Review Article

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PHARMACOLOGICAL AND PHYTOCHEMICAL ASPECTS OF LICHEN *PARMELIA PERLATA*: A REVIEW

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ABSTRACT

Parmelia Perlata (Huds.) Ach. belonging to Parmeliaceae family is a lichen (a close symbiotic association between algae and fungi), commonly called 'Stone Flower' and 'Charila' in India. It is widely distributed in hilly areas of Indian subcontinent. The lichen was found to contain several unique chemical constituents like usnic acid, lecaronic acid, salazinic acid, atronin etc and has been traditionally prescribed in bronchitis, excessive salivation, vomiting, toothache, boils, inflammations etc. It has also been indicated in seminal weakness, nocturnal emission, amenorrhoea, leucorrhoea, dyspepsia, calculi, blood and heart diseases, stomach disorders, enlarged spleen, bleeding piles, scabies, leprosy, general pains etc. It tones up the urinary tract and suppresses calculi formation. It has been used as traditional food by Rai and Limbu communities of East Nepal and also as light brown dye for wool as well as bio-indicator of air pollution due to heavy metals. Although it has already been substantiated for antimicrobial, antiurolithiatic, anticancer, antidiabetic potentials etc. yet not fully explored for therapeutic effects and thus remained pharmaceutically unexploited. It is probably due to difficulties in identification, bulk collection and lack of updated scientific reports on lichens.

The present manuscript is mainly focused to explain various updated aspects like synonyms, common names, taxonomy, botanical descriptions, traditional uses, chemical constituents, pharmacological activities etc. of *P. perlata,* and is the first such scientific compilation that can be an important tool for researchers interested in studying this lichen.

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

INTRODUCTION

Ever since the birth of mankind, human beings have been dependent on plants to fulfil their basic need of life like food, shelter, clothing and even for the maintenance and restoration of health. Lichens represent a unique group of plants that consists of two unrelated organisms i.e. a fungus and an alga, growing together in a close symbiotic association. It is an excellently successful group, exploiting a wide range of habitats throughout the world, and dominating about 8% of terrestrial ecosystems. Since the time of the first Chinese and Egyptian civilizations, these have been medicinally used in traditional system of medicines. The literary records of traditional knowledge of Indian medicinal plants demonstrated the lichen in Rigveda, a text where the first authentic record of 'Aushadhi' (medicine) has been described. Further the use of lichen in folklore as medicine has been mentioned in different pharmacopoeias of the world [1, 2].

India has a rich diversity of lichens represented by about 2450 species. These are abundantly found in the temperate and alpine regions of the Himalayas and hilly regions of Peninsular India. Since ancient times, these have been used as one of the natural drug and about 700 biologically active components have been structurally identified that were quite unique with respect to those of higher plants [3-5]. The lichens are well known to have many characteristic secondary metabolites that contribute remarkable biological activities such as antiviral, antibacterial, antifungal, antitumor, antioxidant etc [2, 6, 7].

In the present manuscript, attempts have been made to describe the lichen *Permalia perlata* (Huds.) Ach. (Fig. 1) belonging to Parmeliaceae family which is commonly known as Chharila. Some other common names like Stone Flower, Patthar Phool, Shilaapushpa etc are probably because of its traditional therapeutic action on ashmari (urinary stone) in ayurvedic system of Indian medicine. Similarly, *Saxifraga ligulata*[8] is also known as Pashanbheda (stone breaker), *Didymocarpus pedicellata*[9] as Patharphori (stone crusher) because of their use in kidney stone. Usnic acid, a major constituent of parmelia species, showed potent antimitotic, antitumor and antimycobacetrial effects while some other unique constituents like diffractic acid, gyrophoric, caperatic acid etc were also isolated and well known for their analgesic, antipyretic, antispasmodic potential and beneficial effects against hyperproliferative skin disease like psoriasis etc[10-12].

Three parmelia species i.e. *P. perlata* (L.) Ach. [Synonym: *Parmotrema chinense* (Osbeck) Hale & Ahti], *P. perofrata* (Wulf.) Ach. [Synonym: *Parmotrema perforatum* (Ach.) Mass.] and *P. sanacti-angelii* Lynge are sold as chharila in Indian market[13]. It contains many chemical constituents like tridecyl myristate, 3-ketooleanane, icosan-1-ol, usnic acid[12], parmelanostene permelabdone[14], atranorin, lecanoric acid, orcin, erythrolein, azolitmin and spaniolitmint[15]. *P. perlata* is generally used as spice to enhance the taste and flavour of food. It has astringent, resolvent, laxative, carminative properties and supposed to possess aphrodisiac potential. It is also useful in treating sores, bronchitis, excessive salivation, tooth-ache, boils, inflammations, seminal weakness, spermatorrhoea, amenorrhoea, dyspepsia, calculi, blood disorders, heart diseases, stomach disorders, enlarged spleen, piles, scabies, leprosy and general pain. Smoke of drug is believed to relieve headache and powder is applied on wounds, besides a good cephalic snuff [4, 12, 16-18].

