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Literature Review

Therapeutic Applicability of Fruticose Lichens: A Brief Review on *Pseudevernia furfuracea*

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Abstract

The distinctness in the chemical profile of fruticose lichens marked their versatile applications from culinary, dyeing, to modern therapeutics. *Pseudevernia furfuracea*, commonly known as Tree Moss, has been used from the Ancient Egyptian era to the Modern World. It has exemplary applicability in embalming the dead bodies and has also been used in perfume-making industries. It is a rich source of distinct bioactive constituents reported to exert different Pharmacological activities. Constituents, including depsides, depsidones, orsellinic acid derivatives, pulvinic acid derivatives, aromatic polyketides, and phenolic acids, have been identified in the species via chromatography and spectroscopic approaches. It has been reported to exhibit anticancer, antioxidant, antimicrobial, anti-inflammatory, enzyme-inhibiting, and antifungal activities. Apart from its reported bioactivities, its biomonitoring potential further strengthens the significance of this species.

More Information

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Keywords: Lichen; Anti-cancer; *Pseudevernia furfuracea*; Tree moss; Embalming; Biomonitoring

Introduction

The healing properties of nature remarkably affect humans in the path of their evolution [1]. Curative principles present in medicinal plants, lichens, and other life forms offer a plethora of compounds capable of exerting diverse bioactivities [2]. They are not only involved in a preventive role but also can modulate the bodily function at the molecular level, thereby providing a permanent solution to a disease and disorder [3]. The applications of lichens in therapeutics led to the discovery of some important lichen-derived constituents. Lichen bioactive constituents, viz. usnic acid, salazinic acid, atranorin, gyrophoric acids, lecanoric acid, and stictic acid, showed their potential in several diseases [4]. Some commonly therapeutically active lichens are *Cetraria aculeata, Cladonia chlorophaea, Pseudevernia furfuracea, Rhizoplaca marginalis,* and *Xanthoria parietina* [5]. Literature review revealed their potential as antioxidants [6], anticancer [7], antimicrobial [8], anti-inflammatory [9], anti-fungal [10], anti-diabetic [11], etc. Some lichens showed a protective role in immune-related disorders [12]. Varied lichens have also been used as nutraceuticals due to the presence of vitamins, minerals, amino acids, proteins, etc. [13]. Apart from their therapeutic applications, lichens have been utilized in the preservation of food [14], the dyeing of fabrics [15], perfumery [16], and for their inherent ecological roles [17]. Historical records of the Egyptian era have deciphered some of their extraordinary applications, such as the mummification of dead bodies [18]. Several lichens served as an essential ingredient used in the preservation of mummies [19]. The expertise of the Ancient Egyptians in preservation facilitated the use of lichens in preserving dead bodies, hence decoding their diverse applications in mummification [20]. Several liches are extremophilic and have been associated with terraforming Mars and might answer to the human quest to survive on outer planets [21]. The environmental applications of lichens in biomonitoring are indispensable. Their inherent biosensing ability promoted their usage in environmental biomonitoring [22].

Materials and methods

A comprehensive literature search was conducted across scientific databases, viz. Google Scholar, PubMed, and Web of Science. This exploration utilized several keywords

relevant to the topic, including 'tree moss', 'fruticose lichens', '*Pseudevernia furfuracea*', and 'Pharmacology of *Pseudevernia furfuracea*', among others. This systematic approach ensured wide coverage of the selected topic and paved the way for further investigation.

Fruticose lichens

Fruticose lichens evolve in such a way to cope with natural stressors, which is reflected in their existing morphological traits. The shrub-like, branched thallus possesses an outermost protective layer (cortex). With some exceptions, the photosynthetic algal layer is often present beneath the cortex, responsible for performing vital functions. The medullary layer (loosely packed fungal hyphae), involved in gaseous exchange and storage tissue for water and metabolites, forms the bulk of the thallus. Some fruticose lichens also possess a specialised central cord providing mechanical strength [23-25]. Fruticose lichens existed in varied life forms, viz., shrubby (*Pseudevernia furfuracea*), hanging (*Alectoria sarmentosa*), cylindrical (*Cladonia*), coralloid (*Tuckermannopsis*), hairy (Usnea spp.), etc. [26-28]. Some common examples of fruticose lichens include *Dendriscocaulon intricatulum, Siphula ceratites, Polychidium muscicola, Aspicilia hispida, Caloplaca coralloides, Cornicularia normoerica, Hubbsia parishii,* and *Lecanora phryganitis* [28]. They have a profound role in biomonitoring [29] and also serve as a food source for a variety of animals [30] and birds [31].

