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BRYOPHYTES AS HIDDEN TREASURE

Assoc. Prof. Dr. Ozlem TONGUC YAYINTAS*

Canakkale Onsekiz Mart University, School of Applied Sciences, Fisheries Technology, Canakkale, Turkey, E-mail: ozlemyayintas@hotmail.com

Assist. Prof.Dr. Latife Ceyda İRKİN

Canakkale Onsekiz Mart University, School of Applied Sciences, Fisheries Technology, Canakkale, Turkey

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ABSTRACT

Bryophytes are the second largest heterogeneous group of terrestrial plants. The bryophytes placed taxonomically between Algae and Pteridophytes, are further divided into three classes; Hornworts (class Anthocerotae), Liverworts (class Hepaticae) and Mosses (class Musci). They are the most captivating exotic species on earth with distinguishing characteristics.

Bryophytes are rich in a variety of secondary biological active compounds. Bryophytes contain potentially useful natural products, including polysaccharides terpenoids, lipids, amino acids and phenylpropanoids. Bryophyte isolated compounds and extracts have cytotoxic, antimicrobial, insecticidal, antiviral, nematocidal effects on smooth and non-striated muscles, weight loss, plant growth regulation and allelopathic activities.

In the present review, the therapeutic uses of bryophytes were focused in detail. This will highlight bryophytes as potential source for phytotherapeutic remedies and chemical products used in different fields of chemistry, pharmacology, bioiogy and different branches of life sciences.

1. INTRODUCTION

The bryophytes comprises the liverworts (Marchantiophyta, 6.000 species), the hornworts (Anthocerotophyta, 300 species) and the mosses (Bryophyta, 15.000 species) were thought to be the second largest group of land pivotal plants after flowering plants in the early land plant evolution (Shaw and Renzalia, 2004). Bryophytes are characterized by dominant perennial gametophytic stages, with small and unbranched sporophyte remain attached to the maternal gametophyte (Cox *et al*., 2010). They may be that are important components in forest ecosystems and constitute a major part of the biodiversity in moist environments and mountain ecosystems (Hallingback and Hodgetts, 2000).

Bryophytes are found in habitats of every ecosystem and play a significant role in each ecosystems for example nutrient cycling, water economy or providing shelter for other organismal groups.

The size of bryophyte species varies from few millimeters to few metres. In liverwort *Monocarpus* to 0.7 m in the self supporting *Dawsonia superba* Turner and *Fontinalis antipyretica* Hedw. to 2 m as observed in the water habitat (Sabovljevic *et al*., 2016).

Some have a cuticle, some absorb water directly through leaf surfaces. They do not have true roots. They instead have multicelled, root like appendages called "rhizoids," which anchor the plants and take in water and minerals.

Bryophytes have pigments, chlorophyll a and b, xanthophyll and carotene. They store starch as energy saver molecule in plastids. Flavonoids are common in this group which is in accordance with their ability to cope with UV radiation (Sabovljevic *et al.,* 2016).

Bryophytes are important environmental indicators and have been used as predictors of climate change to validate climate models and potential indicators of global warming (Rao, 2009).

Bryophytes also can be important contributors to the total stream metabolism, nutrient cycling, food web interactions in streams and as direct food source for some vertebrates (Andrea *et al*., 2011). More importantly, some species are of great source for herbal medicine. Bryophyte are used as indicator species for erosion control, bioindicators of heavy metals in air pollution, aquatic bioindicators, radioactivity indicators, as material for seed beds, fuel, medicines and food sources, pesticides, nitrogen fixation, moss gardening, treatment of waste, construction, clothing, furnishing, packing, genetic engineering, for soil conditioning and culturing (Chandra *et al*., 2016).

Bryophytes are small biomass in various ecosystems and seldom part of ethnomedicine that rarely subject to medicinal and chemical analyses. Hundreds of natural products have been isolated from bryophytes. Bryophytes have potentially useful natural products, like polysaccharides, terpenoids, amino acids, lipids, quinones, phenylpropanoids and other specialized metabolites (Sabovljevic *et al*., 2016).

This slow growing group of plants is stockroom of naturally occurring materials and have been investigated for the antimicrobial, antioxidant, anti-inflammatory, anti-venomous and anti-leukemic activity (Mishra *et al*., 2014).