The present manuscript is mainly focused to describe the research work of various scientists on this drug and other data including common names, taxonomical classification, botanical descriptions, traditional uses, ayurvedic properties, pharmacological activities, chemical constituents, marketed formulations etc. Further, this manuscript is the first scientific report of such diverse aspects of lichen *P. perlata* and shall be of immense importance for researchers interesting in studying any such aspects of this drug.

Synonym
Parmotrema chinense (Osbeck) Hale & Ahti[13]

Vernacular Names[19-22, 28]
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
Germen: 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

Taxonomical Classification[23]
Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Solamaceae
Family: Parmeliaceae
Genus: Parmelia
Species: Perlata

Habitat
P. perlata is a native of Indian subcontinent, usually found throughout India especially in Northern India, growing in rocky areas and old tree trunks. It is especially seen in Himachal Pradesh, Punjab, Kerla, Bengal and cultivated in Kashmir hills and Himalayas [24, 25].

Ayurvedic Properties[20, 26-28]
Rasa (Taste): Tikta (pungent), Kasaya (astringent)
Guna (Property): Laghu (light), Snigdha (slimy)
Virya (Potency): Sheet (cold)
Vipaka (Post digestive effect): Katu (bitter)
Karma (Effect on dosha/disease): Hrdya (Heart diseases), Pittahara, Stambhaka (Semen thickening agent), Kapha-pitthara.

Botanical Description
Thallus is flattened, adnate, 3-8 cm broad, foliose structure, greenish mineral grey (or yellowish-white on top and black on the lower surface) in color having sublinear to irregular 2-4 mm wide lobes. The marginal cilia are distinct, 0.3-0.7 mm long. The upper surface of thallus is plane and continuous, which is moderately to densely isidiate i.e. having isidia or soralia. Each isidia or soralia (both are bud-like vegetative structures present on upper surface of thallus) is cylindrical, erect, simple to branched, up to 0.5 mm high. The lower surface of thallus is moderately rhizinate i.e. having rhizines. The rhizines (rootlets that attach the lichen to its substrate) are delicate, simple or in part sparsely furcated. Apothecia are adnate, 1-3 mm in diameter and amphithecia is also isidiate[20, 22, 28-29].

Traditional Uses
P. perlata is generally used as spice to enhance the taste and flavour of food. It is astringent, carminative, demulcent, bitter, resolvent, emollient, laxative, sporofic, sedative, diuretic and considered to be used in treating sores, bronchitis, excessive salivation, vomiting, tooth-ache, boils, inflammations etc. It is very good aphrodisiac and indicated in seminal weakness, spermatorrhoea, nocturnal emission, amenorrhoea, leucorrhoea etc. It is also useful in dyspepsia, calculi, blood disorders, heart diseases, stomach disorders, enlarged spleen, bleeding piles, scabies and leprosy. It is externally used for pain in renal and lumbar region. It is also used in pain of liver, womb and other general pains. The powdered drug is applied on wounds, considered as a good cephalic snuff and is also a good agent for improving digestion. It tones up the urinary tract and suppresses the calculi formation. It also suppresses respiratory disorders and maintains normal body temperature. The paste of drug is helpful in reducing inflammations. Smoke of drug is believed to relieve headache. It is also used as an important ingredient in cosmetics [19, 24, 30].
Ayurvedic pharmacopoeia of India has mentioned that *P. perlata* is therapeutically useful in kandu (itching), kustha (skin diseases), asmari (calculi), daha (burning sensation), visa (poison), hrllasa (angina pectoris), trsna (thirst), varna (ulcer), hrdaya-roga (heart diseases), rakta-vikara (blood disorders), svasa (asthma), mutrakrchra (dysuria), jvara (fever), mutraghata (urinary obstruction) and sriah-sula (headache)[20, 28].

