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Antioxidative Potential of Bryophytes: Stress Tolerance and Commercial Perspectives: A Review

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Abstract: Background: Bryophytes, phylogenetically placed between the algae and the vascular plants, are divided into three classes viz. Liverworts, Hornworts and Mosses. This small, slow-growing group of plants is often associated with disturbed habitat, barren rock surface and extreme climatic condition. Traditional system of medicine throughout the world has been utilizing the small group of plants to treat various ailments. Recent pharmacological investigations have proven that the active principles present in the group are quite unique and having tremendous therapeutic potential. Compounds present in bryophytes have been investigated for antiinflamatory, antimicrobial, antioxidant, antivenomous and cytotoxic activity. Bryophytes possess strong antioxidative enzymatic machinery which helps them to cope up with extreme climates and stresses. Results: The present review deals with the literature covering the potential of bryophytes as antioxidative agent, pharmacological investigations of antioxidants and induction of antioxidative system due to different kinds of stress *viz*. heavy metals, desiccation, radiation, salt etc. A number of antioxidative enzymes were found to be activated due to stress response. Some bryophytes were found to hyperaccumulate metals, some were able to sequester the toxic metal ions. These bryophytes are used as biomonitoring agents. **Conclusions:** In the present study the authors have found several reports of antioxidative properties found in liverworts and mosses. Herbs have already been used as a potent source of antioxidant in cosmetic and food supplement industry. Bryophytes can serve as a natural source of antioxidants which can be exploited in medicine and cosmetics. Although, the clinical efficacy of the active principles are subjected to further investigation, the therapeutic potential of this small plant group should not be ignored.

Key words: Bryophytes, antioxidants, heavy metal, desiccation, stress, nutrition

INTRODUCTION

Bryophytes are considered to be among the oldest land plants. Lack of economic importance, insignificant number and size and inconspicuous distribution have made bryophyte apparently of no use when compared to its tracheophyte cousins (Glime, 2007; Harris, 2008). Bryophytes have been investigated extensively for active constituents and pharmacological activity. Cytotoxic, anticancer and antitumour activity (Shi *et al*., 2008, 2009; Shen *et al*., 2010), antifugal (Niu *et al*., 2006; Veljic *et al*., 2010) and antibacterial property (Mitre *et al*., 2004; Ivanova *et al*., 2007), anti inflammatory response (Ivanova *et al*., 2007) in liverworts and mosses have been reported. The present review deals with the literature covering the antioxidative aspect of bryophytes.

Antioxidants are an endogenous defense system against Reactive Oxide Species (ROS) and are used in cosmetic and medicinal applications (Bhattarai *et al*., 2008a). Excessive accumulation of ROS leads to cellular injury in terms of damage to the DNA, protein and lipid membrane (Mittler, 2002). Excessive ROS must be eliminated from the living system by cells endogenous antioxidative defense mechanism activating an array of enzymes.

Different plant species have shown to have antioxidative potential. Antioxidants have been reported from angiosperms (Bernaert *et al*., 2011; Vanzani *et al*., 2011), gymnosperms (Seccon *et al*., 2010; Zhou *et al*., 2010), pteridophytes (Hort *et al*., 2008; Fu *et al*., 2010), fungi (Zan *et al*., 2011; Ozen *et al*., 2010), lichen (Bhattarai *et al*., 2008b; Kosanic and Rankovic, 2011), algae (Vijayavel and Martinez, 2010; Souza *et al*., 2011). Use of antioxidant as an alternative and complementary medicine against cancer is common at certain parts of the world (Thomas-Schoemann *et al*., 2011). In another study,

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the role of Manganese (Mn) superoxide dismutase in skin cancer has been recorded (Robbins and Zhao, 2011).

In this study, antioxidative potential of bryophytes have been discussed with a note on stress induced activity of antioxidative enzymes. Heavy metal, desiccation and ultraviolet radiation were found to activate an array of different enzymes in bryophytes. Photoperiod was found to play a role in antioxidative metabolism of this group.

