BRAZILIAN BRYOPHYTE AS MEDICINAL PLANTS: A FORGOTTEN POT OF GOLD?

Milena Evangelista dos Santos[1,2], Maiara Bernardes Marquesa[2], Moan Jéfter Fernandes Costa[2], Pedro Henrique Sette-de-Souza[2]

[1] Author contact: milenaevangelista16@gmal.com
[2] Programa de Pós-Graduação em Saúde e Desenvolvimento Socioambiental – Universidade de Pernambuco campus Garanhuns – Garanhuns, Pernambuco, Brazil Programa de Pós-Graduação em Saúde e Desenvolvimento Socioambiental - PPGSDS, Universidade de Pernambuco campus Garanhuns - Rua Capitão Pedro Rodrigues, 105 - São José – Garanhuns/PE – Brasil. CEP: 55294-902. Phone/Fax: +558738226626.

Abstract

Constituting the second largest group of plants, bryophytes are characterized by not having lignified conducting vessels, thus belonging to the group of non-vascular plants. They have great ecological importance and have recently gained notoriety in medicinal studies. In Brazil, studies are still incipient, but they have already demonstrated the potential of some species against some microorganisms. This work aims to review the studies carried out in Brazil in order to gather the main information and serve as a basis for future studies. Linked to this factor, the pioneering study being carried out by the authors at the University of Pernambuco (UPE) is published, in which previously selected species occurring in the Caatinga are being tested against oral microorganisms.

Keywords: Medicinal plants; Mosses; Marchantiophyta; Anthocerotophyta.

Resumo

Constituindo o segundo maior grupo de plantas, as briófitas são caracterizadas por não apresentarem vasos condutores lignificados, sendo, assim, pertencentes ao grupo das plantas avasculares. Possuem grande importância ecológica e recentemente tem ganhado notoriedade frente aos estudos medicinais. No Brazil, os estudos ainda são insipientes, mas já demonstram a potencialidade de algumas espécies frente a alguns microrganismos. Esse trabalho, visa, fazer uma revisão dos estudos realizados no Brasil no intuito de reunir as principais informações e servir de base para estudos futuros. Atrelado a este fator, é divulgado o estudo pioneiro que está sendo realizado pelos autores na Universidade de Pernambuco (UPE), no qual, espécies previamente selecionadas, ocorrentes na Caatinga estão sendo testadas frente a microrganismos bucais.

Palavras-chave: Plantas Medicinais; Musgos; Marchantiophyta; Anthocerotophyta.

INTRODUCTION

Bryophytes constitute the second largest group of plants and represent the earliest plants to colonize terrestrial environments. This plant group exhibits diminutive, relatively simple structures, non-lignified conducting cells arranged for the transport of water and nutrients. Morphologically distinct from vascular plants, they are primarily characterized by a heteromorphic life cycle with a predominant gametophytic generation and a temporary sporophytic generation dependent of gametophyte for water and nutrition. They are distributed across three divisions: Marchantiophyta (liverworts), Anthocerotophyta (hornworts), and Bryophyta (mosses) (Goffinet, Buck, Shaw, [1] 2009).

The biological activity of medicinal plants has been the subject of intense scientific investigation. Given the search for new antimicrobials, drugs of plant origin stand out, as Brazil possesses the world's greatest biodiversity, and a variety of plants have been used and tested for numerous applications. Studies have shown that among plants, the most studied taxa are the group of angiosperms, little information is provided on other groups of plants, such as bryophytes, which include mosses, liverworts, and hornworts (Asakawa, [2] 1981). Although most plant medicines come from higher plants, including angiosperms, some species of mosses also have recorded antioxidant and antibacterial activity (Makajanma, Taufik, Faizal, [3] 2020).

Bryophytes are considered an important source of medicines and other pharmacological products, although some studies report the use of bryophytes as sources of antimicrobial compounds, antifungal, cytotoxic, antitumor, and insecticidal properties (Cascaldo-Cobianchi et al., [4] 1988; Asakawa, [5] 2007; Üçüncü, et al., [6] 2010). The medicinal potential of bryophytes and their applications is well known. In this context, a review of studies involving Brazilian bryophyte species for medicinal purposes will be presented. We also present a compilation of studies on the use of bryophytes and the status of studies in Brazil. It's work emphasizing the importance of researching compounds derived from bryophytes, given that they have long been overlooked in assays for obtaining pharmaceuticals and other pharmacologically relevant products. While there are some studies addressing the use of bryophytes as a source of bioactive compounds, there's a need for

further research aimed at elucidating the existence and potential of such bioactive compounds, particularly in Brazil.

