



PHYTO-PHARMACOLOGICAL ACTIVITY AND NOVEL ASPECT OF LICHEN *PARMELIA PERLATA*: A REVIEW

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Abstract: The lichen *Parmelia perlata*, often called black stone flower or Chharila, is a member of the Parmeliaceae family. It is spreading over the steep region of the Himalaya and North East India, growing in between the rocks, tree trunks, and ground. The plant's exterior coat is greenish black and white, and the thallus, which can grow up to 15 cm in diameter, is only weakly attached to the substrate. Its smooth upper surface is orbicular greyish white, while the lower surface is backish brown and hairy. Usnic acid, lecaronic acid, salazinic acid, and atronin, among other unique chemical components discovered in the lichen, have been traditionally given for bronchitis, excessive salivation, vomiting, toothaches, boils, and other inflammations. Aside from these conditions, it has also been linked to seminal weakness, nocturnal emission, amenorrhea, leucorrhea, dyspepsia, calculi, blood and heart conditions, stomach problems, enlarged spleen, bleeding piles, scabies, leprosy, general aches, etc. It strengthens the urinary system and inhibits the development of calculi. The primary goal of the current manuscript is to discuss the pharmacognostic information and pharmacological activity of this lichen.

Keywords: Lichen, *Parmelia perlata*, Chharila, Pharmacological profile, Phytochemical aspects

I. INTRODUCTION

Parmelia perlata is a well-known lichen of family Parmeliaceae. A lichen is an association of an alga and fungus, living together in a symbiotic relationship. It is a very effective group that exploits a variety of environments worldwide and controls around 8% of terrestrial ecosystems [1], *Perlata Parmelia* (Huds.) Ach. is a species of perennial lichen, Common names for them include Stone Flower, Patthar phool, Kalpashee, Chhadila, Dagad phool, and Charela [2] Traditional medicine employed it to treat edoema, arthritis, toxicosis, fever, obesity, eczema, heart tonic, refrigerant, and gout, among other conditions. According to folklore, it is effective in treating dyspepsia, diarrhoea, dysentery, antiulcer, spermatorrhea, amenorrhea, as an astringent and diuretic, as well as in accelerating wound healing [3,4]. By using gas chromatography, Indian and Serbian researchers discovered phenolic substances like olivetol, orcinol, as well as dibenzofuran derivatives known as lichen acids - atranorin, lecarinic, and usnic acids - in various *Parmelia* members. Among terpene chemicals, simarenol, fridelan, and lupeol were found [5]. The anti-inflammatory, antifungal, antibacterial, and painkilling properties of limonene, borneol, camphor, thymol, and pulegone are demonstrated [6-8]

II. Vernacular Name: [9, 10]

Arabian: Hinna-i-Korisha, Rumman, Barri, Shaibah, Shaibat

Ayurvedic: Bhuri-charilla, Shaila, Shaileya, Shailaka, Shaileyaka, Shailpushpa, Shilaapushpa, Shilaadaaru, Shilodbhava, Shitashiva, Sthavira, Vrddha,