Bryophyte extracts and isolated compounds may be shown antimicrobial, antiviral, cytotoxic, nematocidal, insecticidal, effects on smooth and non-striated muscles, weight loss, plant growth regulators and allelopathic activities (Sabovljevic *et al*., 2016). In the recent years bryophytes has emerged as a potential biopharming tool for production of complex biopharmaceutiticals. Bryophytes considered as 'remarkable reservoir' of natural products and secondary metabolites, which show interesting biological activity could be used in medicine.

Bryophytes especially moss and liverworts are the source of many biologically active novel compounds pertaining to pharmaceutical uses (Singh *et al*., 2007). About 3.2 % of mosses and 8.8 % of liverworts have been chemically investigated. Species like *Bryum, Marchantia, Sphagnum, Octeblepharum*, *Riccia*, *Barbula*, and *Fontinalis* are used to treat different diseases such as cardiovascular diseases, fever, inflammation, lung diseases, infections, skin diseases and wounds (Glime, 2007).

Bryophytes are known to produce secondary metabolites to combat a number of stress condiotions such as microbial decomposition predation, extreme temperature and UV-radition. They are the large variety source of secondary metabolites, thus provide a great potential for biotechnological and biopharmaceutical applications for bryophytes (Xie *et al*., 2009).

Although bryophytes are important source of various plant derivatives but only few studies have been conducted to get an in depth knowledge regarding role of various metabolites of bryophytes. Present review focused on the therapeutic uses of bryophytes and the various phyotochemical and pharmaceutical constituents obtained from the bryophytes.

2. MATERIAL AND METHODS

In the present review, information about bryophytes, their medicinal properties and biochemical properties was gathered searching scientific databases including Elsevier, Google Scholar, PubMed, Springer, related books and manuscripts online or offline.

3. AIM OF THE PRESENT REVIEW

In the present review, scientific databases and pharmacological properties of bryophyte species were given.

4. MEDICINAL PROPERTIES

4.1. Ethnomedicinal Properties

In general, bryophytes never play a direct role in human life because the uses of bryophytes by ethnic people (for their healthcare or other needs) have been not exactly understanded. It is clear that these little plants do not have ethnobotanical importance in different cultures (Alam *et al.*, 2015). Because bryophytes produce little biomass per locality and are not often used as medicinal plants. However, the small size of these plants as well as usually not huge biomass in the nature, made these plants neglected for wide use.

Miller and Miller (1979), stated that the ancient method of determining the medicinal properties of a plant is 'doctrine signature'deals with resemblence of plant parts to structure and shape of organs in animal or human body for which it is remedial. As an example, some liverworts (e.g. *Marchantia polymorpha* L.) were believed to treat liver aliments because of its shape like liver. Similarly, *Polytrichum commune* Hedw. called hair cup moss, was used for hair treatment (Miller and Miller, 1979).

The first medicinal mosses are mentioned already in Renaissance herbals (by Fuchs, 1543 and Lobelius, 1581). From the 18th century, physicians were interested in using bryophytes as medicinal alternatives (Drobnik and Stebel, 2014).

Flowers (1957), indicated that the majority use of bryophytes as ethnomedicine reported from Chinese, Indian and Native American medicines. Bryophytes are highly used in horticulture in Far East, and Chinese and Indian people use them widely in ethno therapeutics (Kumar *et al*., 2000; Ando and Matsuo, 1984).

Chemical constituents of these plants have been used as biologically active agents. Many bryophyte compounds have shown biological activity with particular properties to their application in medicine and agriculture (Pant and Tewari, 1998). For example *Polytrichum commune* which is used as antipyretic and anti-inflammatory agent or boiled as a tea for treating the cold. *Rhodobryum giganteum* Schwägr is another species used to treat cardiovascular diseases or angina (Ando and Matsuo, 1984). In different parts of the world, different ethnic groups used plants to cure various diseases. Gaddi tribes people in India, used *Plagiochasma appendiculatum* Lehm. et Lind. for treating skin diseases (Kumar *et al*., 2000). Irular tribe used also *Targionia hypophylla* L. for skin diseases in Kerala state. In South India, people used hair-like thallus *Frullania ericoides* (Nees) Mont for hair-related afflictions (Remesh and Manju, 2009).

Gasuite Indians (Utah, USA) used species such as *Philonotis*, *Bryum*, *Mnium* and some hypnaceous forms to alleviate burn pains (Sabovljevic *et al*., 2001). Ding (1982) indicated that 40 species have been used in Chinese traditional medicine.