The biological potential of Brazilian Bryophytes

According to The Plant List [7] (2023), they encompass approximately 20,000 species worldwide, with records of 1,710 species in Brazil (Flora and Funga do Brasil, [8] 2020). According to Costa & Peralta [9] (2015) the biomes with the highest number of species continues to be the Atlantic Rainforest, with 1,337 species, followed by the Amazon Rainforest (570 species), Cerrado (478), Pantanal (176), Pampa (120), and Caatinga (96). Studies about bryophytes in the country primarily focus on floristic investigation, taxonomy, ecology, and molecular aspects. In recent years, studies evaluating the chemical compounds and demonstrating biological activity in some bryophytes have been introduced into the realm of science, including in Brazil. However, the Brazil's contribution is still incipient, with only six of the published works.

In the table 1 was constructed based on the studies cited here and those mentioning bryophyte species occurring in Brazil, totaling 15 species. Mostly moss species are represented; no studies on hornwort species have been reported in the country. Given the above, the necessity for the development of investigative studies focusing particularly on the antimicrobial and antioxidant potential of bryophyte species becomes evident. The first Brazilian works in this thematic in the literature are conducted by Pinheiro, Lisboa, Brazão, [10] (1989) and analyzed bryophytes as a source of antibiotic compounds. In their study, the authors employed 25 bryophyte species, including mosses and liverworts, gathered from various periods and locations within the states of Amazonas and Pará. Only ten species exhibited positive results against the tested microorganisms, indicating a seasonal divergence.

Studies regarding the antibacterial activity of mosses, such as the study by Vidal et al., [12] (2012) evaluated the antibacterial effect of the moss *Octoblepharum albidum* Hedw. This work is the first to describe the modulation of antibiotic activity of the bryophyte *O. albidum* extract. According to authors previously mentioned the phytochemical screenings has revealed the presence of compounds such as tannins phlobaphenes, tannins pyrogallates, anthocyanins, flavones,

flavonols, flavonones, aurones, proanthocyanidins, alkaloids, and terpenes.

More recently, Costa et al., [12] (2018) analyzed the diversity of secondary metabolites in *Syzygiella rubricaulis* (Nees) Steph. in populations from Mexico, Venezuela, Ecuador, and Brazil, confirming the existence of 50 different components, with the predominance and richness of sesquiterpenes. The results demonstrate the increased solar radiation and the lower temperature at higher altitudes are assumed to have the most profound influence on plant secondary metabolism, corroborate by Zidorn, [13] (2010) and Shukla et al., [14] (2016).

Family	Specie	Medicinal implications	Citation
MARCHANTIOPHYTA			
Calypogeiaceae	*Calypogeia miquelii* Mont.	Inhibitory action of bacterial growth (*Edwardsiela tarda*)	Pinheiro, Lisboa, Brazão, [10] (1989)
Jamesoniellaceae	*Syzygiella colorata* (Lehm.) K. Feldberg et al.		
Lejeuneaceae	*Lejeunea boryana* Mont.	Inhibitory action of bacterial growth (*Staphylococcus aureus*)	Pinheiro, Lisboa, Brazão, [10] (1989)
Marchantiaceae	*Marchantia polimorfa* L.	Treatment for tuberculosis and liver conditions	Roig, Mesa, [15] (1945)
BRYOPHYTA			
Bryaceae	*Bryum capillare* Hedw.	Antimicrobial, antibiofilm, antioxidant, antigenotoxic and anticancer activities	Onbasli, Yuvali, [16] (2021)
Calymperaceae	*Calymperes lonchophyllum* Schwägr.	Inhibitory action of bacterial growth (*Escherichia coli*)	Pinheiro, Lisboa, Brazão, [10] (1989)
	Octoblepharum albidum Hedw.	Inhibitory action of bacterial growth (*Escherichia coli*, *Klebisiella pneumoniae*, *Pseudomonas aeruginosa*, *Shigella flexneri*, and *Staphylococcus aureus*)	Vidal et al., [11] (2012) and Onbasli, Yuvali, [16] (2021)