Bengali: Shailaj

English: Litho Lichen, Rock Moss, Stone Flower, Yellow Lichen

French: *Parmelia des murs* German: Wandschildflechte

Guajarati: Chhadilo, Ghabilo, Patthar Phool

Hindi: Chhadila, Charela, Chharila, Pathar ka phool

Kannada: Kallu-hoovu, Kallu-huvu, Shilapushpa

Malayalam: Kalppuvu, Sheleyam

Marathi: Dagad phool

Persian: Davala

Punjabi: Ausneh, Chhadila

Sanskrit: Silapuspa, Silavalka, Sitasiva

Tamil: Kalpashee

Telugu: Kallu-pachi, Ratipuvvu

Unani: Dowala, Charelaa, Hazaz-al-Sakhr

Urdu: Chhadila, Pariyo, Ushna

III. Taxonomical Classification: [11]

Kingdom: Fungi

Division: Ascomycota

Class: Lecanoromycetes

Order: Lecanorales

Family: Parmeliaceae

Genus: Parmotrema

Species: *P. perlatum*

IV. Botanical description:

The foliose species of lichen known as *Parmelia perlata*, also known as *Parmotrema perlatum*, is used as a spice in India and is known locally as black stone flower, shaileyam in Sanskrit, kalpasi in Tamil, and chadila, among other names. It is a member of the Parmeliaceae family. [12] *P. perlata* is found in the temperate Himalayas, northeast India, eastern Nepal, the west of Britain, and tropical climates. It primarily grows on trees/trunks and rocks. This lichen's thallus is big, patch-shaped, light grey to pale blue, with rounded lobes, and it frequently has black hairs at the borders [13, 14].

V. Phytochemical screening:

P. perlata is claimed to include proteins, tannins, sugars, phenols, vitamins A and C, alkaloids, glycosides, steroids, and terpenes [15] among other substances. Additionally, it contains lichen acids such usnic acid, lecanoric acid, and atranorin. Lanoset-2-en type triterpene is one of two novel terpenes and labdane type diterpenoid [16] and two dibenzofuran i.e. 2-acetyl-9b-carbomethoxy-7,9-dihydroxy-8-methyl-1,3(2H,9bH)-dibenzofurandione and 2,6-diacetyl-7,9-dihydroxy-8,9b-dimethyl-1,3(2H,9bH)-dibenzofurandione known as (+)-Usnic acid, were also identified and isolated from *P. perlata*. Icosan-1-ol, 3-ketooleanane, tridecyl myristate, and others are isolated components. A hot methanolic extract of the drug also comprised the constituents (4-amino-3-hydroxy-6-methoxy-2-methylcyclohexa-1-3-diene-1-carbaldehyde), (5-amino 2-ethoxy-4-methylcyclohexa-1, 3-diene-1-carboxylic acid), and (5-methoxy-2-(methoxymethyl)-3-methylpyrazine). [17]

VI. Traditional Applications:

Parmelia perlata is commonly used as a spice to enhance the taste and flavour of food. It has astringent, carminative, demulcent, bitter, resolvent, emollient, laxative, sporofic, sedative, and diuretic properties and is used to treat sores, bronchitis, excessive salivation, vomiting, toothache, boil and inflammations, among other things. It is an excellent aphrodisiac and is used to treat seminal weakness, spermatorrhoea, nocturnal emission, amenorrhoea, leucorrhoea, and other conditions. Additionally, it helps with leprosy, scabies, enlarged spleen, bleeding piles, dyspepsia, calculi, blood problems, heart ailments, stomach disorders, and calculi. It is applied topically to relieve lumbar and kidney discomfort. It is also used to treat general symptoms, including liver and womb pain. The powdered medication is used to treat wounds, is regarded as a good cephalic snuff, and also works well to aid in digestion. It strengthens the urinary system and inhibits the development of calculi. Additionally, it controls respiratory issues and keeps the body's temperature within normal range. The medication paste can assist to lessen inflammations. Headaches are said to be relieved by drug smoking. Additionally, it is a key component of cosmetics. [18,19]

VII. Pharmacological Profile.

VII.1. Antiuro lithiatic Effects

P. perlata extract exhibited significant antiuro lithiatic potentials against CaOx calculi in experimental rats. It significantly restored the normal renal architecture and improved the renal functions by restoring the EG + AC mediated biochemical changes in urine, serum and kidney tissue homogenate parameters of experimental rats towards normal.[20]

VII.2. Antiulcer Activity

Ethanol extract of *P. perlata* (100 mg/kg, p.o.) showed significant gastroprotective potential against cold restraint, aspirin, alcohol and pyloric ligation induced gastric ulcer models in adult Sprague Dawley rats. [21]

VII.3. Antioxidant Potential

Methanolic extract of *P. perlata* showed significant antioxidant activity when tested in DPPH (2,2'-diphenyl-2-picrylhydrazyl) and phosphomolybdenum reduction assay³⁵. The ethanol extract also showed significantly good free radical scavenging effects and antioxidant potential. [22]

