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Pharmacological potential of genus *Marchantia*: A Review

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Abstract
Bryophytes are the second largest group of plants in the plant kingdom containing about 24000 species; they are well known to create an incredible range of biologically active compounds Marchantia is a dioecious liverwort found all over the world. It belongs to family Marchantiaceae. Marchantia has been mentioned in ancient Greek medical texts as a very useful plant, used in the prevention of infection and inflammation on open wounds. It has been used as a model system for investigating biological processes. Marchantia and liverworts are rich in flavonoid, tannins and phenolic compounds, the main constituent being Marchantian A which is an anticancer agent. This review article is an attempt to explore the pharmacological aspects of this miracle bryophyte.

Context: This review focuses on the study and compilation of pharmacological and therapeutic activities of genus Marchantia.

Aims: It was noted that pharmacological details related to genus Marchantia is not well documented. The present we have tried to compile information on pharmacological and therapeutic properties of genus Marchantia.

Methodology: Information related to Marchantia and related species, their pharmacological properties was gathered via extensively searching scientific databases which included Elsevier, Google Scholar, PubMed, Springer etc. and other related online/offline material.

Conclusions: This work congregates the botanical and pharmacological, information on Marchantia and related species. These plants have shown a huge potential in the field of medicine, and are being majorly used in treatment of hepatic disorders by various tribal communities all over the world. Studies on medicinal properties of marchantia are being carried in various laboratories regarding treatment of cancer, cardiovascular, hepatic and skin diseases. Development on new drug from marchantia is another field with a huge scope for the future.

Keywords: bryophytes, liverworts, marchantia, pharmacological uses

1. Introduction
Medicinal plants are being used all over the world for the treatment of ailments since ancient times, hence becoming a integral part of traditional medicinal systems at various parts of the world which basically include Ayurveda, Unani, Tibetan, Chinese and African medicine system with only a few differences on bases of culture [1].

Bryophytes contain 960 genera & 24000 species worldwide and yet they are considered insignificant for the economy. This is due to its small size and biomass. Bryophytes are used in ethno-therapeutics in India and China [2]. Although used as medicine, the use of bryophytes in research with respect to effect on human health has not been fully explored yet [3].

Bryophytes are well known to create an incredible range of biologically active compounds known to possess a typical odour, tanginess, and bitter taste, and they exhibit curious bioactivities and medicinal properties. Bryophytes are like stockroom of naturally occurring chemicals. Many of these chemicals show substantial biological activity. Investigations used to be hindered because of very little amount of plant material [4].

Despite of a long history of medicinal use by various communities throughout the world, significant utilization of bryophytes in medicines is still limited due to the lack of ethnobotanical information and scarcity of material. Harris documented the use of bryophytes as medicine in various parts of the world and compiled a list of about 150 species. According to the document bryophytes were explored medicinally by Natives of North America (28%) followed by China (27%). In India *Hortus Malabaricus* contains detailed account on use of bryophytes as medicine [5].

Marchantia is a common liverwort found all over the world. In the last decade extensive work has been carried out on genus Marchantia. Marchantia species have been described in ancient Greek medical texts as a plant that is useful in application on open wounds to prevent infection and inflammation. *M. polymorpha* is the only liverwort described in the earliest

floras after the Renaissance. *Marchantia* is a representative of an ancient lineage of land plants that colonized our planet millions of years ago hence becoming an important plant in the field of genetics [6, 7].

Fig 1: *Marchantia ploymorpha*

2. Material and Methods

Information related to Marchantia and related species, their pharmacological properties was gathered via extensively searching scientific databases which included Elsevier, Google Scholar, PubMed, Springer etc. and other related online/offline material.

3. Aim of review

It was noted that pharmacological details related to genus Marchantia is not well documented. The present we have tried to compile information on pharmacological and therapeutic properties of genus Marchantia.