Hedwigiaceae	*Hedwigia ciliata* (Hedw.) P. Beauv.	Antioxidant, antitumor, antiproliferative, anti-inflammatory, neuroprotective, antibacterial, and antifungal	Canli et al., [17] (2012) and Lunić, Božić, Nedeljković, [18] (2022)
Lembophyllaceae	*Orthostichella rigida* (Müll.Hal.) B.H.Allen & Magill	Inhibitory action of bacterial growth (*Cryptococcus neoformans*, *Listeria monocytogenes*, *Staphylococcus aureus*, and *Salmonella enteritidis*)	Klegin et al., [19] (2020)
Leucobryaceae	*Campylopus savannarum* (Müll. Hal.) Mitt.	Antioxidant, antibacterial, and antifungal	
	Leucobryum martianum (Hornsch.) Hampe *ex* Müll. Hal.	Inhibitory action of bacterial growth (*Escherichia coli* and *Salmonella* sp.)	Pinheiro, Lisboa, Brazão, [10] (1989)
Leucomiaceae	*Leucomium strumosum* (Hornsch.) Mitt.	Inhibitory action of bacterial growth (*Edwardsiela tarda*, *Klebisiella pneumoniae*, *Proteus vulgaris*, and *Staphylococcus aureus*)	Pinheiro, Lisboa, Brazão, [10] (1989)
Polytrichaceae	*Polytrichum commune* L. *ex* Hedw.	Treatment of kidney and gallbladder stones	Roque, [20] (1941)
Sphagnaceae	*Sphagnum papillosum* Lindb.	Synergistic activity (*Staphylococcus aureus*)	Mellegard et al., [21] (2009)
	Sphagnum magellanicum Brid.	Antimicrobial activity	Klavina et al., [22] (2015)

The study by Klegin et al., [19] (2020) evaluated the antimicrobial activity in *Orthostichella rigida* (Müll. Hal.) B. H. Allen & Magill, collected at different times of the year. The extracts from the summer, autumn and winter seasons were more efficient to reach Seasonal influence is statistically evident in spring, which has demonstrated minor antimicrobial activity when compared with the other seasons. In this study, the compounds of *O. rigida* has demonstrated a rising potential for future research and possible use as a natural antimicrobial.

The more recent work published, Muniz et al., [23] (2023), evaluated the chemical composition and the antimicrobial, antioxidant, and cytotoxic potential of the fractionated extract of *Campylopus savannarum* (Müll. Hal.) Mitt. The authors can be found alkaloids, triterpenoids, steroids, and phenol in this specie. The evaluation of the biological potential of the fractionated extracts of *C. savannarum* showed promising data, in the search for natural antimicrobial compounds. Also, here we provided consistent findings that indicate the antimicrobial, antioxidant, and non-toxic potential.

Currently, a group of researchers, including the authors of this article, are leading investigations to assess the antioxidant, antimicrobial, and antibiofilm potential using bryophytes from the Caatinga. In addition to identifying the chemical compounds present in the studied species, researchers are conducting more specific tests with bacterial strains related to oral health. It is a pioneering effort that promises significant contributions to science. Despite an increase in studies evaluating the antimicrobial activity of bryophytes, particularly in the last 5 years, publications on this topic are still scarce in the word, especially in Brazil. This indicates a wide field of study to be explored, invested in, and published, primarily due to the vast diversity of moss species occurring in the country. Furthermore, this study contributes to a better understanding of the state of the art regarding antimicrobial activity in bryophytes, enabling a more targeted approach to research aimed at filling gaps and making an effective contribution to science.

Phytochemical profile of Brazilian bryophytes with biological activity

Brazilian bryophytes, particularly species from the Bryaceae, Calymperaceae, and Hedwigiaceae families, display a diverse phytochemical profile (Supplementary 1). *Bryum capillare*, a species within Bryaceae, is rich in flavonoids like luteolin, apigenin, and their glycoside derivatives, known for their antimicrobial, antioxidant, and anti-inflammatory effects. These flavonoids directly impact bacterial cell walls, destabilizing membranes and inhibiting protein synthesis, contributing to significant antibacterial activity against pathogens such as *Staphylococcus aureus*. The synergistic effects of these compounds with other plant metabolites enhance their antimicrobial potency, particularly against biofilm-associated infections, which are common in hospital environments where bacterial resistance poses substantial challenges (Onbasli, Yuvali, [24] 2021).

In the Calymperaceae family, *Octoblepharum albidum* stands out due to its composition of terpenes and fatty acids, including dodecanoic acid and neophytadiene. These compounds exhibit robust antimicrobial action against bacteria. Terpenes and fatty acids are known to disrupt bacterial cell membranes and metabolic pathways, thus reinforcing the plant's broad-spectrum antibacterial activity. Additionally, these bioactive molecules have anti-inflammatory properties, which not only combat bacterial infections but also mitigate inflammation, making *Octoblepharum albidum* suitable for treating infections that involve inflammatory responses (Vidal et al., [11] 2012; Onbasli, Yuvali, [24] 2021).

