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Chemistry, ethnobotanical uses and biological activities of the lichen genus *Heterodermia* Trevis. (Physciaceae; Lecanorales; Ascomycota): A comprehensive review

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ABSTRACT

Lichens are composite organisms comprised of a photobiont (an alga or a cyanobacterium) and a mycobiont (an ascomycete or basidiomycete fungus) and represent a stable, ecologically obligate symbiotic association. The lichen genus *Heterodermia* Trevis (Physciaceae; Lecanorales; Ascomycota) is one of the lichen genera distributed worldwide. The thallus is foliose, dichotomously or irregularly branched and the genus *Heterodermia* differs from other foliose lichen genera in the family Physciaceae mainly on the basis of its prosoplectenchymatous upper cortex in combination with atranorin (a cortical lichen substance). In this review, an attempt is made to compile data (by referring books, journals and various search engines such as Google Scholar, PubMed, and ScienceDirect) available on the chemistry, traditional uses and biological activities of species of *Heterodermia*. Atranorin and zeorin are the major metabolites found in *Heterodermia* species. Besides these, salazinic acid and norstictic acid are also found in several *Heterodermia* species. *Heterodermia* species are used ethnobotanically as a flavoring agent, in preparation of perfumes and for treatment of wounds and infections. Literature survey revealed the potential of extracts and isolated constituents of *Heterodermia* species to exhibit biological activities such as antimicrobial, antioxidant, cytotoxic, antinociceptive, anti-inflammatory, insecticidal, immunomodulatory and anthelmintic activity.

INTRODUCTION

Lichens are composite organisms (holobionts) and represent a stable, self-supporting symbiotic relationship between a photosynthetic partner (also called photobiont, representing a microalga or a cyanobacterium) and a fungal partner (referred as mycobiont; represents the majority of the portion of lichens). They are known to be the first colonizers of the earth. Lichens are used traditionally as medicine (to cure dyspepsia, bleeding piles, bronchitis, scabies, stomach disorders, and many disorders), spice, flavoring agents (as an ingredient of garam masala, meat masala, and sambhar masala) and sources of dyes and perfumes. Traditional systems of medicine such as Ayurveda and Unani make use of lichens (Upreti *et al*., 2005; Gupta *et al*., 2007; Nguyen *et al*., 2013; Shah, 2014; Behera *et al*., 2016). Lichens are distributed universally and occur in varied climatic conditions ranging from the poles to the tropics. They grow on various substrates such as rock (saxicolous), leaves (foliicolous), soil (terricolous), bark (corticolous) and wood (lignicolous) and exhibit one of the different growth forms such as a) crustose-spreading rapidly over the surface b) foliose-leafy and loosely attached to the surface and c) fruticose-branched and shrubby, hanging from tree twigs or branches, with a single attachment (Sanders, 2001; Pinokiyo *et al*., 2006; Spribille *et al*., 2008; Kumar, 2009).

Lichens are shown to be the best indicators of air pollution as they are very sensitive to changes in the environment and usually disappear from the area in case of pollution (Gunathilaka *et al*., 2011; Rodríguez *et al*., 2016). Lichens produce a number of secondary metabolites which seldom occur in plants, animals, and other organisms. Most of these metabolites are produced by

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mycobiont and some of the metabolites are formed only in the lichenized state. These substances are often known by name lichen substances or lichen metabolites and are small molecules with complex structure. More than 1000 of such secondary metabolites are known and are derived from acetyl polymalonyl, mevalonic and shikimate pathways (Müller, 2001; Stocker-Wörgötter, 2008; Nguyen *et al*., 2013). Studies on lichens have shown that solvent extracts and purified compounds exhibit potent bioactivities such as antioxidant, hepatoprotective, analgesic, antimicrobial, antiviral, cytotoxic, insecticidal, antinociceptive, anthelmintic, neuroactive, anti-inflammatory, enzyme inhibitory, immunomodularoty and anticancer activity (Müller, 2001; Karunaratne *et al*., 2005; Oksanen, 2006; Verma *et al*., 2008a; Russo *et al*., 2012; Brisdelli *et al*., 2013; Córdova *et al*., 2013; White *et al*., 2014; Thadhani *et al*., 2015; Reddy *et al*., 2016).