The liverworts *Conocephalum conicum* (L.) Dumort and *Marchantia polymorpha* (Hedw.) mixed with vegetable oils, are used as ointments for burns, eczema, cuts and bittes (Sabovljevic *et al*., 2016). For eye diseases, Chinese used Peat-moss *Spaghnum teres* (Schimp.) Ångstr. ex Hartm and for tonsillitis, bronchitis, cystitis and timpanitis. *Haplocladium microphyllum* (Hedw.) Broth. and *Polytrichum commune* Hedw. is widely used as a medicinal cure to antipyretic, diuretic and hemostatic properties (Chandra *et al*., 2016).

136 species bryophytes have been reported that used in ethnobotany for a variety of purposes (Harris, 2006). Nearly half of these species used for their pharmaceutical constituents (Table 1).

Asakawa (2001) indicated that, 500 bryophytes have been studied with respect to their chemistry, pharmacology and application as cosmetics and medicinal drugs in Asia.

Today, ethnobotany has become a crucial area of research and development in resource management of biodiversity. As tribal communities has their own health care systems. Their ancient knowledge referred to as ethno-therapeutics, has provided a more useful and effective strategy for the discovery of active drugs.

4.2. Therapeutical Properties

Bryophytes are natural reservoir products of secondary metabolites. These metabolites have shown biological activity used in pharmacology. Bryophytes especially moss and liverworts are the source of biological active constituents pertaining to pharmaceutical uses (Nath and Singh, 2007).

In past few years, more than 400 chemical compounds were isolated from bryophytes (Asakawa, 2007). Biologically active compounds obtained from mosses includes biflavonoids, terpenes, terpenoid and flavonoids whereas liverworts to contain a large variety of lipophilic mono-, di- and sesquiterpenoids aromatic compounds like bibenzyls, benzoates, cinnamates and naphtalenes (Asakawa, 2007).

Secondary metabolites of plants that are the potential therapeutic introduction of novel drugs has increased in recent years. Investigations on secondary metabolites of bryophytes have revealed the few original compounds, some of which are not isolated from higher plants.

Antibiotic resistant bacteria have motivated researchers to look forward for new plant based natural active compounds. Botanist and microbiologist indicated precious antibiotic substances in bryophytes. They have compounds such as alkaloids, polyphenolic acids and flavonoids.

The antibiosis of bryophytes has been studied in recent years. Some of the species of bryophytes like *Polytrichum* sp. and *M. polymorphya* are used against pulmonary tuberculosis and to treat gingivitis.

Antibiotic polyphenols were identified in *Atrichum, Dicranum, Mnium, Polytrichum* and *Sphagnum* sp. (McCleary and Walkington, 1966). Apigenin, luteolin, kaempferol and orobol glycosides and their dimers are also found in mosses (Zinsmeister *et al*., 1991; Basile *et al.*, 1999). Extracts of various medicinal plants containing flavonoids have been reported to show antimicrobial activity (Waage and Hedin, 1995).

Table 1. Ethanomedicinal uses of bryophytes

Species	Medicinal uses	References
Liverworts		
Riccardia sp.	anti-leukemic activity	Alam, 2012
Plagiochasma appendiculatum	skin diseases	Shirsat, 2008
Reboulia hemisphaerica	blotches, hemostasis, external wounds, and bruises	Asakawa, 2007
Conocephalum conicum	antimicrobial, antifungal, antipyretic, antidotal activity	Ding, 1982
Herbertus sp.	antiseptics, antidiarrheal agents, expectorants *and* astringents	Azuelo *et al.*, 2011
Frullania tamarisci	antiseptic activity	Asakawa, 2007
Frullania ericoides	to get rid from head lice and nourishment of hair	Remesh, 2009
Marchantia polymorpha	inflammation, used as diuretics, for liver ailments, insect bites, used to cure cuts, fractures, poisonous snake bites,	Hu, 1987
Marchantia convoluta	treatment of hepatitis, fever and gastric intolerance	Rao, 2009
Marchantia palmata	acute inflammation caused by the touch of fire and hot	Tag *et al*., 2007
Marchantia paleacea	skin tumefaction, hepatitis and as antipyretic	Sabovljevic *et al*., 2011
Dumortiera hirsuta	source for antibiotics	Azuelo *et al*., 2011
Pallavicinia sp.	antimicrobial agent	Azuelo *et al*, 2011
Plagiochila sp.	anti-leukemic activity/anti-microbial activity and used as perfumes or as perfume components	
Plagiochila beddomei	wound healing	Alam, 2012
Riccia sp.	mixed with jiggery and given to the children affected by the ringworms.	Lubaina *et al*., 2014