Fruticose lichens were also reported to exert a wide array of biological activities in relevance to their ethnomedicinal uses, as represented in Figure 1 & Table 1, viz., antioxidant (*Evernia prunastri*), anti-cancer (*Usnea longissima*), anti-inflammatory (*Cladonia gracilis*), anti-viral (*Cetraria islandica*), antimicrobial (*Usnea undulata*), and Antidermatophytic (*Usnea orientalis*) [32-41].

Table 1: Common examples of therapeutically active fruticose lichens.

Common name	Fruticose lichen	Pharmacology	Reference
Oakmoss	*Evernia prunastri*, Parmeliaceae	Antimicrobial, antioxidant	[32]
Iceland moss	*Cetraria islandica*, Parmeliaceae	Antiviral	[33]
Old man's beard	*Usnea baileyi*, Parmeliaceae	Anticancer	[34]
Beard lichen	*Usnea orientalis*, Parmeliaceae	Antidermatophytic	[35]
Methuselah's beard lichen	*Usnea longissima*, Parmeliaceae	Anticancer	[36]
Undulated old man's beard	*Usnea undulata*, Usneaaceae	Antibacterial	[37]
Smooth cup lichen	*Cladonia gracilis*, Cladoniaceae	Antioxidant, anti-inflammatory	[38]
Snow lichen	*Stereocaulon massartianum*, Stereocaulaceae	Antioxidant	[39]
Granular bush lichen	*Ramalina polymorpha*, Remalinaceae	Antioxidant	[40]
-	*Ramalina dendriscoides*, Remalinaceae	Antimicrobial	[41]

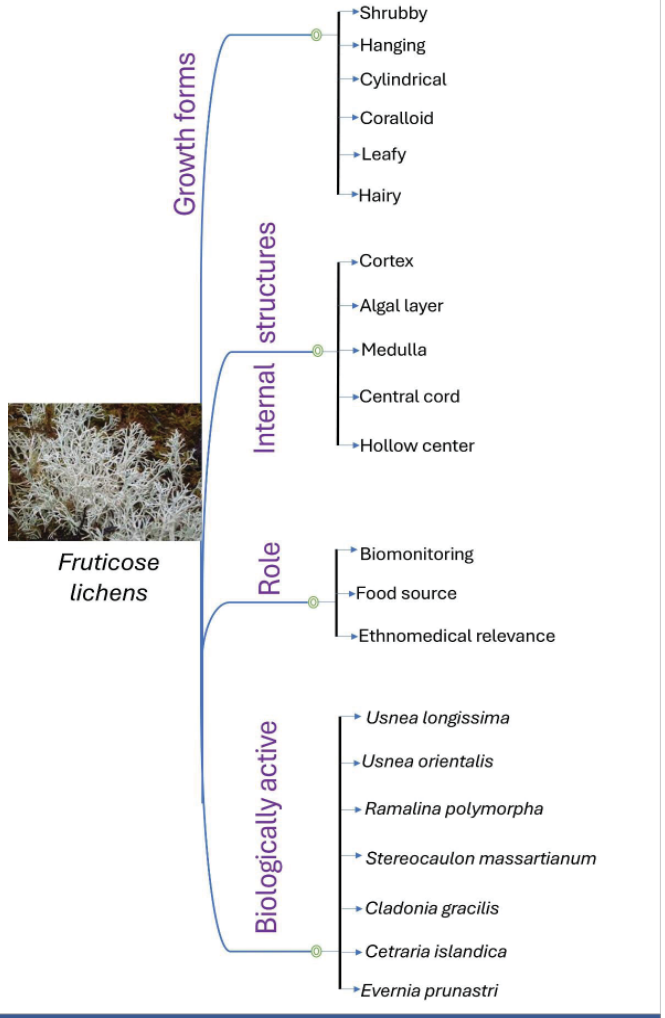

Figure 1: Applications of Fruticose Lichens.

Botanical description of *Pseudevernia furfuracea*

The tree moss (*Pseudevernia furfuracea*) exists in a symbiotic association among algae (*Trebouxia*) and fungus and serves as a unique habitat for microfauna. It dwells on the bark of trees like birch, pine, and spruce [42], and rarely on saxicolous form [43]. This fruticose lichenized species predominantly inhabits cool-temperate regions [44]. The thallus, having forked lobes, has a silver grey or light greyish upper surface and a black mottled lower surface. The peg-like isidia of *P. furfuracea* involved in vegetative reproduction emerge as the propagules of the lichen cortex [45,46].