METAL STRESS TOLERANCE

In trace amount, metal ions are essential for metabolic activity, growth and development of living species. But excessive amount of these metal ions are extremely harmful and toxic to the cells (Cinquetti *et al*., 2003). Others are known as non-essential elements without having any known metabolic function Heavy metals are non essential elements generated by environmental pollution and anthropogenic activities (Choudhury and Panda, 2004). Lack of significant cuticle or epidermis and well-developed conduction system, presence of one celled thick leaves have made them potent metal absorber, bioindicator and biomonitoring agent (Glime, 2007). Morphological, physiological and cellular response due to the heavy metal stress in bryophytes have been an interesting area of study for several years. Bryophytes serve as important bioaccumulators, because of their high absorbing and ion exchange capacities (Basile *et al*., 2005). Capacity of metal absorption enables using bryophytes as possible biomonitoring agent against environmental pollution. Species that thrive in metal rich habitat become tolerant due to hyperaccumulation of metals or sequestering of excessive metal ions without disturbing metabolic machinery. Heavy metal induced toxicity in plants includes alteration of enzyme activities, damage to chlorophyll biosynthesis and content, proline content and other physio morphological characteristics. Plants have evolved different enzymatic and non enzymatic processes to prevent oxidative damage. Oxidative damage due to heavy metals involves production of ROS like OH^- and O_2^- radicals. Membrane disintegration and lipid peroxidation are associated with oxidative response (Panda *et al*., 2003; Mishra and Choudhuri, 1996). As a result of which the levels and activity of antioxidative enzymes like superoxide dismutase (SOD), catalase (CAT), peroxidase (POD), ascorbate peroxidase (APX), glutathione reductase (GRD) and guaiacol peroxidases (GPX) are changed.