Ayurvedic Formulations
P. perlata is an important constituent of many herbal formulations used in different systems of medicine. It constitutes a vital part of several dosage forms used in both Ayurvedic and Allopathic systems of medicine, like Neeri (Aimil Pharmaceuticals India Ltd.), Calcury (Charak Pharma Pvt. Ltd.), Pathrina (Shri Baidyanath Ayurved Bhawan Pvt. Ltd.) etc. These formulations are especially used in renal stone and restoring the functions of kidney. It constitutes an important ingredient of many formulation e.g. Confido, Speman, V-Gel, Speman Vet (The Himalya Drug Company) used for sexual problems and improving sexual health. Further, it is an important ingredient of many Unani formulations like Dawa-ul-misk, Dawa-ul-misk motadil, Erqember, Laboob-e-kabir muqquawie bah, Ma-ul-leham, Majun shabab awar, Majun muqwwi mumsik, Mufarrhe yaquti motadil, Mumsik be nazir, Roghan-e-surkh, Sharbat mufarrhe muqawwi-e-qalb (Hamdard Laboratories) and Dawa-ul-misk mutadil, Dawa-ul-misk mutadil jawahar wali, Demaghi, Laboob khas jawahar wala (Qarshi Industries Pvt. Ltd.) It is also used in Mahanarayan Oil[21, 27, 30].

Phytochemical Aspects
P. perlata is reported to contain proteins, tannins, glucose, phenols, Vitamin A, Vitamin C[32], alkaloids, glycosides, steroids, and terpenes[33]. It also contains lichen acids like lecanoric acid, atranorin and usnic acid[20, 24]. Two new terpenes i.e. lanoset-2-en type triterpene (Fig. 2) and labdane type diterpenoid (Fig. 3)[14] and two dibenzofuran i.e. 2-acetyl-9b-carbmethoxy-7,9-dihydroxy-8-methyl-1,3(2H,9bH)- dibenzofurandione (Fig. 4) and 2,6-diacetyl-7,9-dihydroxy-8,9b-dimethyl-1,3(2H,9bH)-

dibenzofurandione (Fig. 5) known as (+)-Usnic acid, were also identified and isolated from *P. perlata*[17].
Some other isolated constituents are tridecyl myristate (Fig. 6), icosan-1-ol (Fig. 7), 3-ketooleanane (Fig. 8)[12]. The constituents shown in Fig. 9 (4-amino-3-hydroxy-6-methoxy-2-methylcyclohexa-1-3-diene-1-carbaldehyde), Fig. 10 (5-amino-2-ethoxy-4-methylcyclohexa-1, 3-diene-1-carboxylic acid) and Fig. 11 (5-methoxy-2-(methoxymethyl)-3 methylpyrazine) have also been isolated from hot methanolic extract of drug[34].

Pharmacological Profile

Antiulcer Activity
Ethanolic 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[18].

Antioxidant Potential
Methonolic extract of *P. perlata* showed significant antioxidant activity when tested in DPPH (2,2'- diphenyl-2-picrylhydrazyl) and phosphomolybdenum reduction assay[35]. The ethanolic extract also showed significantly good free radical scavenging effects and antioxidant potential[32].

Hypolipidemic Potential
Methonolic extract of *P. perlata* was proved to have significant hypolipidemic activity when tested by employing in-vitro anticholesterol assay using Simvastatin as standard[35].

Cytotoxic Activity
Methonolic extract of *P. perlata* was found to have cytotoxic activity and showed antiproliferation against colon cancer cell lines HCT 116[35].

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[36].
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[37].

Hepatoprotective Activity
Aqueous slurry *(*0.7g/kg and 1.0g/kg, p.o.*)* of *P. perlata* was found to have significant hepatoprotective activity in CCl_4 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[38].

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[4]. 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 *Klebseilla pneuomoniae* in agar well diffusion method. This antibacterial potential might be due to the presence of usnic acid[39].
The 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 hot methanolic extract were also found to have remarkable antibacterial potential against *Clavibacter michiganensis, Pseudomonas solanacearum* and *E. coli*. Antibacterial effect of crude extracts was more on *C. michiganensis*, moderate on *P. solanacearum* and less on *E. coli*. The constituents I and II showed more antibacterial effect than constituent III. Constituent II was more effective against *C. michiganensis* and *P. solanacearum*; less against *E. coli* while constituent I and III were more active against *C. michiganensis*, moderately active against *P. solanacearum* and less active against *E. coli* [15, 34].
Further, methanolic extract was observed to have significant antibacterial effect against some Gram positive food borne bacteria[33]. Aqueous-methanolic extract was also effective against *B. cereus, P. aeruginosa, Bacillus pumilus, E. coli, Citrobacter freundii, S. aureus, Streptococcus pneumoniae* and *K. pneumonia* in agar well diffusion method[40]. Two new isolated terpenes i.e. lanoset-2-en type triterpene and labdane type diterpenoid also showed good antibacterial potential against *S. aureus* and *E. coli*[14].

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[15, 34]. Further aqueous methanolic extract also showed significant action against *Candida albicans* and *A. niger* in agar well diffusion method[40].

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[41].

Antiurolithiatic Activity
The hydroalcoholic extract of *P. perlata* showed significant in-vitro antiurolithiatic activity against APMH (Ammonium Magnesium Phosphate Hexahydrate) crystals of struvite stone in single diffusion gel growth technique[42].