The *Hedwigia ciliata* from the Hedwigiaceae family contains an array of luteolin and apigenin derivatives, which contribute to its powerful antioxidant, antimicrobial, and anti-inflammatory properties. These antioxidants neutralize free radicals, reducing oxidative stress and aiding tissue regeneration during infections. The antimicrobial action extends to both bacterial and fungal pathogens, suggesting a dual role in managing infections while supporting cellular health. Such properties make *Hedwigia ciliata* particularly valuable for topical formulations aimed at preventing microbial infections and soothing inflammation in cutaneous conditions (Canli et al., [17] 2012; Lunić, Božić, Nedeljković, [18] 2022).

The diverse range of specialized metabolites in Brazilian bryophytes further highlights their pharmaceutical potential. *Calymperes lonchophyllum* and *Lejeunea boryana* contain various phenolic compounds and terpenes, which play a critical role in antibacterial action by interacting with microbial enzymes and disrupting essential cellular processes. This action not only hinders bacterial growth but also demonstrates selective efficacy against drug-resistant strains, providing an alternative approach to conventional antibiotic therapies, which are increasingly challenged by resistance (Pinheiro, Lisboa, Brandão, [10] 1989).

Furthermore, the presence of complex bioactive structures in *Polytrichum commune*, from the Polytrichaceae family, including compounds such as ohioensins and communins, contributes significantly to its medicinal efficacy. Known for its use in traditional medicine, *Polytrichum commune* contains monoterpenes and diterpenes that possess anti-inflammatory, diuretic, and potentially nephroprotective properties, making it beneficial for treating conditions like kidney and gallbladder stones. The antimicrobial properties of these terpenes are also notable, as they create hostile environments for bacterial pathogens by disrupting lipid membranes and inhibiting cellular respiration. Such multifunctional attributes illustrate the potential for these bryophytes in addressing both microbial infections and inflammatory conditions simultaneously (Roque, [20] 1941).

Another remarkable species, *Sphagnum magellanicum* from the Sphagnaceae family, produces a spectrum of fatty acids, including octadecanoic and hexadecanoic acids, alongside compounds like squalene and betulin (Klavina et al., [22] 2015). These compounds offer a dual role in enhancing antimicrobial and antioxidative defense. Squalene and betulin contribute to skin barrier protection, supporting wound healing while preventing microbial invasion. *Sphagnum* species have been traditionally utilized for their synergistic effects against *Staphylococcus aureus*, demonstrating a unique combination of wound-healing and antimicrobial properties that could be harnessed for developing advanced topical and wound-care products.

Together, these findings reveal that Brazilian bryophytes, with their diverse phytochemical profiles, not only offer targeted antimicrobial and anti-inflammatory benefits but also present opportunities for comprehensive therapeutic applications. Their natural efficacy against bacterial, fungal, and inflammatory conditions highlights their value in both traditional and modern medicine, providing a rich foundation for further exploration in pharmacology and clinical applications.

References

1. Goffinet B, Buck WR, Shaw AJ. Morphology, anatomy, and classification of the Bryophyta. Pages 55-138, In: Goffinet B, Shaw AJ. (Editors), Bryophyte Biology, 2 ed. Cambridge University Press, Cambridge; 2009. 610 p.

2. Asakawa Y. Biologically active substances obtained from bryophytes. The Journal of the Hattori Botanical Laboratory. 1981;50:123-142.

3. Makajanma MM, Taufik I, Faizal A. Antioxidant and antibacterial activity of extract from two species of mosses: *Leucobryum aduncum* and *Campylopus schmilii*. Biodiversitas Journal of Biological Diversity. 2020;21:1-66.

4. Cascaldo-Cobianchi R, Giordano S, Basile A, Violante U. Occurrence of antibacterial activity in *Conocephalum conicum*, *Mnium undulatum* and *Leptodictyum riparium* (Bryophytes). Giornale Botanico Italiano. 1988;122:303-311.

5. Asakawa Y. Biologically active compounds from bryophytes. Pure and Applied Chemistry, 2007;79(4):557-580.

6. Üçüncü O, Cansu TB, Ozdem˙IRT, Karaoglu SA, Yayli N. Chemical composition and antimicrobial activity of the essential oils of mosses (*Tortula muralis* Hedw., *Homalothecium lutescens* (Hedw.) H. Rob., *Hypnum cupressiforme* Hedw., and *Pohlia nutans* (Hedw.) Lindb.) from Turkey. Turkish Journal of Chemistry. 2010;34(5):825-834.