4. Botanical Description

Marchantiales are Hepaticae in which the thallus is composed of several distinct layer of tissue, of which the upper most, the chlorophyll – bearing layer, nearly always enclosed air chambers, which have communication with the exterior through pores. The rhizoids are of two kinds, smooth and tuberculated. The sex organs are generally united in replicates often borne on long stalked archegoniophores respectively [8].

All species are terrestrial and cosmopolitan in distribution. The habitat of the species is moist and shady places like wet open woodlands, banks of streams, wood rocks or on shaded rocks, it is often seen that the plant grows best after the forest fire on burnt soil. The genus marchantia is distributed all over the world including about 65 species and out of these 11 species have been reported to be present in India. These species include *M. emarginata* (*M. palmata*), *M. assamica*, *M. paleacea* (*M. nepalensis*), *M. subintegra*, *M. polymorpha*, *M. robusta* (*M. indica*, *M. kashyapii*), *M. linearis*, *M. pandei*, *M. papillata* subsp. *grossibarba*, *M. hartlessiana* and *M. gemminata* [9, 10, 11].

The position of marchantia in Plant Kingdome is dipected in the following table.

Table 1: Systematic position of genus *Marchantia* in plant kingdom

Class	Hepaticopsida
Order	Marchantiales
Family	Marchantiaceae
Genus	Marchantia

5. Chemical Constituents

The major constituents of Marcantia include triterpenoids, flavonoids, and steroids. The flavonoids include quercetin, luteolin, apigenin and their glycosides [43]. Marchantin A, (cyclic bis (bibenzyl ether) and plagiochin E (macrocyclic *bis* (bibenzyl) was isolated from *M. emarginata* and *M. polymorpha* which was responsible for its anti cancer and antifungal activity respectively [18, 20]. In a study carried out on ether extract of *M. polymorpha* Gas chromatography-mass spectrometry (GC-MS) reviled the presence of isoprenoid compounds. These included thujopsene, acoradiene, ß-chamigrene, cuparene, ß - himachalene, γ-cuprenene, and α - chamigren-9-one [44] On analysing the volatile content of *M. convolute* obtained by Supercritical Fluid Extraction (SEF) method (using CO_2) and pet-ether extraction. 11 compounds were identified (using GCMS) that made up 73.62% of the SEF extract, ome of these compounds were 22, 23-dihydro-stigmasterol (31.26%), n-hexadecanoic acid (20.35%), stigmasterol (4.55%) and octadecanoic acid (5.75%), while pet-ether extract contained Hexadecanoic acid ethyl ester (36.97%), ethyloleate (10.47%), E-11-hexadecenoic acid ethyl ester (9.77%) and linoleic acid ethyl ester (4.63%) [43].

6. Pharmacological Activity of Marchantia

"Doctrine of Signatures" is an ancient method of determining the medicinal properties of plants it deals with resemblance of plant body part to the shape and structure of human or animal organ for which it is remedial. As per this philosophy, *Marchantia polymorpha* is used to cure hepatic disorders as its structure represents liver [12]. Plants belonging to Marchantiaceae family are well-known as traditional Chinese medicinal herbs, extensively used to treat skin swelling. These are used as hepatoprotectives for treatment of hepatitis, and as antipyretics [13, 14, 11].

6.1 Anticancer Activity

Xiao tested the cytotoxicity of three extracts (petroleum ether, ethyl acetate and n-butanol) from *Marchantia convoluta*, on human non-small cell lung carcinoma (H1299) and liver carcinoma (HepG2) cell lines. Cytotoxicity was determined by the 3-(4, 5-dimethylthiazol- 2-yl)-2, 5-diphenyltetrazolium bromide assay and reported in terms of cell viability. The ethyl acetate extract had a significant cytotoxicity against lung and liver carcinoma cells [15]. *Marchantia polymorpha*, showed the anticancer activity against human carcinoma of the nasophaynx [16, 12]. Marchantin A obtained from *Marchantia palacea*, *M. polymorpha*, and *M. tosana*, has shown cytotoxicity against the leukemic KB cells [17]. Huang WJ extracted Marchantin A from *Marchantia emarginata* sub sp. *tosana* which effectively actuated cell development restraint in human breast cancer cells (MCF-7) breast disease cells. Fluorescence microscopy and Western blot investigation demonstrated that Marchantin A initiated apoptosis of MCF-7 cells [18]. Sophie tested Marchantin A obtained from Icelandic *M. polymorpha* species, and found that Marchantin A prompts decrease in cell viability of breast malignancy cell lines A256, MCF7, and T47D. Fluorescence microscopy affirmed the antimicrotubular impact of Marchantin A [19].