Ethnomedicinal uses

Traditionally, it has been used in the treatment of wounds, eczema, and several conditions of respiratory, intestinal weakness. Literature revealed the usage of this foliose lichen by ethnic people in culinary practices and food preservation due to its aromatic properties [47].

Chemistry of *P. furfuracea*

Pseudevernia furfuracea contains a reservoir of distinctive compounds capable of exhibiting a wide array

of pharmacological activities, as represented in Figure 3. Lichen majorly contains depsides (squamatic acid, olivetoric acid, atranorin, chloroatranorin, boninic acid, lecanoric acid, dihydropicrolichenic acid, imbricaric acid, microphyllinic acid), depsidones (alectroronic acid, physodalic acid, oxyphysodic acid, menegazziaic acid), orsellinic acid derivatives (β-orsellinic acid, methyl orsellinate, orsellinic acid), phenolic acids (atraric acid, evernic acid), polysaccharides (Arabic acid), aromatic polyketides (olivetonide), hydroxybenzaldehydes (atranol), etc. [48-55].

Pharmacological status of *P. furfuracea*

The methanolic extract of tree moss (*P. furfuracea*) demonstrated its anti-metastatic potential in colorectal carcinoma (HCT-116, SW-480) by inhibiting the migration and invasion of respective cell lines [56]. Petrova, et al. [57] reported the effectiveness of acetone extract and physodic acid in a selected breast cancer cell line, i.e., MCF-10A. Atraric acid reported in *P. furfuracea* demonstrates significant activity against PA-1 cells (ovarian cancer), inhibiting their growth and potentially acting as an EGFR inhibitor [48]. Lichen-derived compounds (atraric acid, methyl hematommate, methyl chlorohematommate) and active fractions showed anti-inflammatory potential [50]. Mitrovik, et al. [49] reported antioxidative, antimicrobial, and antibiofilm potentials of various extracts of *P. furfuracea* and found proficient results. Several lichen-derived constituents (evernic acid, usnic acid, physodalic acid) showed potential when evaluated in vitro involving antioxidant and antibacterial activities [53]. Physodic acid isolated from tree moss showed its effectiveness in haematological malignancies, thereby inhibiting apoptosis in Jurkat cells [54]. The aqueous extract of *P. furfuracea* revealed its potential in oxidative damage when evaluated in vitro [58]. Essadki, et al. [59] detected the presence of several volatile constituents capable of exerting antimicrobial activities against multidrug-resistant bacteria. The ethanolic extract of *P. furfuracea* revealed its relevance as an antifungal candidate evaluated in vitro [60] along with enzyme inhibitory activities [52]. The phytopharmacological potential of tree moss has been represented in Table 2, Figure 2.

Other uses

Tree moss (*Pseudevernia furfuracea*) has been used in culinary and perfumery since ancient times to the present day [61]. Its characteristic woody odour and fixative properties aid its usage in perfumery [62]. Major phenolic volatile compounds have been identified in this species by GC-MS, contributing to its odorous properties [50].

The fruticose lichen *P. furfuracea* has been widely used to monitor trace elements and environmental contaminants in several locations in Italy, contributing to its biosensing properties. The major locations in Italy were reported as Torino, Bergamo, Sondrio, Trento, Bolzano, Belluno, Udine,