7. The plant List. Bryophytes. Available on < https://wfoplantlist.org/> accessed 10 Jun 2023.

8. Flora and Funga do Brasil. Briófitas. Available on: https://floradobrasil.jbrj.gov.br. Accessed 10 Nov. 2024.

9. Costa DP, Peralta DF. Bryophytes diversity in Brazil. Rodriguésia. 2015;66(4):1063-1071.

10. Pinheiro MFS, Lisboa RCL, Brazão RV. Contribuição ao estudo de briófitas como fontes de antibióticos. Acta Amazonica. 1989;19:139-145.

11. Vidal CAS, Sousa EO, Fabíola FGF, Campos AR, Lacerda SR, Costa JGM. Phytochemical screening and synergistic interactions between aminoglycosides, Selected antibiotic and extracts from the bryophyte *Octoblepharum albidum* Hedw. (Calymperaceae). Archives of Biological Sciences. 2012;64(2):465-470.

12. Costa DP, Amado-Filho GM, Pereira RC, Paradas WC, Miyataka H, Okamoto Y, Asakawa Y. Diversity of secondary metabolities in the liverwort *Syzygiella rubricaulis* (Ness) Steph. (Jamesoniellaceae, Marchantiophyta) from Neotropical high mountains. Chemistry & Biodiversity. 2018;15(9):e1800239.

13. Zidorn C. Altitudinal variation of secondary metabolites in flowering heads of the Asteraceae: trends and causes. Phytochemical Reviews. 2010;9:197-203.

14. Shukla V, Patel DK, Bajpai R, Semwal M, Upreti DK. Ecological implication of variation in the secondary metabolites in Parmelioid lichens with respect to altitude. Environmental Science and Pollution Research. 2016;23:1391-1397.

15. Roig J, Mesa JT. Plantas medicinales, aromáticas o venenosas de Cuba. Hahana, Ministério de Agricultura, Servicio de Publicidad y Divulgation. 1945. 75 p.

16. Onbasli D, Yuvali G. *In vitro* medicinal potentials of *Bryum capillare*, a moss sample, from Turkey. Saudi Journal of Biological Sciences. 2021;28:478-483.

17. Canli K, Cetin B, Altuner EM, Turkmen Y, Uzek U, Dursun H. In vitro Antimicrobial Screening of *Hedwigia ciliata* var. *leucophaea* and Determination of the Ethanol Extract Composition by Gas Chromatography/Mass Spectrometry (GC/MS). Journal of pure and applied microbiology. 2012;8(4):2987-2998.

18. Lunić T, Božić B, Nedeljković BB. Immunomodulatory Potential of *Hedwigia ciliata* and *Hypnum cupressiforme*. Living reference work entry. 2022;46:1-29.

19. Klegin C, Enio LJ, Eduardo ME, et al. Evaluation of the antimicrobial activity of ethanol extracts from *Orthostichella rigida* (Mull. Hal.) B.H Allen Magill (Bryophyta) on pathogenic microorganisms. Journal of Medicinal Plants Research. 2020;14(3):98-104.

20. Roque JM. Flora Medicoguatamalteca. I. Guatemala, La tipografia Nacional. 1941. 200 p.

21. Mellegard H, Stalheim T, Hormazabal V, Granum PE, Hardy SP. Antibacterial activity of sphagnum acid and other phenolic compounds found in *Sphagnum papillosum* against foodborne bacteria. Letters in Applied Microbiology. 2009;49:85-90.

22. Klavina L, Springe G, Nikolajeva V, Martsinkevich I, Nakurte I, Dzabijeva D, Steinberga I. Chemical composition analysis, antimicrobial activity and cytotoxicity screening of moss extracts (moss phytochemistry). Molecules. 2015;20:17221-17243.

23. Muniz AR, Jesus LS, Marques EJ, Vale VLC, Valente EB. Chemical and biological profile of the fractionated extract of the species *Campylopus savannarum* (Müll. Hal.) Mitt. Journal of Biology. 2023;83:e273243.

24. Onbasli D, Yuvali G. *In vitro* medicinal potentials of *Bryum capillare*, a moss sample, from Turkey. Saudi Journal of Biological Sciences. 2021;28: 478-483.