6.2 Anti-microbial Activity

Plagiochin E (PLE) obtained from *Marchantia polymorpha L*. is an antifungal macrocyclic bis (bibenzyl). Xiu-Zhen studied the effects of PLE on *Candida albicans*. It was observed through Transmission Electron Microscopy (TEM) that the

structure of *C. albicans* cell divider was affected, which suggested that, the antifungal activity of PLE on *C. albicans* by inhibiting cell division [20]. Wu also illustrated that when exposed to PLE there is a decrease in ATP level of mitochondria, due to inhibitory effect on the activity of the mitochondrial dehydrogenases and increase of mitochondrial F_0F_1-ATPase. This demonstrated the antifungal mechanism of action of PLE [21]. Wu displayed that, Plagiochin E (PLE) initiated the apoptosis in *Candida albicans*. He inferred that PLE actuated apoptosis in *C. albicans* through a metacaspase-subordinate apoptotic pathway [22].

Ling gave detailed account of the impact of fluconazol (FLC) as antifungal action on Candida albicans by connecting Plagiochin E, Result of the study demonstrated that PLE inhanced FLC antifungal property by interfering with the FLC focused on ergosterol biosynthesis instrument [23].

Sabovljevi conducted experiments on *Marchantia polymorpha* growing naturally and on axenic media and evaluated them against five fungal species namely *Aspergillus versicolor, Penicillium ochrochloron, Trichoderma viride, Aspergillus fumigatus and Penicillium funiculosum*. All *Marchantia polymorpha* extracts showed activity against all the fungal stains. It was also noted that *Marchentia* grown *invitro* conditions displayed better antifungal activity compared to those extract prepared from plant material grown in nature [24].

Gahtori & Chaturvedi tested antifungal and antibacterial potential of methanol and chloroform extract of *Marchantia polymorpha* against gram negative bacterial strains of *Xanthomonas oryzae* pv *oryzae, Pasturella multocida* and *Salmonella enterica* and four fungal strains, *Tilletia indica, Fusarium oxysporum f. Sp. lini, Sclerotium rolfsii* and *Rhizoctonia solani.* Both extracts displayed significant activity against *X. oryzae* and *Pasturellamultocida*. The fungal strains S*clerotium rolfsii* and *Fusarium oxysporum*. Bacterial strain *Salmonella enterica* was resistant to both the extracts [25].

Crude methanol extract of *Marchantia polymorpha* was screened against three bacterial strains, namely, *Escherichia coli, Proteus mirabilis* (Gram negative), and *Staphylococcus aureus* (Gram positive), and four fungal strains, *Aspergillus flavus, A. niger, Candida albicans,* and *Trychophyton mentagrophytes*. The extract showed best activity against *S. aureus*. It was also noted that all the microorganisms were sensitive against the extract [26]. On testing methanol extract and free flavonoids extract of *M. polymorpha it was observed that* free flavonoids extract showed high percentage inhibition of *Fusarium oxysporum* (76.40%) while growth of *Rhizoctonia solani* was completely inhibited (100%) by methanolic extract and free flavonoids extract of *M. polymorpha* [27].