VII.4. Hypolipidemic Potential

Methanolic extract of *P. perlata* was proved to have significant hypolipidemic activity when tested by employing in-vitro anticholesterol assay using Simvastatin as standard. [23]

VII.5. Cytotoxic Activity

Methanolic extract of *P. perlata* was found to have cytotoxic activity and showed antiproliferation against colon cancer cell lines HCT 116. [24]

VII.6. Antidiabetic Activity

Aqueous extract of leaves of *P. perlata* (200mg and 400mg/kg body weight) administered for 60 days showed significant antidiabetic activity compared to glibenclamide against alloxan induced diabetes in rats. The extract reduced the fasting blood glucose, HbA1C level, increased plasma insulin level and normalises the activities of glucose metabolizing enzymes. It also significantly improved serum lipid profile by reducing serum triglyceride, cholesterol, LDL (low density lipoprotein), VLDL (very low density lipoprotein), free fatty acids, phospholipids and increasing HDL (high density lipoprotein) level in dose dependent manner. [25]

Methanolic extract also showed significant blood glucose lowering potential in oral glucose tolerance test, significant alpha-glucosidase inhibitory activity and free radical scavenging activity in streptozotocin induced diabetes in Wistar rats. [26]

VII.7. Hepatoprotective Activity

Aqueous slurry (0.7g/kg and 1.0g/kg, p.o.) of *P. perlata* was found to have significant hepatoprotective activity in CCl₄ intoxicated albino Wistar rats. It decreased the levels of biochemical markers. The histopathological analyses were also in compliance with the findings of haematological biochemical parameters. [27]

VII.8. Antibacterial Activity

The methanolic, ethyl acetate and acetone extracts of *P. perlata* were found to have significant antibacterial activity against *Staphylococcus aureus* when tested by using Kirby and Bauer disc diffusion and Mueller-Hinton agar plate methods. Further hydro-alcoholic extract was also found to be significantly active against *Bacillus cereus*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *S. aureus*, *Corynebacterium xerosis*, *Escherichia coli* and *Klebsiella pneumoniae* in agar well diffusion method. This antibacterial potential might be due to the presence of usnic acid. [28]

VII.9. Antifungal Activity

Methanolic, chloroform, petroleum ether and acetone extracts as well as isolated constituents I (4-amino-3-hydroxy-6-methoxy-2-methylcyclohexa-1-3-diene-1-carbaldehyde), II (5-amino-2-ethoxy-4-methylcyclohexa-1,3-diene-1-carboxylic acid) and III (5-methoxy-2-(methoxymethyl)-3-methylpyrazine) from *P. perlata* showed antifungal potential against *Aspergillus niger*, *Rhizopus nigricans* and *Fusarium oxysporum*. Constituent II was having more, I having moderate and III having less antifungal effect. The constituent II was more active against *F. oxysporum* and *R. nigricans*. Further aqueous methanolic extract also showed significant action against *Candida albicans* and *A. niger* in agar well diffusion method. [29]

VII.10. Antiviral Activity

The cytotoxicity of polysaccharide fraction of *P. perlata* was investigated on HEP-2, Vero and L20 cell lines. The antiviral properties were determined against yellow fever, poliomyelitis and infectious bursal disease virus of chickens using the end-point cytopathic effect assay. The order of sensitivity of cell lines was found to be L20 > HEP-2 > Vero. The fraction was found to possess specific antiviral potential against yellow fever virus. Attack on the viral envelope by the polysaccharide fraction of lichen was postulated as the major mechanism of inhibition of yellow fever infection. [30]

VII.11. Gastroprotective effect

Potential anti-ulcer activity of the ethanol extract of the *P. perlata* was observed against CRU (50.0%), AS (37.5%), AL (65.41%) and PL (50.00%) induced ulcer models. The reference drug omeprazole (10mg/kg, p.o.) showed 77.40% protection against CRU and 57.08% against AS and 69.42% against PL model. Sucralfate, another reference drug (500 mg/kg, p.o.) showed 62.50% protection in AL induced ulcer model. The ethanol extract of the *P. perlata* reduced free acidity (19.04%), total acidity (14.43%) and upregulated mucin secretion by 14.17% respectively. [31]

VII.12. Antifertility activity

Oral administration of *Parmelia perlata* reduces the weight of testis, and secondary sex organ. Marked decrease in the sperm cell counts specially the number of secondary spermatocyte and rounded spermatid also reduces the testis weight. Reduced protein content may be another reason for low sperm density as the growth rate of any organ is proportional to its protein content. [32]

VII.13. Anti-inflammatory Activity and Antiarthritic Effect.