Increased concentration of Lead (Pb) and Nickel (Ni) was found to be responsible for increased POD and decreased SOD and catalase CAT activity in *Thuidium cymbifolium*. ROS and malondialdehyde (MDA) were accumulated in a dose dependent manner due to Pb and Ni stress. Thus POD plays an important role in elimination of ROS. *T. cymbifolium* can be used as a biomarker in pollution monitoring of Pb and Ni (Sun *et al*., 2009a). Pb and Ni had synergistic effect in moss *H. plumaeforme* to induce oxidative stress in high concentration. Single and combined metal stress was responsible for elevation of POD indicating its important role to resist ROS. The fluctuation CAT activity, hydrogen peroxide (H_2O_2) level and MDA content due to the metal stress could be exploited in the process of biomonitoring (Sun *et al*., 2009b). Dose-dependent accumulation of H_2O_2 was induced by Pb and Ni in *Hypnum plumaeforme*. Combined metal stress also resulted in increase of POD activity and decrease of APX activity. The data showed that Pb was more severe than Ni and both the metals had a synergistic effect in inducing oxidative stress in the moss (Sun *et al*., 2010a). *Brachythecium piligerum*, collected from Shanghai, China had shown different levels of SOD, POD, CAT, APX and lipid peroxidation and proline content when exposed to metal stress indicating its usefulness to be used as a possible biomarker (Sun *et al*., 2010b). *H. plumaeforme*, *T. cymbifolium* and *B. piligerum*, when exposed to short-term Pb and Ni stress showed different responses in terms of SOD and CAT activity. POD activity was increased in all three though. Studied indicated that to Pb and Ni stress, the most sensitive species is *B. piligerum* and the most tolerant species is *T. cymbifolium* among the three (Sun *et al*., 2011). Increased levels of SOD, CAT, APX, GRD and GPX were noted in the aquatic bryophyte *Fontinalis antipyretica* when exposed to different heavy metals, Cadmium (Cd), Copper (Cu) , Pb, Zinc (Zn) at different concentrations. MDA and lipid peroxidation levels were also changed. The species can be used as a potential biomarker in freshwater biomonitoring (Dazy *et al*., 2009). The activity of antioxidant enzymes was increased due to stress induced by Chromium (Cr) salts. Nitrate of Cr(III) was equally harmful as Cr (VI) (Dazy *et al*., 2008). Previously, correlation between polycyclic aromatic hydrocarbons (PAHs) accumulation and antioxidant enzymes was recorded in *F. antipyretica* (Roy *et al*., 1996). Phenanthrene, a PAH is responsible for oxidative stress in the aquatic liverwort *Riccia fluitans* (Burritt, 2008). The moss *Leptodictyum riparium* had shown antioxidant activity when stressed with Cd, Pb, salinity and heat shock. Activity of the acetone extract was tested by a chemiluminescence assay. Cd was found to be the most potent antioxidative agent among the four (Basile *et al*., 2011). CAT, GPX, GRD and SOD levels were changed, MDA content was increased, Nitrate Reductase (NR) was inhibited and total chlorophyll content was declined as a result of oxidative stress imposed by Cr, Cu and Zn in the moss *Polytrichum commune*. The enzymes CAT, GPX, GRD and SOD were also affected by metal toxicity (Panda and Choudhury, 2005). Increased amount of glutathione in Chilean endemic bryophyte *Thuidium* species could be in response to oxidative stress caused by Cd (Leinenweber *et al*., 2009). GPX and SOD activity in the leaves of the moss *Plagiomnium cuspidatum* was increased as an antioxidant defense reaction against H_2O_2 and superoxide anion (O_2(.-)) when treated with Cu (Wu *et al*., 2009). Following ultraviolet-B (UV-B) and Cd treatment the level of ascorbate, SOD and POD was found to be increased whereas CAT activity was decreased in *Riccia* sp. Generation of ROS, accumulation of H_2O_2 and inhibition of CAT activity were responsible for the oxidative damage when exposed to UV-B and Cd (Prasad *et al*., 2004). It has been reported that the genes of plant metabolic pathways are up or down regulated by Cd stress in the liverwort *Lunularia cruciata* (Basile *et al*., 2005). Oxidative stress in the moss *Taxithelium* sp. due to heavy metal has been reported (Panda, 2003). *T. nepalense*, when exposed to Pb and Arsenic (As), an increase in SOD and decrease in CAT, POD and GRD were noticed (Choudhury and Panda, 2004). DPHH assay was carried out and total phenol content was measured to evaluate antioxidant efficacy of some Colombian bryophytes *Breutelia chrysea*, *Dicranum frigidum*, *Leptodontium luteum*, *Sphagnum recurvum*, *Sphagnum* sp. and *Thuidium peruvianum* along with Inhibitory effect against the myotoxic phospholipase A_2 activity of *Bothrops asper* snake whole venom and the authors have tried to correlate the two (Pereanez *et al*., 2010).

DESICCATION TOLERANCE

Being the earliest land plants, Bryophytes are well adapted against oxidative stress (Nagae *et al*., 2008). Bryophytes are among the pioneer colonizers on barren rock surface and are found in certain extreme climates. They have adapted themselves in these conditions and have become stress tolerant species.

Antioxidants play a modulating role in tolerance to desiccation for long survival in the desiccated state by scavenging free radicals with a number of antioxidative enzymes (Kranner and Birtic, 2005). The correlation between desiccation tolerance and various activated oxygen-processing enzymes in the mosses *Tortula ruraliformis* and *Dicranella palustris* was reported (Seel *et al*., 1992). Oxidative stress was induced and SOD, GRD and APX levels were elevated when vanadate, an abiotic elicitor was added to the suspension-cultured cells of the liverwort *Calypogeia granulata* (Nakagawara *et al*., 1993). Damaging forms of activated oxygen may be prevented by a stable and carbon-centred radical when compared in some desiccation tolerant and intolerant moss species *in vivo* (Seel *et al*., 1991). SOD and CAT were not found to be responsible for desiccation tolerance induced by hardening treatment in the moss *Atrichum androgynum* (Mayaba and Beckett, 2003). Increase in MDA content in the gametophytes of thalloid liverwort *Monoclea forsteri* was indicated by oxidative damage during dehydration (Hooijmaijers, 2008). A novel extracellular 120 kDa germin-like protein (GLP) with Mn-SOD activity was isolated from the moss, *Barbula unguiculata* (Yamahara *et al*., 1999). Cu/ZnSOD gene was found to be induced by Cu in *B. unguiculata* (Nagae *et al*., 2008). GLP with Mn-SOD activity was also detected in the same species when exposed to salt stress (Nakata *et al*., 2002). GLP gene was reported from the moss *Physcomitrella patens* (Nakata *et al*., 2004). ROS metabolism in desiccation-stressed liverwort *Dumortiera hirsuta* thallus have been reported by Beckett *et al*. (2004). The ascorbate system is being utilized in *Brachythecium velutinum* and *Marchantia polymorpha* to remove H_2O_2 by APX. Less sensitivity of mosses towards draught could be due to an efficient water stress tolerance by ascorbate recycling system (Paciolla and Tommasi, 2003). Desiccation tolerance mechanism in the moss *Tortula ruralis* has also been reported by Oliver *et al*. (2000).