Targionia hypophylla	mixed with two tablespoons of coconut oil for scabies itches and other skin diseases	Remesh and Manju, 2009
Hornworts		
Ceratophyllum demersum	purgative, astringent, constipating and antipyretic	Pullaiah, 2006
Mosses		
Cratoneuron filicinum	heart disease	Pant and Tewari, 1998
Leptodictyum riparium	antipyretic in uropathy	Pant and Tewari, 1998
Philonotis fontana	to relieve pain of burn and heal burns, adenopharyngitis, antipyretic	Flowers, 1957
Philonotis sp.	heal burns, for adenopharyngitis, as antipyretic and antidote	Asakawa, 2007
Plagiopus oederi	sedative, epilepsy	Pant and Tewari, 1998
Bryum argenteum	antidote, antipyretic, antifungal	Asakawa, 2007
Rhodobryum giganteum	to treat cardiovascular problem and nervous prostration, to cure angina, anti-hypoxia, diuretic, antipyretic, and antihypertensive	Pant and Tewari, 1998
Rhodobryum roseum	to treat nervous prostration and cardiovascular diseases sedative	Wu, 1977
Leucobryum bowringii	body pain, paste of leaf tips mixed with *Phoenix sylvestris*	Lubaina *et al*., 2014
Oreas martiana	anodyne (pain), hemostasis, external wounds, epilepsy, menorrhagia and neurasthenia (nervosism, nervous exhaustion)	Asakawa, 2007
Ditrichum pallidum	for convulsions, particularly in infants	Pant and Tewari, 1998

Entodon flavescens	used during earache, leaf juice is used as ear drops, during cold, leaf juice is administered daily twice	Lubaina *et al.*, 2014
Fissidens nobilis	for growth of hairs and diuretic activity	Azuelo, 2011
Funaria hygrometrica	hemostasis, pulmonary tuberculosis, bruises, skin infection	Pant and Tewari, 1998
Fontinalis antipyretica	used in chest fever	Drobnik and Stebel, 2014
Taxiphyllum taxirameum	for external wounds, hemostasis	Asakawa, 2007
Aerobryum lanosum	used during burns, decoction of whole plant boiled in goat urine is applied externally	Lubaina *et al.*, 2014
Mnium cuspidatum	for hemostasis, nose bleeding	Pant and Tewari, 1998
Mnium sp.	to reduce pain of burns, bruises and wounds	Azuelo *et al.*, 2011
Plagiomnium sp.	for infections and swellings	Azuelo *et al.*, 2011
Octoblepharum albidum	used as febrifuge and anodyne	Singh, 2011
Dawsonia superba	used as diuretics, hair growth	Azuelo *et al.*, 2011
Polytrichum commune	used for hemostasis, wound healer, antipyretic, antidotal activity, dissolve kidney and gall bladder stones, to speed up labor process during child birth	Turner *et al.*, 1983
Polytrichum juniperinum	to treat prostate, uninary difficulties and skin ailments	Gulabani, 1974
Pogonatum macrophyllum	to reduce inflammation and fever, also used as detergent diuretic, laxative and hemostatic agent	Alam, 2012

Barbula unguiculata	to treat fever and body aches	Azuelo *et al.*, 2011
Barbula indica	used during menstrual pain and intermittent fever	Lubaina *et al.*, 2014
Hyophila attenuata	used during cold, cough and neck pain, leaf decoction is administered with a pinch of pepper powder daily	Lubaina *et al.*, 2014
Weisia viridula	to treat cold and fever	Asakawa, 2007
Sphagnum sericeum	used for dressing wounds, with anti-microbial properties for skin ailments (insects bites, scabies, acne), haemorrhoids and to treat eye diseases	
Sphagnum teres	to treat eye diseases	Ding, 1982
Haplocladium microphyllum	to treat cystisis, bronchitis, tonsillitis pneumonia and fever	Ding, 1982

Studies on *Platyphylla* and *D. scoparium* showed antimicrobial effects on the gram-positive bacteria *Bacillus subtilis*, *Staphylococcus aureus* and *Sarcinalutea*, but no activity against gram-negative *Escherichia coli* (Pavletic and Stilinovic, 1963).

Bryophytes have shown antibacterial activities against gram negative and gram positive bacteria (Basile *et al*., 1999).