The objective of this study was to evaluate the anti-inflammatory and antiarthritic potential of *Parmelia perlata*. Methods: The relative study is based on in vitro anti-inflammatory and antiarthritic activity using hydroalcoholic extract of *P. perlata* (HAEPP). The preliminary phytochemical tests showed the presence of various phytochemical compounds such as alkaloids, flavonoids, and glycosides since the lichen species of *P. perlata* has the folklore claim of anti-inflammatory activity, thus it was studied by human red blood cells membrane stabilization method, and arthritic activity was carried using protein denaturation method using diclofenac as a standard. Results: The results showed eminent anti-inflammatory and antiarthritic activity in a dose-dependent manner. The membrane stabilization showed the maximum effect at 78.54% at the concentration of 1000 µg/, and the protein denaturation was also found maximum at 1000 µg/ml concentration at 79.43%. Thus, our research states the potent anti-inflammatory activity and antiarthritic effect in *P. perlata*. Conclusion: The HAEPP has a potent anti-inflammatory activity and antiarthritic activity. A further study has to be conducted to establish the pharmacological evidence behind the compound and the mechanism of action of the HAEPP on the inhibition of the inflammation process. [33]

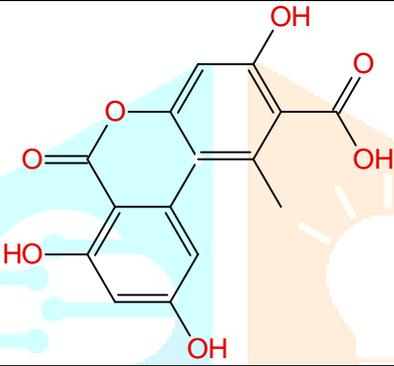
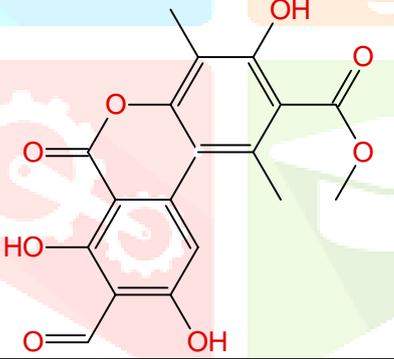
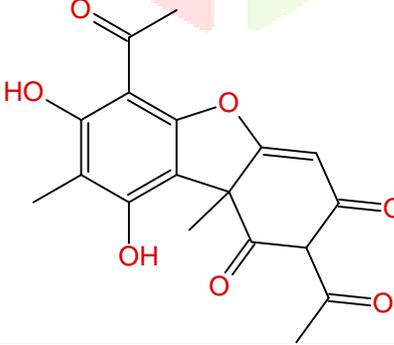
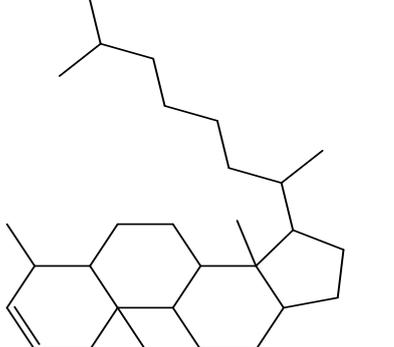
VIII. Role of *Parmelia* in Environmental and Ecological aspect:

