*. Besides, N- (4’- Bromophenyl)-2, 2-Diphenylacetanilide and curarimimetic indoles were reported from flowers of giant reed *A. donax*.

The biochemicals have been isolated and identified from *Juncus effuses* plant which had the allelopathic potential for interactions [203]. Various glucosides have been reported from the pith of culms [204]. Allelochemicals present in *Juncus* sp. allelopathy was demonstrated [205]. These allelochemicals were, namely, antioxidant phenanthrenes from *Juncus acutus* [206], carotenoids, coumarins, sterols [207], A triterpene, cyloartanes [208], and phenol Juncunol [209] have been isolated and identified from *Juncus* sp. The biological activities of these compounds revealed their cytotoxic and antioxidant properties, and help to protect neurotransmitters, that is, anti-acetylcholinesterase [210].

Higher quantities of phenolic compounds and flavonoids have been documented in this macrophyte [211]. Antieczematic potential of *J. acutus* was reported due to the presence of phenolic glycosides, canthoside B, and caffeic acid. The rhizome of *J. acutus* exhibited antioxidant potential due to the presence of 8,8′-bidehydrojuncusol, juncunol, 5,7-dihydroxychromone, and flavone products (apigenin, luteolin, chrysoeriol, luteolin-7-O-β-glucoside, and hydrocarbon) [206]. These antioxidant compounds acted as anti-inflammatory, anti-algal, cytotoxic, and anti-leukemic elements. Moreover, Rodrigues [212] detected a significant *in vitro* cytotoxic effect of phenol, juncunol on human cancer cells (HepG2, MDA-MB468, and HeLa), possibly due to the radical scavenging activity of *J. acutus* species.

A perennial emergent tall grass of genus *Typha* possessed several natural products such as saponins, coumarins, and flavonoids. The phenolic compounds-typhaphthalide, typharin, flavonoids-afzelechin, epiafzelechin, [+]-catechin, and [-]-epicatechin and phytosterol-sitosterol were isolated from rhizomes of *Typha capensis* Rohrb. [213,214], fatty alcohol nonacosanol, and triterpene-lupeol acetate were detected in dry flowers and leaves of *Typha angustifolia*. Further, the cerebrosides, 1-O-(beta-d-glucopyranosyloxy)-(2S,3S,4R,8Z)-2-((2′R)-2′-hydroxy-tricosanoyl-amino]-8-nonadecene-3,4-diol) and 1-O-(beta-D-glucopyranosyloxy)-(2S,3R,4E,8Z)-2-((2′R)-2′-hydroxynonadecanoylamino)- 4,13-nonadecene-3-diol have been reported from pollen grains of the same species [215].

Typha species being medicinal grass have health benefits. Roots and rhizome are rich in starch and used as flour. They have observed significant antioxidant, cytotoxic [216], and immunosuppressive activity from pollen grains [217] in *T. angustifoli* while leaves and flower extracts of *Typha* sp. exhibited strong antibacterial potential against *Salmonella typhimurium*, *Pseudomonas aeruginosa*, *Escherichia coli,* and *S. aureus* [218]. Moreover, silver nano-sized particles made using *T. angustifolia* leaf extract harmed bacteria *E. coli* and *Klebsiella pneumonia* with greater antibiotic efficiency [219].

The phytochemical studies of *Cyperus rotundus* rhizomes have revealed the presence of polyphenol, a flavonol glycoside, saponin, sesquiterpenoids, essential oils, and Vitamin C. The most important biologically active compound reported from *C. rotundus* is cyperine. This volatile compound is used in Ayurveda as a tonic, diuretic, diaphoretic, and stimulant, hypotensive and anti-inflammatory. Alkaloids and terpenes have also been reported from rhizomes [220]. They have isolated 10 alkaloids and 25 phenolic compounds from this plant by GC-MS analyses. These compounds demonstrated inflammatory, anticancer antidiabetic, and antioxidant anti-antimicrobial properties [221,222]. Further, it contained a huge amount of tannins [223]. Its roots and rhizome have multidimensional therapeutic potential, including a diuretic and digestive juice and appetizer [224]. Acetone and methanol extract (70%) of the rhizome of *C. rotundus* possesses a good source of antioxidants [225]. Secondary metabolites such as phenols, flavonoids, and alkaloids produced by *C. rotundus* are valuable sources of modern drug design for chronic diseases such as cancer [226,227].