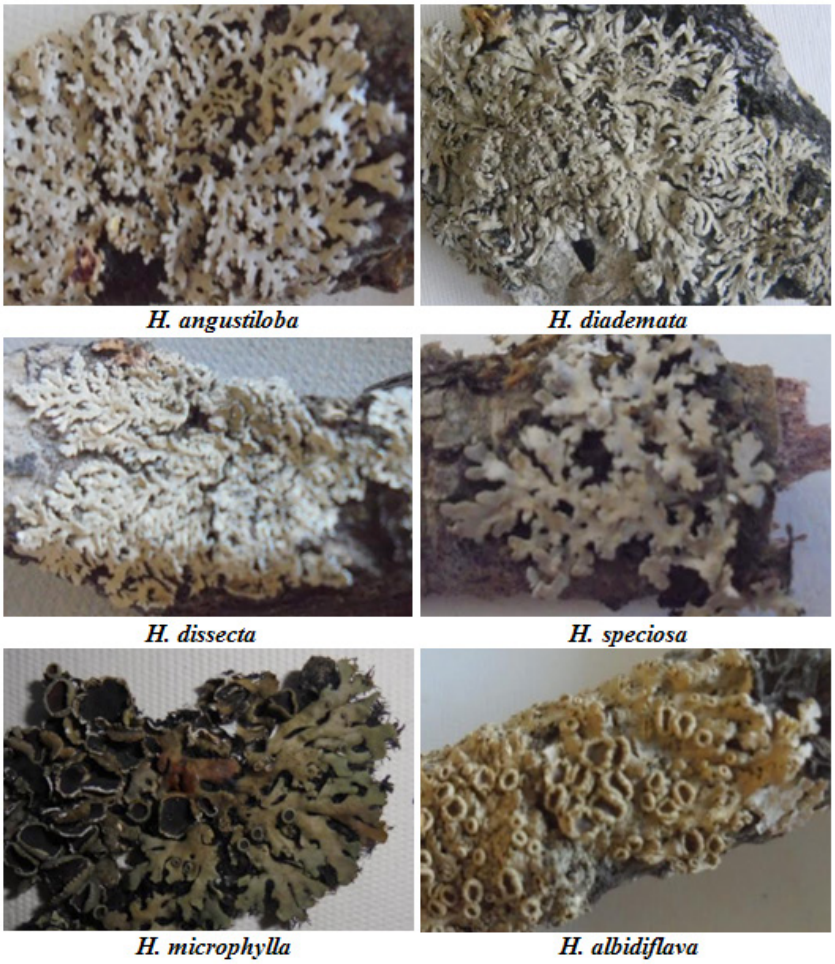

Fig. 1: Some *Heterodermia* species (Photographs by Vinayaka K.S).

THE GENUS *HETERODERMIA*

The lichen genus *Heterodermia* Trevis. (Physciaceae; Lecanorales; Ascomycota) is one of the most commonly found foliose macrolichens (Figure 1) found distributed in tropical and subtropical regions. Earlier, all species of *Heterodermia* were included in *Anaptychia* Körb. until thick-walled spores and the presence of atranorin were considered as useful characters for separating these two genera. The genus *Heterodermia* is distinguished from other foliose lichen genera in the family Physciaceae chiefly on the basis of its prosoplectenchymatous upper cortex in combination with atranorin (as a cortical lichen substance). Most *Heterodermia* species are also characterized by the production of abundant marginal cilia (that resembles rhizenes), lack of a lower cortex and the presence of norstictic and salazinic acids as the common medullary substances. Thallus of *Heterodermia* is foliose, adnate, suberect, rosulate to pendulous, irregularly or dichotomously branched, heteromerous and corticated on the upper side or both sides. The upper cortex is unevenly or uniformly thick. The photobiont is a green alga. Apothecia are laminal, sessile to pedicellate; asci 8-spored; ascospores 2-celled (Awasthi, 2007; Luckling *et al*., 2008; Wang *et al*., 2008; Wei *et al*., 2008). Some species of *Heterodermia* are used traditionally in certain countries as medicine and as spice and flavoring agent (Upreti *et al*., 2005; Rawat, 2016). In this review, we focus on traditional uses, chemistry and biological activities of *Heterodermia* species. A detailed and extensive literature survey was carried out on various aspects of the lichen genus *Heterodermia* by referring standard flora, journals, and

various search engines including Google Scholar, PubMed, and ScienceDirect.