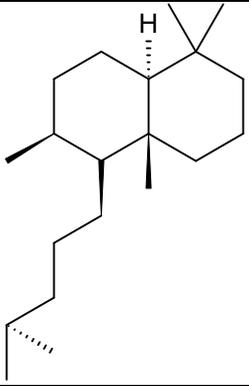
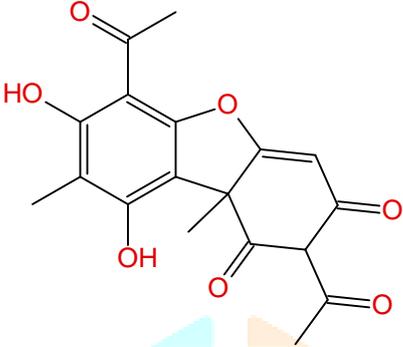
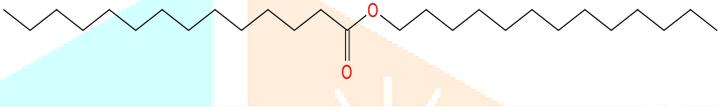
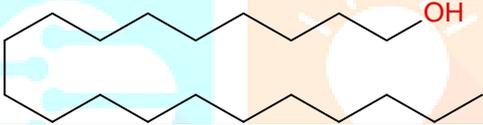
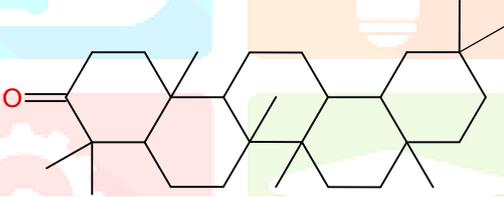
When compared to other species from different genera, *Parmelia* lichens have been largely studied regarding their environmental biomonitoring capacity, their biological activities and phytochemistry. The reason could be attributed to the early description of the genus (the first references date back to 19th century) and its wide geographical distribution. Within generic diversity, *Parmelia*

Parmelia sulcata Taylor is probably the lichen species that has involved the deepest research, being even employed in many works aimed at understanding the ecological physiology of lichens [43]. The morphology-based selection of specimens could have led to the use, under the name of *Parmelia* sp., of lichen species that actually belonged to different genera.

In general, lichens are organisms with a great sensitivity to changes concerning the chemistry of the air. Air pollution and its sediments are deposited on the outer layer of lichen thalli and penetrate inside by infiltration owing to the lack of covering and protecting cuticle. Element uptake in lichens depends on several factors, such as the morphological characteristics of the given specimen, the chemical nature of the pollutant element, and diverse environmental factors. [44,45] Lichenic symbioses react physiologically towards pollution in industrial areas through readjustments between the photobiont and the mycobiont; it has been evidenced, for E. González-Burgos, et al. *Phytochemistry* 165 (2019) 112051 2 instance, by the altered conductivity correlated to contamination level that was found in various *P. sulcata* specimens. In response to high levels of pollutants, the algal cell proportion slightly increases while fungal cells decrease within the medulla and the photobiont cells exhibit increased lipid droplets in the cytoplasm and thicker cell walls. Thanks to such ecological properties, together with their ubiquitous distribution in both clean and polluted ecosystems (including cities), *Parmelia* lichens are advantageously utilized in analytical and chemical research as environmental indicators. [46,47] To date, several *Parmelia* species were demonstrated to be efficient tools for measuring geographical variances in air pollution by trace elements, mainly heavy metals. [48,49]

Table 1 [34] Chemical Constituents of *Parmelia perlata*

| Sl.no. | Chemical structure | Chemical name |
|--------|---|------------------------------|
| 1. |  | Lecanoric Acid |
| 2. |  | Atranorin |
| 3. |  | Usnic Acid |
| 4. |  | Lanoset-2-En Type Triterpene |

| | | | |
|----|---|--|------|
| 5. |  | Labdane Diterpenoid | Type |
| 6. |  | 2,6-diacetyl-7,9- dihydroxy-8,9b- dimethyldibenzofuran- 1,3-dione | |
| 7. |  | Tridecyl myristate | |
| 8. |  | Icosan-1-ol | |
| 9. |  | 3-keto oleanane | |