On examining ethanolic extracts of *Marchantia linearis* for antifungal activity. It was found that fungicidal impacts of naturally dynamic mixes from *Marchantia linearis* thallus ethanolic concentrate can be utilized as great possibility for the *in vivo* organic control of pathogenic growths, restricting the manhandle of synthetic fungicides [28].

Antibacterial action of Marchantin A was tested against Gram-positive (Streptococcus viridans, S. pyogenes, and *S. faecalis*, and Staphylococcus aureus) and Gram-negative (*Escherichia coli, Pseudomonas aeruginosa, Neisseria meningitidis, Pasteurella multocida. Haemophylus influenzae,* and *Proteus mirabilis*) organisms. The results showed that Marchantin A can be helpful in treatment of diseases cause due to *Staphylococcus aureus* and *Streptococcus pyogenes*. Marchantin A was active against Gram-negative *Pasteurella tnulfocida* and *Pseudotnonas aeruginosa*. Effectiveness of Marchantin A against *Neisseria meningitidis* and *Haemophylus influenzae* was moderate [29].

Antibacterical impact of *Marchantia convolute* extract (MCF) was studied using *Candida albicans, Pneumococcus, Streptococcus* pyogenes, *Salmonella typhi, Staphylococcus aureus, Bacillus enteritidis, Escherichia coli,* and *Pseudomonas aeruginosa* for the study. MCF repressed *S. typhi, S. aureus, Pneumococcus, Streptococcus* pyogenes, *B. enteritidis* and *E. coli*, It had no impact on *B. dysenteriae, C. albicans* and *P.aeruginosa* [14].

Rubina Khanam studied the *in-vitro* antibacterial activity of different extracts (petroleum ether, benzene, acetone, methanol, ethanol, and aqueous) of *Marchantia palmate* tested these extracts against the development of four human pathogenic gram negative microorganisms in particular *Escherichia coli, Pseudomonas aeruginosa, Proteus mirabilis, Klebsiella pneumonie* and two gram positive microscopic organisms *Bacillus subtilis* and *Staphylococcus aureus*. The plant demonstrated huge antibacterial activity against each one of the microorganism. The most extreme antibacterial activity was seen in metabolic extract against *E.coli* and least action was seen in petroleum ether remove against *K.pneumonie* [31]. *Marchantia convolute* extract is a potent inhibitor of coli bacillus, typhoid bacillus, *Staphylococcus aureus, Bacillus enteritidis*, hemolytic *Streptococci* type B and *Diplococcus pneumonia* [14]. Alam extracted Marchantin A from various *Marchantia* species like *M. chenopoda, M. polymorpha, M. paleacea, M. plicata,* and *M. tosana*. Marchantin A displayed significant antibacterial activity against *Acinetobacter calcoaceticus* [31].

6.3 Antioxidant Activity

Marchantia Sp. are rich source of natural antioxidant compounds (flavonoid, tannins and phenolics) playing a major role as free radical scavenging agents, hence giving the plant antioxidant property. Gokbulut Tested *M.polymorpha* for DPPH radical scavenging and ABTS antioxidant activity result showed that the IC_{50} value of the methanol extract of *M. polymorpha* was 0.4495 ± 0.029 mg/mL, and the ethyl acetate extract was 0.2756 ± 0.01 mg/mL, and ABTS antioxidant activity results show that IC_{50} value of the methanol extract of *Marchentia polymorpha* was 0.2441 ± 0.009 mg/mL, and the ethyl acetate extract was 0.2126 ± 0.01 mg/mL. This experiment established antioxidant activity of *M. polymorpha*. Phenolic compound (Luteolin) obtained from methanolic extract of *Marchantia* thallus and phenolic acids such as gallate, vanilate, chlorogenate, cinnamate, protocatechol, coumarate, ferulate, sinapic, caffeate and hydroxyl benzoate present in *M. polymorpha* are responsible for antioxidant activity [11, 32, 33].

