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Therapeutic potential of bryophytes and derived compounds against cancer

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ABSTRACT

Bryophytes, taxonomically placed between the algae and the pteridophytes, are divided into three classes such as Liverworts, Hornworts and Mosses. Indigenous use involves this small group of plants to treat various diseases. Bryophytes have been investigated pharmacologically for active biomolecules. Several constituents with therapeutic potential have been isolated, characterized and investigated for antibacterial, antifungal, antiviral, antioxidative, antiinflamatory and anticancerous efficacy. The present review deals with the literature covering the anticancerous potential of bryophytes. Apart from the examples of the compounds and the containing bryophyte genera, the authors have tried to include the examples of cancer cell lines on which the efficacy have been tested and the mode of action of certain cytotoxic agents. Crude extracts and isolated compounds from bryophytes were found to possess potent cytotoxic properties. Different types of terpenoids and bibenzyls have been reported among the most potent cytotoxic compounds. Most of these compounds were found to induce apoptosis by activating a number of genes and enzymes. Biochemical markers such as DNA fragmentation, nuclear condensation, proteolysis of poly (ADP-ribose) polymerase, activation of caspases, inhibition of anti-apoptotic nuclear transcriptional factor-kappaB, activation of p38 mitogen-activated protein kinase etc. have been found to be associated with apoptotic and necrotic response. This review summarizes recent scientific findings and suggests further investigations to evaluate the cytotoxic efficacy of bryophytes.

1. Introduction

Plants and natural products have been used as a source of potential anticancer agents[1–8]. Antitumor agents such as vincristine, vinblastine the epiodophyllotoxin derivatives, maytansine, bruceantin, thalicarpine, camptothecin, and lapachol have been reported from higher plants and their pharmacology have been reported[9]. Members of Algae[10,11], Lichen[12,13], Fungi[14,15], pteridophytes[16,17], gymnosperms[18,19] and angiosperms[20,21] have been evaluated for cytotoxic properties. Traditional anticancerous and antitumourogenic plant reports have been pharmacologically investigated and in many cases scientists have found positive correlation between folklore use and scientific analyses[22,23].

Bryophytes are a small group of plants devoid of true vascular tissue. Being small and of insignificant use, bryophytes have been neglected in scientific investigations. Chemical analysis of active constituents and phytopharmacology of bryophytes came into the field only in the last few decades. With the advent of modern techniques and methods such as gas chromatography, gas chromatography-mass spectrometry, nuclear magnetic resonance, high performance liquid chromatography, high performance thin layer chromatography and X-ray crystallography, it has been possible to isolate and structurally elucidate bioactive molecules present in bryophytes[24]. Bryophytes serve as a source of biologically active, naturally occurring material[25–27]. Antifungal[28,29], antibacterial and antiviral[30–32], anti inflammatory[33], and antioxidative[34,35] potential in liverworts and mosses has been recorded.

The present review deals with the literature covering the cytotoxicity and related therapeutic potential of bryophytes. Several bryophytes have been screened for cytotoxic activity[36,37]. Crude extracts or various bioactive compounds have been isolated from liverworts and mosses for anticancerous

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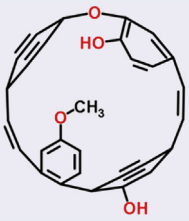
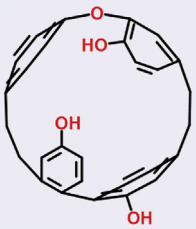
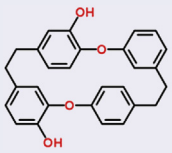
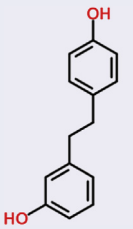
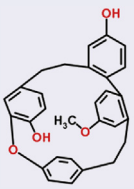
efficacy on cancer cell lines such as pharyngeal squamous carcinoma (KB), P-388 murine leukemia tumor, liver hepatoblastoma (HEP-G2), lung carcinoma (A549), breast ductal carcinoma (MDA-MB-435), and colon adenocarcinoma (LOVO) cell lines, glioma A172 cells, T98G, U87 glioma, osteosarcoma U2OS, leukemia HL-60, K562 and MDR K562/A02, MCF-7 breast cancer *etc*. For reversal activity analyses of multidrug resistance cancer cell lines, adriamycin-resistant K562/A02 cells, vincristine-resistant KB/VCR lines *etc* have been utilized. Cytotoxic efficacy of the bryophytes was reflected in terms of several biochemical markers of apoptosis and necrosis induction such as DNA fragmentation, nuclear condensation, proteolysis of poly (ADP-ribose) polymerase (PARP), activation of caspases (a family of cysteine aspartic proteases), inhibition of antiapoptotic nuclear transcriptional factor-kappaB, activation of p38 (mitogen-activated protein kinase) *etc*. Most/some of these genetic and biochemical machinery play a crucial role in apoptosis induction. Table 1 depicts the cytotoxic compounds isolated from bryophytes with their chemical structures, systematic names and molecular formula. Structures were taken from the chemical structure database http://www.chemspider.com.

2. Cytotoxic compounds from bryophytes

2.1. Liverworts

Liverworts contain a number of bioactive molecules which have been utilized to classify them chemosystemically[38,39]. Terpenes are naturally occurring hydrocarbons made up of several combined isoprene units. Bryophytes possess a number of terpenoid compounds such as mono, sesqui, di and triterpenoids, flavonoids, sterols and characteristic phenolic bibenzyls. Bibenzyls or dihydrostelbene are characteristic phenolic compounds found in liverworts. Apart from its occasional existence in some higher plants, these are absent in hornworts and mosses. Bis (bibenzyls) are derived from two bibenzyl units linked by some ether linkage[24]. The chemicals

Table 1
Structures of cytotoxic phytochemicals from bryophytes.

Cytotoxic phytochemicals from hepatics	Scientific names and molecular formulae
 Riccardin A	Systematic name (8Z,20Z)-5-Methoxy-14-oxapentacyclo[20.2.2.2^{10,13}.1^{15,19}.0^{2,7}]nonacosa-2,4,6,8,11,15(27),16,18,20,23,25,28-dodecaene-16,24-diol Molecular formula: $C_{29}H_{26}O_4$
 Riccardin C	Systematic name 14-Oxapentacyclo[20.2.2.2^{10,13}.1^{15,19}.0^{2,7}]nonacosa-1(24),2,4,6,10,12,15(27),16,18,22,25,28-dodecaene-5,16,24-triol Molecular formula: $C_{28}H_{24}O_4$
 Riccardin B	Systematic name 2,14-Dioxapentacyclo[20.2.2.2^{10,13}.1^{3,7}.1^{15,19}]triaconta-1(24),3(30),4,6,10,12,15(27),16,18,22,25,28-dodecaene-4,12-diol Molecular formula: $C_{28}H_{24}O_4$
 Lunularin	Systematic name 3-[2-(4-Hydroxyphenyl)ethyl]phenol Molecular formula: $C_{14}H_{14}O_2$
 Plagiochin D	Systematic name 19-Methoxy-2-oxapentacyclo[22.2.2.1^{3,7}.0^{10,15}.0^{16,21}]nonacosa-1(26),3(29),4,6,10,12,14,16,18,20,24,27-dodecaene-4,12-diol Molecular formula: $C_{29}H_{26}O_4$

(*continued on next page*)