Different species of lichen and its activity

| Lichen species | Activities | Extracts | Results | Ref |
|--------------------------------------|-------------------|---|--|------|
| <i>Parmelia arseneana</i> Gyeln | Antimicrobial | Acetone extract | Moderate antibacterial and antifungal activity. (31) | [35] |
| | Antioxidant | | Moderate antioxidant activity (DPPH - IC ₅₀ : 612.75 µg/ml; and superoxide anion. | |
| | Cytotoxic | | Cytotoxic effects on LS174 cell line (IC ₅₀ : 11.61 µg/ml), K562 cell line (IC ₅₀ : 13.84 µg/ml), Fem-x cell line (IC ₅₀ : 16.86 µg/ml) and moderate on A549 cell line (IC ₅₀ : 47.06 µg/ml). | |
| <i>Parmelia caperata</i> (L.) Ach. | Antimicrobial | Acetone, aqueous, diethyl ether, ethanol, ether, methanol, and n-hexane extracts Protocetraric acid | Significant antibacterial activity against <i>S. aureus</i> . | [36] |
| | Antioxidant | | Moderate antioxidant activity: acetone extracts > methanol extracts > aqueous extract. | |
| | Cytotoxic | | Cytotoxic effect: hexane extract against DU145 cells (IC ₅₀ : 7.90 µg/ml) and acetone. | |
| <i>Parmelia centrifuga</i> (L.) Ach. | Antioxidant | Methanol extract | Strong antioxidant activity: inhibition of the linoleic acid (54.19%). | [37] |
| | Antimicrobial | | Strong antimicrobial activity: antibacterial and antifungal | |
| <i>Parmelia cirrhatum</i> Fr. | Antimicrobial | Aqueous extract | Significant antifungal activity against <i>Cladosporium cladosporioides</i> , <i>Curvularia lunata</i> and <i>Fusarium oxysporum</i> . | [38] |
| <i>Parmelia crinita</i> Ach | Antimicrobial | Methanol extract | Antibacterial and antifungal activities. | [39] |
| | Antioxidant | | Moderate antioxidant activity (16% inhibition of the linoleic acid peroxidation). | |
| <i>Parmelia erumpens</i> Kurok | Antimicrobial | Chloroform extract | Antimicrobial activity: 2-hydroxy-4-methoxy-3,6-dimethylbenzoic acid was active against the bacteria <i>V. cholera</i> , <i>K. pneumonia</i> and <i>S. typhi</i> and the fungi <i>C. gastricus</i> and <i>C. tropicalis</i> | [40] |
| | Cytotoxic | 2-hydroxy-4-methoxy-3,6-dimethylbenzoic acid, Atranorin, Usnic acid | Cytotoxic activity against A549 cells (IC ₅₀ 60.19 mg/ml), B16F10 cells (IC ₅₀ 2.53 mg/ mL) and Caski cells (IC ₅₀ 2.69 mg/mL) | |
| <i>Parmelia nepalensis</i> Taylor. | Antiproliferative | Gyrophoric acid, Usnic acid Diffractaic acid Methyl orcinolcarboxylate Ethyl hematommate Atranorin Protolichesterinic acid | Antiproliferative activity: gyrophoric acid (IC ₅₀ : 1.7 µM), usnic acid (IC ₅₀ : 2.1 µM) and diffractaic acid (IC ₅₀ : 2.6 µM). β- Inhibitors of leukotriene B4 (LTB4) biosynthesis in polymorphonuclear leukocytes: atranorin (IC ₅₀ : 6 µM), diffractaic acid (IC ₅₀ : 8 µM) and protolichesterinic acid (IC ₅₀ : 9 µM). | [41] |
| <i>Parmelia omphalodes</i> (L.) Ach | Antioxidant | Methanol extract | High/moderate antioxidant activity (ORAC 3.15 µmol TE/mg dry extract; DPPH 680 µg/mL; FRAP 174 µmol Fe ²⁺ eq/g sample). | [42] |
| | Cytotoxic | | Cytotoxic effects on MCF-7 cells (LD ₅₀ 138 µg/mL) and HepG2 cells (LD ₅₀ 260 µg/mL) | |

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