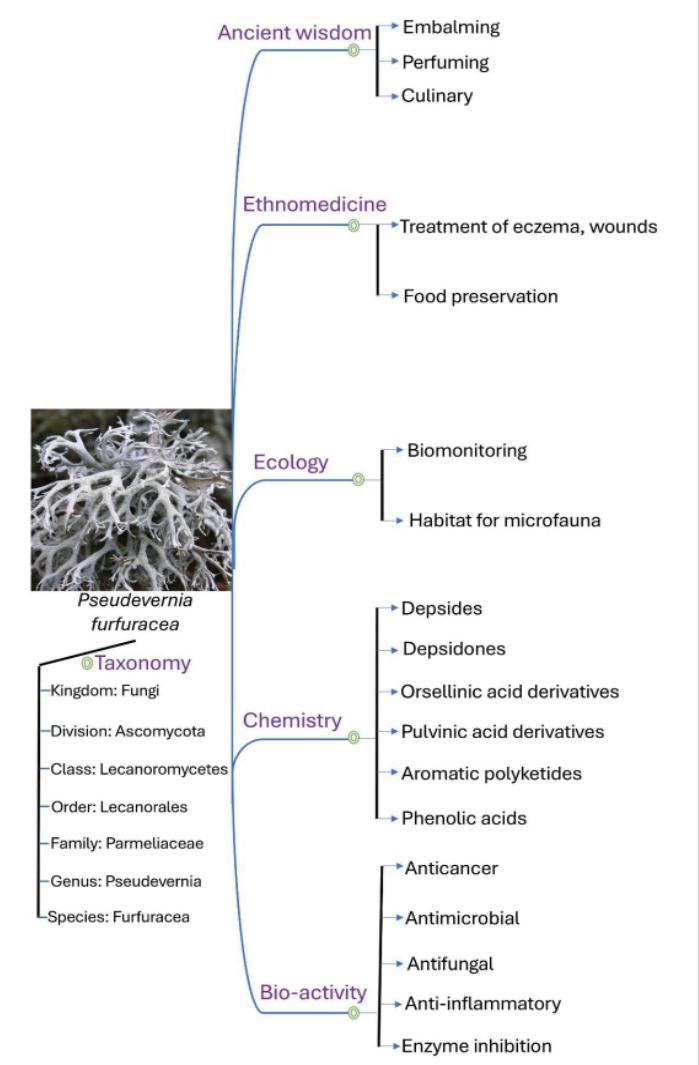

Figure 2: Applications of *P. furfuracea*.

Lucca, and Catanzaro [63], as well as the urban area in Naples [64]. The outer locations outside Italy where the biomonitoring potential of this lichen was established are Central Anatolia [65], Slovakia [66].

The ancient Egyptian practice of preserving dead bodies involved injecting solutions containing natural substances, such as resins, gums, oils, and lichens, as well as inorganic materials [67]. The historic text highlights the significance of *P. furfuracea* in the preservation of dead bodies [68,69], as it has been found stuffed inside the corpse's body cavities and also detected in the linen cloth used for wrapping mummies [70].

Safety considerations

Rapid metallic pollution raised due to industrialization and increased man-made activities tends to alleviate the presence of toxic elements in the environment [71]. Lichens, being bioaccumulators, absorb pollutants [72], which can lead to toxicity in them [73]. It is necessary to conduct quantitative heavy metal detection from sophisticated instrumentation methods like Inductively Coupled Plasma Mass Spectrometry,

Table 2: Pharmacological status of *P. furfuracea.*

Extract /Derived compound	Targeted study area	Outcome	Reference
Methanol extract	Colorectal carcinoma (HCT-116, SW-480)	Inhibition of cancer cell migration	[56]
Acetone extract, Physodic acid	Breast cancer (MCF-10A)	Suppression of TGF-β signalling	[57]
Atraric acid	Ovarian cancer (PA-1)	Atraric acid-mediated inhibition of EGFR	[48]
Atraric acid, methyl hematommate, methyl chlorohematommate	Anti-inflammatory	Fractions containing active constituents displayed significant anti-inflammatory activities.	[50]
Extracts (acetone, ethyl acetate, methanolic extract)	Antioxidative, antimicrobial, antifungal	Extracts showed prominent activities viz. antioxidant (IC_{50} 95.33 µg/mL), antimicrobial (MIC 0.005 mg/mL to 2.5 mg/mL), antifungal (0.04 mg/mL to 2.5 mg/mL)	[49]
Evernic acid, usnic acid, physodalic acid	Antibacterial, antioxidant	Extracts showed prominent activities as determined by their MIC values	[53]
Physodic acid	Anti-leukemic	Physodic acid induced apoptosis in Jurkat cells	[54]
Aqueous extract	Antioxidant	Significant improvement in the antioxidant defense system and prominent reduction in oxidative stress associated with type 1 diabetic rats	[58]
Volatile compounds	Antimicrobial	Volatile compounds showed activity against multidrug-resistant bacteria, fish pathogens, and *Candida albicans*	[59]
Ethanolic extract	Antifungal	The extract showed prominent antifungal potential against the selected Aspergillus strains.	[60]