Eleocharis sp. was used in Chinese folk medicine for the treatment of pharyngitis, laryngitis, enteritis, cough, hepatitis, and hypertension [228]. It also inhibits natural acrylamide formation during food processing. It has diverse pharmacotherapeutic applications such as antioxidant, anti-depressant, and neuro disorders [229], a phenolic glucoside, leonuriside A, 2-hydroxymethyl-6-(5-hydroxy-2-methyl-phenoxy-methyl)-tetra-hydro-pyran-3,4,5-triol, and 1,4 dihydroxy 3-methoxy-phenyl-4-O-β-D-glucopyranoside showed good acrylamide formation activity.

Aquatic medicinal herbaceous plant *Bacopa monnieri*, a creeping small tropical plant with oblong leaves and light purple flowers, is known for its pharmacological effects due to the presence of chemical constituents isolated in India (*B. monnieri* Monograph 2004). It contains beta-sitosterol and linoleic acid. The former reduces inflammation in prostrate, whereas the latter is an anticancerous compound. Another medicinal plant *Eclipta alba* is a moisture-loving herb with small white flowers. Leaves of this plant contain resins, an alkaloid called eclitine chemical wedelolactone, etc. Wedelolactone, luteolin, and apigenin are antioxidant compounds isolated from this medicinal aquatic plant active against hepatitis C Virus [230].

The strong fungicidal effect of *B. monnieri* was illustrated due to the presence of high antioxidant activity [231]. They have identified flavonoids, glycosides, phenols, tannin, phlobatannin, saponin, steroid, and alkaloids from this medicinal plant. Major compounds were 9,12-octadecadienonic acid (36.96%), 9,17-octadecadienal (26.65%), 9-octadecenoic acid (7.79%) and *in vitro* roots yielded 9,12-octadecadienonic acid (25.62%), 9-octadecenoic acid (23%), and 9,17-octadecadienal (16.08%). *In vitro* roots subjected to salicylic elicitation comprised of 1,3-dihydroxyacetone dimmer (15.69%), 1-hexadecena (7.74%), 1-tetradecene (6.78%), eicosane (6.57%), 1-octadecene (5.29%), 1-decene (4.60%), E-15-heptadecenal (4.45%), and heptacosane (3.45%). *In vitro* elicited roots showed 36 compounds and an increasingly higher percentage of sesquiterpenoids and higher alkenes.

Schoenoplectus belonging to the family Cyperaceae, Bulrush (New World species) is closely related to Genus *Scirpus*. Secondary metabolites of this species have been isolated and identified. The biological activity test revealed that they exhibited toxicity to unicellular. More than 50 biochemicals have been reported from emergent *Schoenoplectus lacustris.* Mostly they are phenolic compounds.

Nasturtium officinale, one of the oldest known leaf vegetables for human beings harvested from a fast-growing aquatic plant belonging to family Brassicaceae, released 2-phenyl isothiocyanate which discouraged feeding by freshwater amphipods, cattle fish, and snails [232]. *Habenaria repens*, an aquatic orchid, contained a compound Habenaria (bis-p- hydroxybenzyl 2- alkyl-2 hydroxysuccinate) that protects the plant from crayfish [233]. Antioxidant activity is found highest in the aquatic tree *Neptunia oleracea* [234,235].

JOURNEY OF SECONDARY METABOLITES FROM AQUATIC TO TERRESTRIAL

Tracing the journey of secondary metabolites from early ancient plants to contemporary angiosperms is rather a difficult task. It is a universal truth that early land plant communities consisted of prokaryotic organisms, namely, bacteria and blue-green algae (Cyanophyceae). Later, being prokaryotic organisms, green algae were placed in photosynthetic bacteria in Monera by Whittaker [236] under five-kingdom classifications. Their secondary metabolites include polyketides, peptides, amino acids derivatives, fatty acids, and some terpenoids. Nevertheless, pathways like flavonoid biosynthesis were completely absent in prokaryotic organisms. The presence of oxidized sterols and xanthophylls in prokaryotes suggests that they were evolved under less availability of oxygen. Alkaloids were also absent in lower organisms.

Secondary metabolites covered a vast journey from primitive antibiotics in ancient groups to complexed flavonoids in higher terrestrial plants. In biological interactions, the most important secondary metabolite is terpenoid. Terpenoids are produced both by lower organisms as well as higher plants in aquatic and terrestrial habitats. They are highly significant in the identification of a taxonomic group in angiosperms. However, no particular secondary metabolite was a marker of a particular phylogenetic group of algae; nevertheless freshwater toxins were reported only from cyanobacteria from selected genera [236].

Volatile monoterpenoids and sesquiterpenoids are major components of essential oils characteristics of many terrestrial families, particularly Asteraceae and Verbenaceae. Like higher plants, terpenoids are also common in marine algae [237].