ROLE OF UV, PHTOPERIOD ETC.

Extreme habitat of certain bryophytes can be explained by high ultraviolet tolerance machinery present in some Antarctic moss (Clarke and Robinson, 2008). Defense mechanism of desiccation tolerance and UV-B tolerance in bryophytes may involve similar pathways (Takacs *et al*., 1999). Antioxidative metabolism in the moss *Atrichum undulatum* grown *in vitro* has been affected by photoperiod. ABTS [2,2'-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid)] method was applied to find out total antioxidative capacity. Bryophyte grown in Long Day (LD) was found to have higher antioxidative potential and phenolic contents when compared to the Short Day (SD) grown plants (Cvetic *et al*., 2009). Leaf litter degradation extracts (LLDEs) was found to enhance oxidative stress response in the aquatic bryophyte *Vesicularia dubyana* (Nimptsch and Pflugmacher, 2008).

SOURCE OF ANTIOXIDANT

Extract of *Plagiochasma appendiculatum*, an ethnomedicine used by *Gaddi* tribe in Kangra valley to treat skin diseases had shown antioxidant activity by preventing lipid peroxidation and increasing SOD and CAT activity. Besides that, the bryophyte was found to be a potent antimicrobial agent with wound healing activity supporting its ethnotherapeutic claim (Singh *et al*., 2006). Antioxidant activity of polar moss *Sanionia uncinata*, from King George Island (Antarctica) was analyzed for its antioxidant potential by BHT (butylated hydroxytoluene) method for reducing power, superoxide scavenging activity, ABTS cation scavenging activity and DPPH (1,1-diphenyl-2-picrylhydrazyl) activity. The data indicated its potentiality to be used as a possible source of antioxidant for medicinal and cosmetic purpose (Bhattarai *et al*., 2008b). Ohioensins F and G, the benzonaphthoxanthenones from the Antarctic moss *Polytrichastrum alpinum* had shown *in vitro* antioxidant property assayed by DPHH and ABTS methods. These mosses from the extreme environment can be exploited as a commercial source of antioxidant (Bhattarai *et al*., 2009). No correlation was found between the antioxidant activity and phenol content in certain mosses analyzed *in vitro* (Chobot *et al*., 2006). Antioxidant activity of ethanol extracts of *Atrichum undulatum*, *Polytrichum formosum*, *Pleurozium schreberi* and *Thuidium tamariscinum* have been evaluated (Chobot *et al*., 2008). Significant level of different isoforms of peroxidase and tyrosinase were present in the apoplast region of *Dumortiera hirsuta* (Li *et al*., 2010). Purification and Characterization of CuZn-superoxide dismutase (SOD) have been proformed from the suspension-cultured cells of liverwort *Marchantia paleacea* var. *diptera* (Tanaka *et al*., 1996; Tanaka *et al*., 1998). SOD and protochlorophyllide oxidoreductase genes in this variety of *Marchantia* are regulated by photosynthetic electron transport (Eguchi *et al*., 2002; Sakaguchi *et al*., 2004). *In vitro* antioxidant properties of acetonic extract of *Lunularia Cruciata* could be mediated by flavonoids and or sesquiterpenes (Ielpo *et al*., 1998). Radical-scavenging properties of Marchantins and some related polyphenols from liverwort were reported (Schwartner *et al*., 1996). Marchantin A had shown to be a potent antioxidative agent having free radical-scavenging activity besides being a cytotoxic molecule (Huang *et al*., 2010). Cytosolic APX from the liverwort *Pallavicinia lyelli* was purified and characterized (Sajitha Rajan and Murugan, 2010). Expression of the peroxide-detoxifying 2-cys peroxiredoxin (2-CP) in the liverwort *Riccia fluitans* chloroplast is regulated by ascorbate-modulated redox regulation involving a serine/threonine-kinase (Horling *et al*., 2001). Herbertane sesquiterpenes from the Tahitian liverwort *Mastigophora diclados* had shown radical scavenging activity (Komala *et al*., 2010a). Indonesian *Marchantia* sp. had investigated for radical scavenging activity. Various volatile sesqui- and diterpenoids could have been responsible for the property (Komala *et al*., 2010b). Subulatin, caffeic acid derivative and an antioxidant was isolated from *in vitro* cultures of some liverworts *Jungermannia subulata*, *Lophocolea heterophylla* and such as *Scapania parvitexta*. Antioxidative assay of the compound was carried out by the erythrocyte membrane ghost system and it was found that it may have a role in preventing photo-oxidative damage in the species (Tazaki *et al*., 2002). Antioxidant properties of *Sphagnum magellanicum* extract was measured by DPPH assay and it was found that the capacity is similar to the cabbage cultivar *Brassica oleracea* cv. *capitata* and superior to pumpkin (*Cucurbita pepo*). Montenegro *et al*. (2009) have suggested its potential use as an antioxidant.