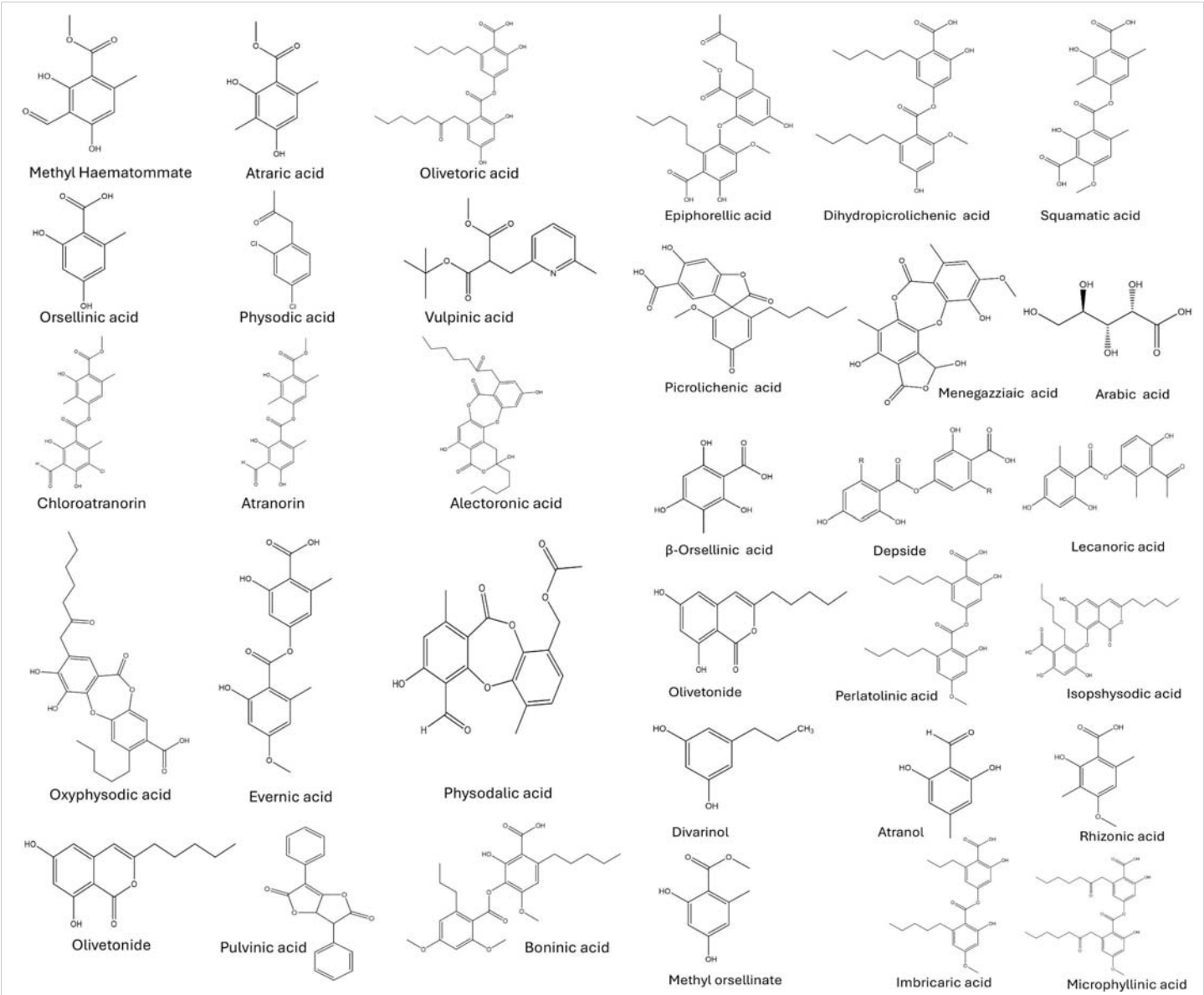

Figure 3: Chemistry of P. furfuracea.

Atomic Absorption Spectroscopy, before its inclusion in any product [74].

Conclusion

The current communication highlighted the potential of fruticose lichen *P. furfuracea* from an ecological to a therapeutic perspective. The ancient use of *P. furfuracea* in embalming the dead bodies and perfume making revealed its commercial importance in the Egyptian era. The biosensing properties of this species further mark its ecological importance in monitoring pollution. The species is found to be a rich source of distinctive depsides, phenolic acids capable of eliciting a wide array of pharmacological activities. The literature revealed its significance as an important antioxidant, anti-inflammatory, and anticancer candidate. Keeping in view its biomonitoring and therapeutic applications, the tree moss *P. furfuracea* should be further explored to harness its complete potential. However, the consideration of several factors, viz., heavy metal content, toxicity prediction, and accurate identification of this species should be monitored to ensure its safe usage in therapeutics.

Author's contribution

Vikrant Arya (VA) initiated the conceptualization of the review article and is responsible for the overall research design, guiding the scope and direction of the work. Anshul Attri (AA) was primarily responsible for drafting the manuscript, ensuring comprehensive coverage of the literature. Both VA and AA collaboratively revised and approved the final version of the article, contributing equally to its intellectual content and accuracy.

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