ETHNOBOTANICAL USES OF *HETERODERMIA* SPECIES

Lichens have traditional uses worldwide. Some species of *Heterodermia* find potential use in the form of medicine and flavoring agents and in the preparation of perfumes. The ethnic group in Sikkim uses *H. diademata* traditionally and applies the thalli on the cuts for protecting from wetting and infection (Upreti *et al*., 2005). The ethnic communities in Madhya Pradesh, India make use of *H. tremulans* as spice and flavoring agent for meat and vegetables (Upreti *et al*., 2005). Together with *Parmotrema*, *H. diademata* is traditionally used as flavoring agent for meat and other food items in Karnataka, India. It is also used medicinally to heal cuts and wounds and is used as a plaster to protect the wound from infection (Vinayaka and Krishnamurthy, 2012). The traditional industries in Uttar Pradesh, India utilize *Heterodermia* species viz. *H. diademata* and *H. boryi* in the preparation of perfumes (Singh *et al*., 2015). The ethnic communities in Nepal use *H. diademata* for treatment of wound and to stop bleeding after the injury. The lichen is mixed with *Artemisia vulgaris* or *Eupatorium odoratum* and used to cure fresh wounds or cuts (Devkota *et al*., 2017). The indigenous Pankararu people in the semi-arid of Pernambuco State, Northeast of Brazil, utilize *H. galactophylla* for treating digestive system related problems such as diarrhea and vomiting and for treating epilepsy (Londoño-Castañeda *et al*., 2017).

COMMON LICHEN SUBSTANCES PRESENT IN *HETERODERMIA* SPECIES

Lichens are capable of producing a number of secondary metabolites which apparently do not occur in other organisms. Most of these metabolites are small molecules but are biologically active and exhibit myriad of biological activities. Besides, these metabolites are also useful in the taxonomy of lichens. Thin layer chromatography is one of the most widely used bioanalytical techniques employed to detect lichen substances. Besides, other techniques such as HPLC, column chromatography, liquid chromatography-mass spectrometry and nuclear magnetic resonance spectroscopic methods have been widely employed to detect and to elucidate the structures of lichen substances. Compounds viz. atranorin and zeorin are known to be the signature compounds to be present in *Heterodermia* species. Besides these compounds, compounds such as norstictic acid and salazinic acid are also present in many of *Heterodermia* species (Awasthi, 2007; Fazio *et al*., 2007; Molnár and Farkas, 2010; Honda *et al*., 2010; Musharraf *et al*., 2015; Kekuda and Vinayaka, 2016). A list of major secondary metabolites detected in some *Heterodermia* species is shown in Table 1 and Figure 2 presents structures of some lichen metabolites.

BIOLOGICAL ACTIVITIES OF *HETERODERMIA* SPECIES

Lichens are shown to display a variety of pharmacological activities. Several studies have been carried out by researchers to investigate biological activities of crude solvent extracts and purified compounds from *Heterodermia* species. Literature survey revealed that species of *Heterodermia* exhibits a range of biological activities such as antimicrobial, antioxidant, antinociceptive, anti-inflammatory, immunomodulatory, enzyme inhibitory, cytotoxic, insecticidal and anthelmintic activities.

Antibacterial activity of *Heterodermia* species

Studies have shown that solvent extracts and purified compounds from *Heterodermia* species exhibit antibacterial properties. Ethanol extract of *H. leucomela* was found to inhibit Mycobacterium tuberculosis strains (Gupta *et al*., 2007). The study carried out by Paudel *et al*. (2012) revealed the potential of methanol extract of *Heterodermia* sp. to inhibit *Bacillus subtilis*. The methanol extract of *H. diademata* was effective in inhibiting *Staphylococcus aureus* (isolates from burn), *Streptococcus mutans* (cariogenic isolates), uropathogenic bacteria (Kambar *et al*., 2014). Extract of *H. obscurata* was effective against gram positive and gram negative bacteria (Kekuda *et al*., 2015). Solvent extracts of *H. boryi* were shown to inhibit gram positive and gram negative bacteria (Prabhu and Sudha, 2015). Kekuda and Vinayaka (2016) observed anticaries activity exhibited by *H. leucomela* against *Streptococcus mutans* isolates. Dichloromethane extract of *H. diademata* and *H. podocarpa* was inhibitory to *Klebsiella pneumoniae* while dichloromethane extract of *H. leucomelos*, *H. indica* and *H. speciosa* was shown to inhibit the growth of *Staphylococcus aureus* and *K. pneumoniae* (Jha *et al*., 2017). Kekuda *et al*. (2017) revealed inhibition of gram positive and gram negative bacteria by an extract of *H. incana*. In another study by Hengameh and Rajkumar (2017), solvent extracts of *H. leucomelos* were effective in inhibiting gram-positive and gram-negative bacteria. Atranorin and sekikaic acid, isolated from *H. obscurata*, were shown to display inhibitory activity against bacteria viz. *E. coli*, *B. subtilis* and *S. typhi* (Thadhani *et al*., 2012).