CONCLUSION

Apart from some ethnic examples, Bryophytes are not used as a common source of food. Number of phenolics and other metabolites prevents them from being palatable (Glime, 2007). But proper investigation of nutritional aspect could generate a possibility of using them as food and/or food supplements. Total dietary fiber content in *Sphagnum magellanicum* was found to be 77%. Antioxidant capacity of the moss was found to be higher than certain common vegetables (Montenegro *et al*., 2009). High level of antioxidants present in liverworts and mosses can serve as a future source for medicinal and cosmetic purpose. Traditional medicinal use of bryophytes includes different ailments *viz*. skin disease, wound healing (Singh *et al*., 2006), inflammation (Tag *et al*., 2007; Namsa *et al*., 2009), viral diseases (Frahm, 2004) etc. The folklore use of bryophytes could be due to certain active compounds having antioxidant capacity. Ethnomedicinal use of different bryophytes should be scientifically investigated for active principles in order to bridge between traditional knowledge and pharmacology. Bryophytes are a rich source of biologically active compounds (Asakawa, 2007). The active constituents include phenolics, bibenzyls, mono, di, tri and sesquiterpenoids, flavonoids, dihydrostelbenes etc. Bibenzyls (Li *et al*., 2009; Cioffi *et al*., 2011), terpenoids (McNamara *et al*., 2005; Utkina *et al*., 2010; Nguelefack *et al*., 2011), flavonoids (Kris-Etherton and Keen, 2002) and phenolics (Pinelo *et al*., 2004; Ozturk and Tuncel, 2011) from the biological sources have been investigated for antioxidatve potential. Pharmacological investigations have been carried out in different bryophytes to find out their cytotoxic (Xiao *et al.*, 2006), antibacterial (Basile *et al.*, 1999), antifungal (Sabovljevic *et al.*, 2011), anti snake venom (Pereanez *et al.*, 2010) efficacy. A positive correlation between the folklore use and scientific evaluation could generate an alternative source of novel medicinal compounds which might overcome the ever expensive synthetic drug based chemotherapy and its long term side effects. Efficacy of these compounds is subjected to be tested clinically in future drug discovery programmes. The lack of literature involving the phytochemical and pharmacological investigation involving hornworts is a big lacuna in bryophyte research. Although this small and evolutionary important plant group has a worldwide distribution, very few reports are found on its active principles. This intermediate group of bryophyte could serve as a source of unique metabolites with antioxidative and other therapeutic potential.

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