Phenolic compounds isolated from *Dicranum, Atrichum, Polytrichum, Mnium,* and *Sphagnum* sp. showed antimicrobial properties (Mishra *et al*., 2014). Also lipids and fatty acids were analyzed in the general of families, *e.g.* Dicranacae, Ditrichaceae and Entodontaceae (Ichikawa *et al.*, 1983; Dembitsky *et al.*, 1993; Wasley *et al.*, 2006).

Nikolajeva (2012), indicated that the antimicrobial activity for two liverwort *Frullania dilatata* and *Lophocolea heterophylla,* and three moss species *Eurhynchium angustirete, Rhytidiadelphus squarrosus* and *Rhodobryum roseum* has been reported.

Decker *et al*., (2003) reported that aqueous extract of few bryophytes have some inhibitory effect on the growth of *E. coli*.

All bryophyte extracts showed a specific antifungal property against the plant pathogenic fungi depending on the concentration. Different crops like tomatoes, wheat and green pepper were infected with *Botrytis cinerea, Phytophora infestans* and *Erysiphe gramini.* After they were treated with alcoholic extracts of different bryophytes species. These alcoholic extracts of different bryophytes species showed antifungal activity for these crops (Frahm, 2014).

Neckera crispa and *Porella obtusata* extracts had showed fungicidal and antifeedant effects several times, and thus commercial product was developed as natural pesticide for Portuguese slug *Aarion lusitanicus* from *Neckera crispa* and *Porella obtusata* extracts (Frahm and Kirchoff, 2002).

Some of the moss and liverworts possess antioxidative activities which helps them to survive in the extreme climate and stress condition (Mishra *et al*., 2014). Heavy metal, desiccation and UV radiation have been found to cause an array of some different enzymes in bryophytes (Dey and De, 2012).

Bryophytes have been found to accumulate some metals and few others were able to insulates the toxic metals.

Antioxidant and free radical scavenging activities are in the focus of pharmacists and nutrition scientists. Free radicals are playing a role in the pathogenesis of many diseases (Castro and Freeman, 2001). Oxidation processes may also decrease the stability of drugs and foods. Bhattarai *et al*., (2009) indicated the potential of Antarctic mosses *Sanionia uncinata* and *Polytrichastrum alpinum* to be used as antioxidants for medicinal and cosmetic purpose.

Antioxidant property, scavenging activities and phenolic content of the aqueous extract of *Brachythecium rutabulum, Calliergonella cuspidata* and *Hypnum mammillatum* have investigated. *B. rutabulum* showed the higher phenolic property than other species (Chobot *et a*l., 2008).

Methanolic and ethylacetate extracts of *M. polymorpha* have also shown antioxidant property. Bryophyte could be the source of many antioxidants which could be used for novel drug discovery (Mishra *et al*., 2014).

Anti-leukemic activity has also been demonstrated in several compounds from leafy liverworts. A new enteudesmanolide called diplophyllin, was isolated from *Diplophyllin albicans* and *D. taxifolium.* Diplophyllin has an alpha-methylene lactone against human epidermoid carcinoma (KB cell culture). Marchantin A from *M. palacea, M. polymorpha,* and *M. tosana,* riccardin from *Riccardia multifida* and perrottetin E from *Radula perrottetii* show cytotoxicity against the leukemic KB cells (Chandra *et al*., 2016). Also compounds from *Plagiochila fasciculata* seemed to inhibit leukaemia (P388 cells) (Saxena and Harinder, 2004).

Apart from ethno-medicinal uses some bryophytes possesses antitumor activities against different cancer cells and thus bryophytes needs to be more focused on the next years.

5. CONCLUSION

Natural products derived from the plants can be used an alternative recipe for development of drug resistance in pathogens. Herbal compounds have been discovered with therapeutic potential. Bioactive compounds used as drugs are a new production system for major problems in medicine.

Bryophytes, a small group of plants, are an important source of biological active compounds. Many of the bryophytes are the source of medicinal recipes with antibacterial, antimicrobial, antifungal and anti-leukemic agents (Bhattarai *et al.*, 2009). Bryophytes being rich source of secondary metabolites could be a source of the bioactive compounds with immense therapeutic potential.

The current researches are going on the medicinal active constituents of bryophytes are used in curing diseases such as skin diseases, cardiovascular diseases, hepatic disorders and many more other ailments.

This evaluation and validation of traditional practices with medicinal active constituents of bryophytes provides significant opportunities for newer drug discoveries for human health care.

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