Antifungal activity of *Heterodermia* species

Extracts and isolated constituents from *Heterodermia* species were shown to display antifungal properties. The aqueous extract obtained from *H. leucomela* was effective in exhibiting antifungal activity against a number of molds including plant pathogenic fungi and dermatophytes in terms of inhibition of spore germination. At 80 µl/ml concentration, 100% inhibition of germination of spores of all test fungi was observed (Shahi *et al*., 2001). Acetone, methanol and chloroform extracts of *H. diademata* were shown to exhibit antifungal activity against phytopathogenic fungi such as *Aspergillus flavus, A. fumigatus, Alternaria alternata, Fusarium roseum, F. oxysporum, F. solani, Penicillium citrinum* (Tiwari *et al*., 2011). The methanol extract of *H. diademata* was effective in inhibiting *Candida albicans, Cryptococcus neoformans, Colletotrichum capsici* (Kambar *et al*., 2014). The methanol extract of *H. obscurata* displayed antifungal activity against *C. capsici*, *F. oxysporum, A. alternata* and *A. flavus* (Kekuda *et al*., 2015). Solvent extracts viz. acetone, methanol and chloroform extracts of *H. leucomelos* were shown to inhibit the growth of *A. niger, A. flavus, F. oxysporum, F. solani, C. falcatum* (Babiah *et al*., 2015). Extracts of *H. comosa* were effective against *F. solani* and *F. oxysporum* (Shivanna and Garampalli, 2016). The methanol extract of *H. incana* was shown to inhibit mycelial growth of seed-borne fungi (Kekuda *et al*., 2017). *Candida albicans* was susceptible to dichloromethane fraction of *H. indica*

and *H. diademata* (Jha *et al*., 2017). Atranorin, isolated from hexane extract of *H. microphylla*, is shown to exhibit antifungal activity against *Colletotrichum gloeospoioides* and *C. musae*. The compound was effective in inhibition germination of spores of the fungi (Bombuwela *et al*., 2008). Methyl β-orcinol carboxylate, derived from atranorin (isolated from *H. obscurata*) was effective in inhibiting yeasts and molds (Thadhani *et al*., 2012). Solvent extracts of *H. boryi* displayed inhibitory activity against *Pestalotia foedans*, *Phomopsis leptostromiformis* var. *occidentalis*, *F. oxysporum*, *Paeciliomyces variotii* (Balasubramanian and Nirmala, 2014a).

Table 1: Major secondary metabolites in various *Heterodermia* species.