Besides terpenoids, algae can synthesize fatty acids, simple nitrogen compounds from amino acid pathways, polyketides, some simple phenolic compounds, tri-tetra terpenoids, and majority as steroids, sesqui, and diterpenes are also common. Mono terpenes are rare [238,239]. Carotenoids from marine algae are more complex and variable than present in terrestrial algae [240]. Tri-terpenes are not very common in marine alga [241]. Only green algae produce some halogenated compounds. Phaeophyceae algae predominate in temperate water bodies. These brown algae only produce polyphenolic compounds. Alkaloids, condensed tannins, and lignins which are peculiar in terrestrial plants are absent in all algal groups.

Land plants originated in the Silurian period from amphibian algae [242]. The former faced environmental stresses in terrestrial dry habitat particularly UV radiation harmful for DNA and protein cofactors [243]. In aquatic organisms, these wavelengths are largely attenuated by water hence did not influence significant mortality in aquatic organisms.

In aquatic environment, plants are suspended in the water column; hence, they require less protection from UV radiation. The evolutionary trend of biochemical products in lower aquatic plants is not evident [244]. They demonstrated that lower organisms (bacteria and algae) produced mycosporine-like amino acids (MAAs) as UV-absorbing compounds while higher plants synthesized flavonoids to protect themselves from ultraviolet rays. Ancestors of present-day land plants were cyanobacteria. They were exposed to a higher UV-B level [245].

Aquatic cyanobacteria and algae produce MAAs as UV absorbing compounds when exposed to UV-B fluxes, whereas upon migration to land, land plants such as pteridophytes, gymnosperms, and angiosperms instead of MAAs synthesized a complex flavonoid in terrestrial plants [245]. They reported that moss, however, does not produce flavonoids on an elevated quantity of UV-B radiation. Nevertheless, both compounds are equally efficient in absorbing UV-B radiations, indicating clearly a demarcation in the type of UV absorbing compounds synthesized by lower (algae) and higher aquatic plants (Hydrophytes). This difference in UV absorbing compounds corroborates the migration of higher aquatic plants from the terrestrial environment to aquatic.