6.4 Anti-inflammatory Activity

M. palmate used in treatment of acute inflammation due to fire or hot water. *M. polymorpha* relives pain from eruption of pimples on face or body other uses are same as *M. palmate.* [36] Ethanolic extract of Marchantia polymorpha was tested for its anti-inflammatory activity using inhibition of albumin denaturation method. The extract showed dose dependent inhibition of albumin. The anti-inflammatory activity was comparable to diclofena sodium [42].

6.5 Insecticidal Activity

In vivo insecticidal examination on *Spodoptera litura*

displayed critical antifeedant, larvicidal and pupicidal exercises at all the fixations against fifth instar hatchlings of *Spodoptera litura* [34].

6.6 Hepatoprotective Activity

Dried *M. convoluta* has been used to protect livers, and to treat tumefaction of skin traditionally in China. Xiao tested the pharmacological properties of *M. convoluta* flavonoids. It was observed that high dose of *M. convoluta* (40μg/mL) reduced the activity of ALT and AST in the serum of mice with acute hepatic injury caused by CCl_4 and increase the contents of TP and ALP. *M. convoluta* inhibited the auricle tympanites of mice caused by dimethyl benzene at high dose [35].

6.7 Miscellaneous Uses

M. polymorpha is used as antipyretic, antihepatic, antidotal, diuretic activity; used to cure cuts, fractures, poisonous snake bites, burns, scalds, and open wounds. Liverwort like *M. tosana* exhibited antifungal, antibacterial and antitumor activity [31, 37, 16]. *M. polymorpha* has been used as a diuretic in France [38, 39]. *M. polymorpha* also causes allergenic contact dermatitis but their allergens have not been isolated yet. [12] The ethnobotanical information on traditional medicinal use of *M. polymorpha* by the *Khampti* community of Arunachal Pradesh, India has been reported for the treatment of inflammation related diseases [40, 11]. *M. palmata* and *M. polymorpha* used as a medicine for treatment of boils. Thick paste of thalli is applied to the skin to reduce swelling and pus formation [41].

Table 2: Summary of Pharmacological Activities of *Marchantia* Species

S. No.	Marchantia Species	Phytochemical Use
1	*Marchantia chenopoda*	Anti bacterial
2	*Marchantia convolute*	Cytotoxic (H1299 & HepG2 cell lines), Anti viral (Hepatitis B), Antibacterial, Hepatitis, Fever and Gastric intolerance, Hepatoprotective, Anti-inflammatory, Diuretic
3	*Marchantia emarginata subsp. tosana*	Apoptosis of MCF-7 cells
4	*Marchantia linearis*	Antifungal, Insecticidal
5	*Marchantia palacea*	Antiviral (HIV-I) Cytotoxic and Apoptotic, Muscle relaxing, Antimicrobial, Antibacterial, Anticancer activity (Leukemic KB cells)
6	*Marchantia palmate*	Anti-inflamatory, Treats Boils, Antibacterial, Paste applied during acute inflammation caused by fire
7	*Marchantia plicata*	Antibacterial
8	*Marchantia polymorpha*	Anticancer, Boils and abcesses, Antipyretic, Antibacterial, Antifungal, Antidotal, Diuretic, Vaso-relaxant, 5-lipoxygenase, Muscle-relaxant, Farnesoid X-receptor (FXR) activation, Cardiotonic, Antioxidant, Antitrypanosomal, Antiviral, Tubulin polymerization inhibition, α-Glucosidase inhibitor, Antimicrobial, Decreases cell viability of A256 and T47D cell lines
9	*Marchantia tosana*	Anticancer, Antibacterial

7. Conclusion and future prospect

The present work congregates the botanical and pharmacological, information on Marchantia and related species. These plants have shown a huge potential in the field of medicine, and are being majorly used in treatment of hepatic disorders by various tribal communities all over the world. Studies on medicinal properties of marchantia are being carried in various laboratories regarding treatment of cancer, cardiovascular, hepatic and skin diseases. Development on new drug from marchantia is another field with a huge scope for the future.

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