Heterodermia sp.	Compounds detected	References
H. squamulosa	Atranorin, zeorin	Wang *et al*. (2008)
H. microphylla	Atranorin, chloroatranorin and zeorin	Bombuwela *et al*. (2008)
H. queensberryi	Atranorin, zeorin	Weerakoon and Aptroot (2014)
H. japonica	Atranorin, zeorin, salazinic acid, norstictic acid	Din *et al*. (2010)
H. appendiculata	Atranorin, zeorin, salazinic acid, norstictic acid, chloratranorin	Din *et al*. (2010)
H. leucomela	Atranorin, zeorin, salazinic acid, glyceryl trilinolate, 6a-hydroxyhop-21bH-22(29)-en, and 3,6-dimethyl-2-hydroxy-4-methoxybenzoic acid	Devkota (2008), Kathirgamanathar *et al*. (2006)
H. upretii	Atranorin, teloschistin and 7-chloroemodin	Joshi *et al*. (2014)
H. diademata	Atranorin, chloratranorin and zeorin	Behera *et al*. (2016)
H. incana	Atranorin and zeorin	Kekuda *et al*. (2017)
H. obscurata	Atranorin, chloratranorin, zeorin, emodin, 7-chloroemodin	Din *et al*. (2010)
H. albicans	Atranorin, zeorin and salazinic acid	Behera *et al*. (2016)
H. angustiloba	Atranorin, zeorin, salazinic acid and norstictic acid	Behera *et al*. (2016)
H. circinalis	Atranorin, zeorin	Boom *et al*. (2007)
H. granulifera	Atranorin, chloroatranorin, salazinic acid, zeorin, hypoconstictic acid, consalazinic acid, norstictic acid, 3-O-methylconsalazinic acid, norhypoconstictic acid	Boom *et al*. (2007)
H. magellanica	Atranorin, zeorin	Boom *et al*. (2007)
H. antillarum	Atranorin, zeorin and salazinic acid	Behera *et al*. (2016)
H. flabellata	Atranorin, zeorin, emodin, 7-chloroemodin	Din *et al*. (2010); Behera *et al*. (2016)
H. isidiophora	Atranorin and zeorin	Behera *et al*. (2016)
H. pseudospeciosa	Atranorin, zeorin, salazinic acid and norstictic acid	Behera *et al*. (2016)
H. punctifera	Atranorin, zeorin and norstictic acid	Devkota (2008)
H. speciosa	Atranorin, zeorin	Devkota (2008)
H. dissecta	Atranorin, zeorin, salazinic acid and norstictic acid	Devkota (2008)
H. indica, *H. albidiflava*, *H. boryi*, *H. comosa*, *H. dactyliza*, *H. firmula*, *H. galactophylla*, *H. hypochraea*, *H. hypoleuca*, *H. lutescens*, *H. pellucida*, *H. togashii*, *H. tremulans*	Atranorin, zeorin	Awasthi (2007)
H. awasthii, *H. barbifera*, *H. himalayensis*, *H. podocarpa*, *H. propagulifera*, *H. rubescens*	Atranorin, zeorin, salazinic acid, norstictic acid	Awasthi (2007)
H. dentrica	Atranorin, salazinic acid, norstictic acid	Awasthi (2007)
H. hypocaesia, *H. rubricosa*	Atranorin, zeorin, salazinic acid	Awasthi (2007)

Cytotoxic activity of *Heterodermia* species

Methanol extracts of some *Heterodermia* sp. were investigated for cytotoxicity by brine shrimp lethality assay. Some species were effective in terms of mortality of shrimps with an IC_{50} value of 100 and 200 µg/ml (Paudel *et al*., 2012). Recently, dichloromethane fraction from *H. indica, H. leucomela, H. diademata, H. punctifera, H. microphylla, H. podocarpa* and *H. speciosa* displayed strong cytotoxicity in brine shrimp assay with >80% mortality (Jha *et al*., 2017).

Antioxidant activity of *Heterodermia* species

Many *Heterodermia* species have been investigated for antioxidant activity. Verma *et al*. (2008b) showed a dose-dependent inhibition of lipid peroxidation by an extract of *H. podocarpa*. Thadhani *et al*. (2011) isolated compounds viz. methyl orsellinate, methyl haematommate, methyl-β-orcinolcarboxylate, atranorin, and m-depside sekikiac acid from *H. obscurata* and evaluated their antioxidant activity by in vitro superoxide radical, nitric oxide radical and DPPH radical scavenging assays. The isolated compounds displayed lower scavenging potential when compared to reference antioxidants. Methanol extracts from *Heterodermia* species were effective in scavenging DPPH and ABTS radicals with marked scavenging potential against DPPH radicals (Paudel *et al*., 2012). Balasubramanian and Nirmala (2014b) screened

antioxidant potential of *H. boryi*. The lichen extract was effective in scavenging DPPH and ABTS radicals and caused inhibition of lipid peroxidation and DNA damage. The study of Behera *et al*. (2016) revealed the antioxidant potential of ethyl acetate extract of *Heterodermia* species by DPPH and TEAC (Trolox equivalent activity capacity) assays. None of the species except *H. pseudospeciosa* exhibited an inhibition of DPPH to >50%. The study of Jha *et al*. (2017) revealed the potential of *H. indica, H. leucomela H. microphylla,* and *H. speciosa* to scavenge DPPH radicals.