Fig. 1 *Parmelia perlata* (Dried sample)

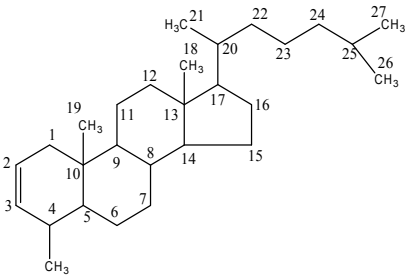

Fig. 2 Lanoset-2-en Type Triterpene

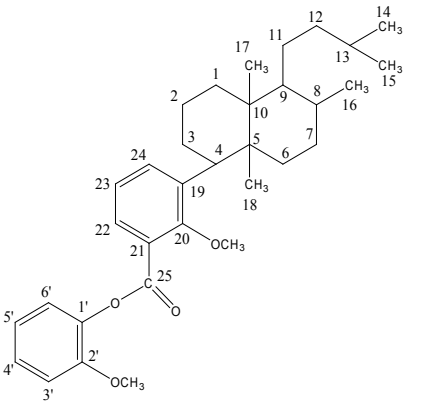

Fig. 3 Labdane Type Diterpenoid

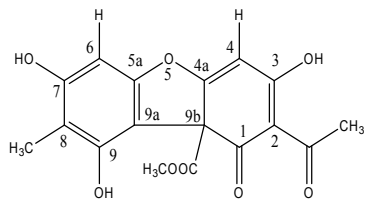

Fig. 4 2-acetyl-9b-carbmethoxy-7,9-dihydroxy 8-methyl-1,3(2H,9bH)-dibenzofurandione

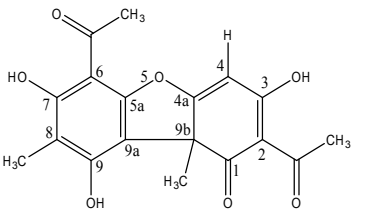

Fig. 5 2,6-diacetyl-7,9-dihydroxy-8,9b-dimethyl-1,3(2H,9bH)-dibenzofurandione

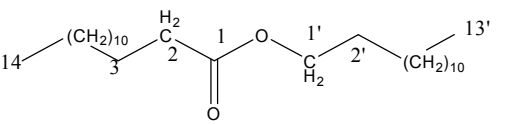

Fig. 6 Tridecyl myristate

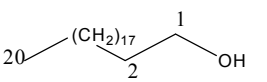

Fig. 7 Icosan-1-ol

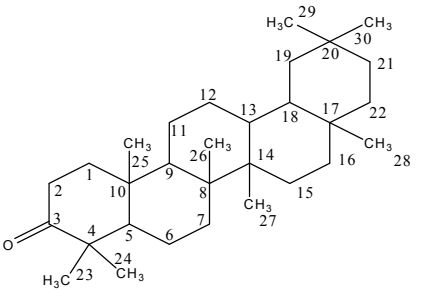

Fig. 8 3-Ketooleanane

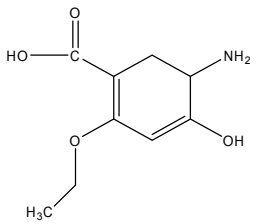

Fig. 10 5-amino-2-ethoxy-4-methyl cyclohexa-1, 3-diene-1-carboxylic acid

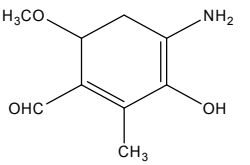

Fig. 9 4-amino-3-hydroxy-6-methoxy-2-methyl-cyclohexa-1-3-diene-1-carbaldehyde

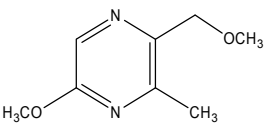

Fig. 11 5-methoxy-2-(methoxymethyl)-3-methylpyrazine

CONCLUSION

This review revealed that *P. perlata* is a very important drug of traditional system of medicine that has multifaceted therapeutic properties out of which only a few like antimicrobial, antidiabetic, antioxidant, antiulcer, hepatoprotective etc are scientifically substantiated. Many of its traditional uses like analgesic, anti-inflammatory, in male sexual problems, menstrual disorders, blood diseases, heart diseases etc are needed to be scientifically explored. Further it also has many unique phytoconstituents that might be responsible for various pharmacological activities but most of them are still unexplored. In nutshell this manuscript, attracts the attention of researchers to pharmaceutically explore *P. perlata* for different pharmacological activities, their underlined mechanisms of action and accountable phytoconstituents; and will be a significant source of information for scientists interested in studying this drug.

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