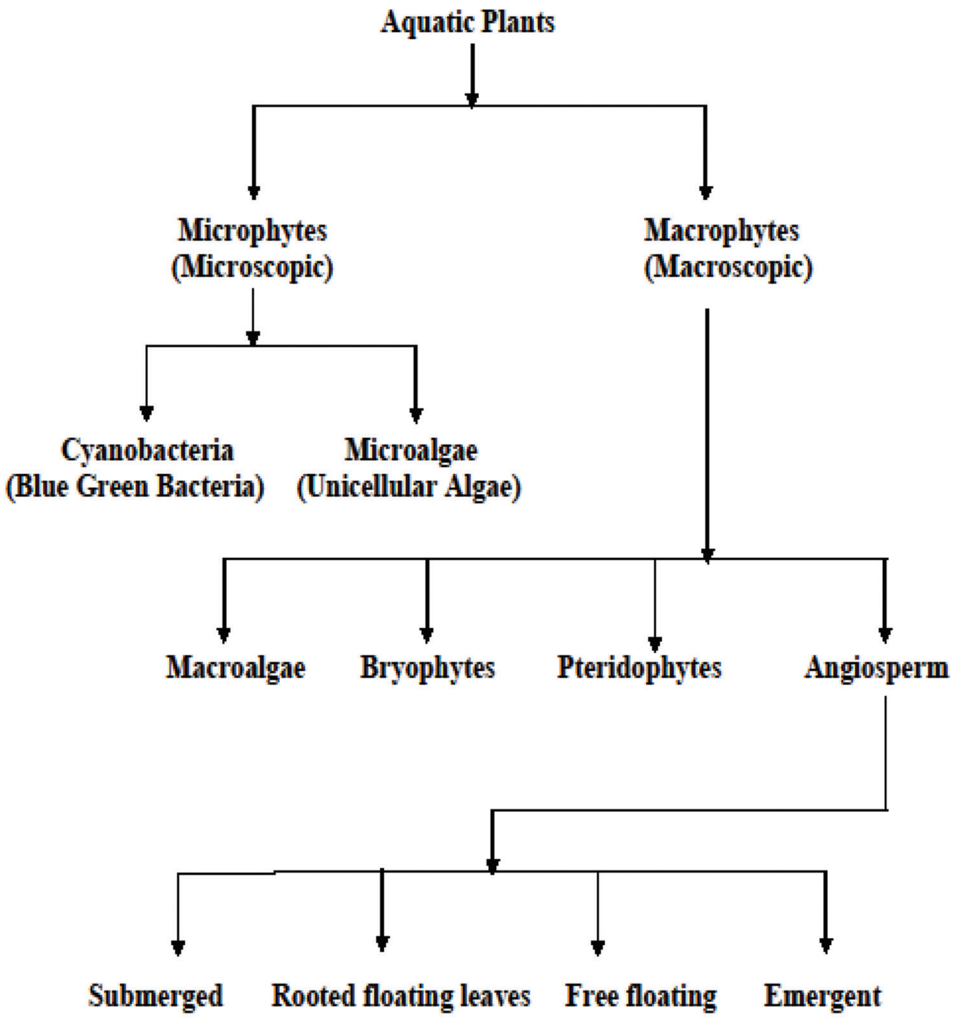

Fig. 2: Classification of aquatic plants

Land plants originated from charophycean lineage of green algae [246,247]. All algae and cyanobacteria produced MAAs as UV-absorbing compound except *Chara aspera*. All land plants possessed flavonoids from bryophytes to higher plants. As Chara (Charophycean) algae are being considered a link between algae and land plants, it does synthesize neither MAAs nor flavonoids [247]. Furthermore, an alga, *C. aspera,* belonging to Charophyceae serves an important link in between primitive aquatic algae and land plants as evidenced by the fact that neither MAAs is present in this species nor flavonoids, both were absent in *C. aspera*.

Importantly, aquatic submerged angiosperms (*C. demersum*, *Batrachium trichophyllum*, and *Potamogeton alpines*) synthesized flavonoids just like higher terrestrial plants. It has been established fact that higher aquatic plants, that is, angiosperms are more advanced than terrestrial plants [248]. It is documented here that higher aquatic plants are not producing MAAs as found in lower aquatic plants (algae). Similarly, monocot plants are more advanced and developed later than dicot plants. This is also evidenced by the fact that in monocot tissues, five but in dicot, only two flavonoids responded at higher UV-B.

The aquatic environment does not provide a vast variety of pathogens and predators as present in the terrestrial environment. That may be the reason aquatic plants have been screened less in search of defense molecules. The terrestrial habitats on the other hand expose more competitive conditions that support a greater number of bioactive biomolecules [249].

Temperature and moisture patterns affect the production of biomolecules. They may be secondary metabolites or allelochemicals. Under hot and dry environment, plant species produce aromatic compounds, whereas in the presence of water species produce phenolic