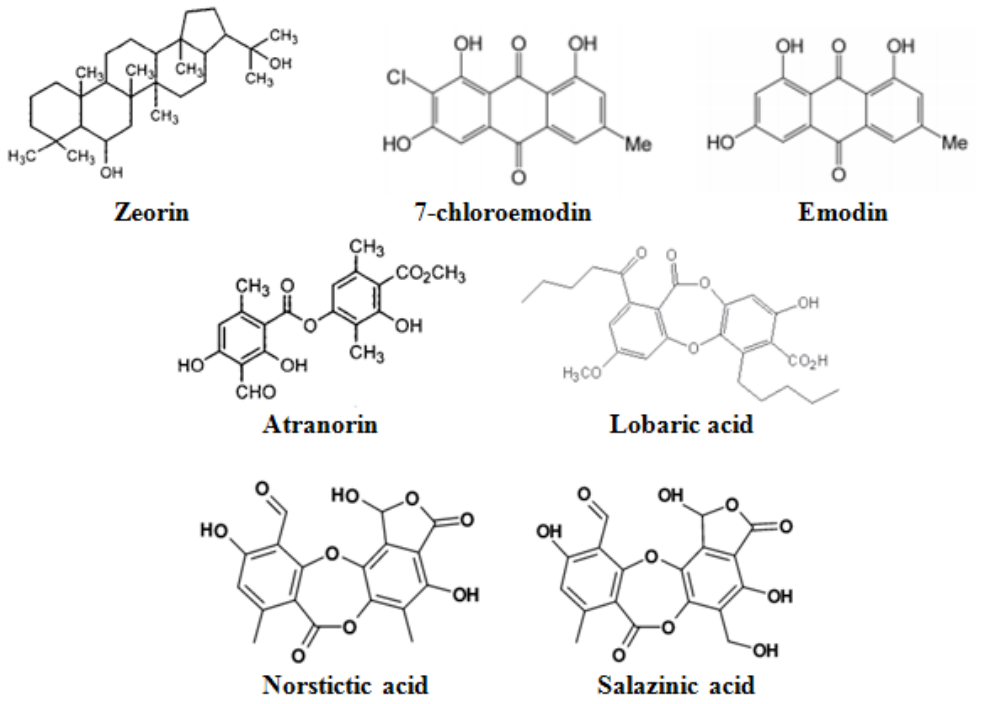

Fig. 2: Structures of some lichen substances.

Table 2: Enzyme inhibitory potential of *Heterodermia* species.

***Heterodermia* species**	**Enzyme inhibited**	**Reference**
H. leucomela	Amylase	Karthik *et al*. (2011)
H. leucomelos	β-Glucosidase	Parizadeh and Garampalli (2016)
H. diademata, H. angustiloba, H. albicans, H. flabellata, H. antillarum, H. isidiophora, H. incana and *H. pseudospeciosa*	Lipoxygenase	Behera *et al*. (2016)
H. leucomelos	Amylase	Hengameh *et al*. (2016)
H. leucomelos	Pancreatic lipase	Shivanna *et al*. (2017)
Heterodermia sp.	Acetyl and butyryl-cholinesterase, phosphodiesterase, β-glucuronidase	Thadhani *et al*. (2014)
H. podocarpa	Tyrosinase	Verma *et al*. (2008b)

Enzyme inhibitory activity of *Heterodermia* species

Studies have shown the potential of some *Heterodermia* species to inhibit certain enzymes of clinical importance such as amylase, lipase, tyrosinase, and glucosidase. A brief detail on the enzyme inhibitory potential of extracts and purified compounds of *Heterodermia* species is presented in Table 2.

Antinociceptive and anti-inflammatory activity of *Heterodermia* species

Glucomannan was obtained from successive aqueous and alkaline extraction of the thallus of the lichenized fungus *H. obscurata*. Intra-peritoneal administration of glucomannan resulted in a marked and dose-dependent inhibition of acetic acid-induced visceral pain with an ID_{50} of 0.6 mg/kg and inhibition of 88 ± 4%. It also reduced leukocyte migration indicating the potential utilization of glucomannan against pain and inflammation (Pereira *et al*., 2010). In another study, glucomannan from *H. obscurata*, was investigated for antinociceptive activity in behavioral models of acute and chronic pain in mice. In the partial sciatic nerve ligation model, the glucomannan was found to reduce the mechanical allodynia and the levels of interleukin 1-β (IL-1β) in spinal cord and nerve. In case of systemic treatment, the polysaccharide inhibited the nociception induced by intraplantar injection of glutamate and by intrathecal injection of N-methyl-d-aspartic acid, (±)-1-aminocyclopentane-trans-1,3-dicarboxylic acid, tumour necrosis factor α and IL-1β. It was concluded that the

glucomannan has significant antinociceptive effect in acute and chronic pain (Córdova *et al*., 2013).