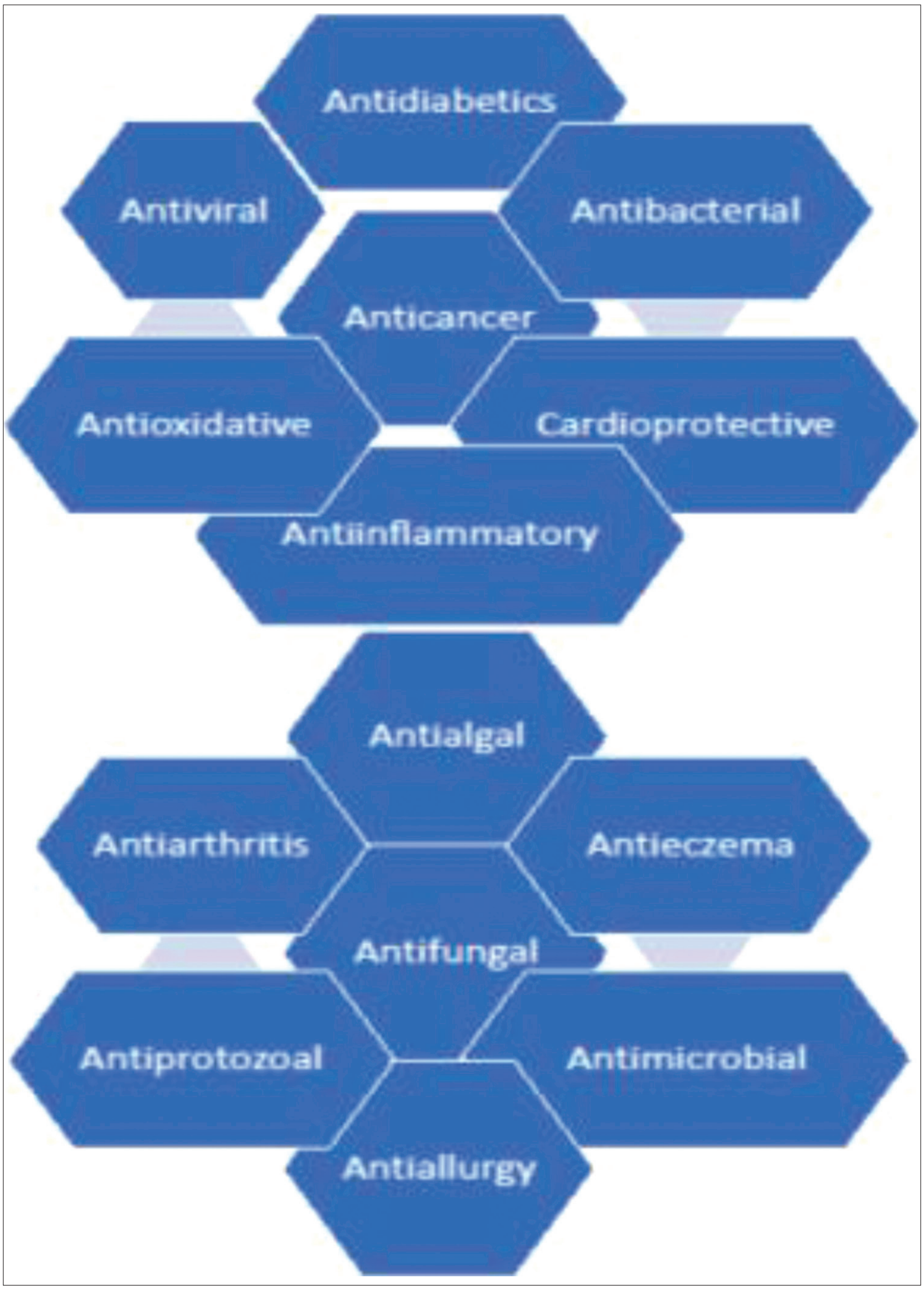

Fig. 3: Biological activity of various natural products isolated from aquatic plants

compounds [250]. He further explained the mechanism of removal of toxic compounds from the plant. Under the aquatic conditions, phenolic compounds are water-soluble hence leached out in the water. Volatile compounds are most efficiently escaped in dry conditions of terrestrial habitats hence more common in these plants.

CONCLUSION AND FUTURE PROSPECTS

Cyanobacteria produce characteristic toxins. Planktons and microalgae synthesize toxins like Microcystins, Domoic acid, Saxitoxins, and Yessotoxins. Chlorophyceae are rich in terpenes, whereas Rhodophyceae and Phaeophyceae produce phlorotannins and polyphenols, respectively (Fig. 2). The first land plants, bryophytes, are known to synthesis polyphenols, tannins, flavonoids, phenolic compounds, and terpenoids. In addition to this, pteridophytes also produce alkaloids. Flavonoids and carotenoids are identifiable markers of vascular aquatic plants and may serve as sunscreen for early land plants. The flavonoids of bryophytes are relatively complex and resemble those of many vascular plants. Terpenoids and phenolics are common secondary metabolites.

Eukaryotes originated from prokaryotes [251]. Therefore, genes for secondary metabolites have been introduced into the eukaryotic genome through prokaryotes called horizontal transfer. Aquatic macrophytes (angiosperms) are evolved from terrestrial plants [252]. It is believed that they somehow migrate to aquatic conditions and used to survive thereafter, developing some adaptation mechanisms in their structure. This is also evidenced by the secondary metabolites present in aquatic macrophytes (alkaloids, phenols, and flavonoids). However, in submerged plants such as *Ceratophyllum* and *Hydrilla* species, alkaloids are absent as plants are not exposed to the aerial environment. All algae and cyanobacteria produced MAAs as a UV-absorbing compound except Chara. All land plants possessed flavonoids from bryophytes to higher plants as a UV absorbing compound.

Further, aquatic plants are a potent source of natural bioactive molecules that can be used for the ailment of chronic diseases (Fig. 3). They are a natural source of antioxidants and are used to cure cancer, viral fever, diabetics, etc., without any side effects. Most of them are highly productive. They synthesize huge biomass in water bodies; therefore, efforts should be made to isolate medicinally important compounds from them. It will be cheaper and safe for human health.

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AUTHORS' CONTRIBUTIONS

MKS prepared overall concept of this review, drafted the manuscript and all aquatic informations and discussion part; NS compiled biochemical part of the script. SK performed all computational and designing work. MPD managed all chemical part of natural products and SD supervised overall written document and final editing.

CONFLICTS OF INTEREST

We all five have no conflicts of interest, neither financial nor personal or any other kind.

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