Immunomodulatory activity of *Heterodermia* species

Lobaric acid, a compound isolated from *Heterodermia* sp., was investigated for immunomodulatory activity by Thadhani *et al*. (2014). The compound was found to exhibit potent oxidative burst inhibitory activity in human polymorphonuclear (PMN) cells. The compound suppressed both the myeloperoxidase dependent and myeloperoxidase independent reactive oxygen species production of PMNs. In another study, compounds viz. methyl orsellinate, methyl haematommate, methyl-β-orcinolcarboxylate, lobaric acid and atranorin isolated from *H. obscurata* were tested for immunomodulatory effect on the basis of their effect on respiratory burst of human whole blood phagocytes, isolated human polymorphonuclear leukocytes and murine macrophages using luminol or lucigenin-based chemiluminescence probes (Thadhani *et al*., 2015). Compounds viz. methyl haematomate and methyl orsellinate displayed moderate effect on whole blood and intra-cellular ROS (reactive oxygen species), however, these compounds strongly inhibited extra-cellular ROS with IC_{50} values 3.3 ± 0.1 µg/ml and 6.1 ± 1.0 µg/ml, respectively. Lobaric acid was shown to suppress myeloperoxidase dependent and myeloperoxidase independent ROS production in PMNs.

Insecticidal activity of *Heterodermia* species

Karthik *et al*. (2011) determined the insecticidal activity of methanol extract of *H. leucomela* in terms of its larvicidal effect against 2nd and 3rd instar larvae of *Aedes aegypti*. Among larvae, marked susceptibility was shown by 2nd instar larvae. In another study 3,6-dimethyl-2-hydroxy-4-methoxybenzoic acid, isolated from *H. leucomelos*, was shown to exhibit larvicidal effect against 2nd instar larvae of *A. aegypti* (Kathirgamanathar *et al*., 2006).

Anthelmintic activity of *Heterodermia* species

The study carried out by Prabhu and Sudha (2016) revealed the anthelmintic activity of various solvent extracts viz. aqueous, methanol, petroleum ether, acetone and chloroform extract of *H. boryi*. The extracts were effective in causing paralysis and death of adult Indian earthworm (*Pheretima posthuma*) in a dose-dependent manner. Acetone and methanol extracts displayed significant anthelmintic activity at the highest concentration tested.

CONCLUSIONS

An extensive literature survey carried out resulted in potential biological properties of *Heterodermia* species. Compounds such as atranorin, zeorin, salazinic acid and norstictic acid are common in many species of *Heterodermia*. The presence of these secondary metabolites might be attributed to the various biological activities displayed by *Hetereodermia* species. Isolation of mycobiont and their mass cultivation for the purpose of obtaining bioactive metabolites should be considered to exploit the lichens for commercial purpose.

SOURCES OF SUPPORT

None.

CONFLICTS OF INTEREST

Author declare there are no conflict of interest.

REFERENCES

Awasthi DD. A compendium of the macrolichens from India, Nepal and Sri Lanka, Bishen Singh Mahendra Pal Singh, Dehra Dun, India, 2007.

Babiah PS, Upreti DK, John SA. Assessment of fungicidal potential of lichen *Heterodermia leucomelos* (L.) Poelt against pathogenic fungi. Current Research in Environmental & Applied Mycology, 2015; 5(2):92-100.

Balasubramanian M, Nirmala P. Antimycobacterial activity of foliose lichens on plant and animal pathogens. International Journal of Pharmaceutical Sciences and Research, 2014a; 5(11):4825-4831.

Balasubramanian M, Nirmala P. Evaluation of anti-oxidant properties of Foliose lichens. Journal of Chemical and Pharmaceutical Research, 2014b; 6(9):177-184.

Behera BC, Morey MV, Gaikwad SB. Anti-lipoxygenase, radical scavenging and antimicrobial activities of lichen species of genus *Heterodermia* (Physciaceae). Botanica Pacifica, 2016; 5(1):79-85.

Bombuwela K, Kathirgamanathar S, Thadhani V, Jayalal RGU, Adikaram NKB, Wijesundara DSA, Andersen R, Wolseley P, Karunaratne V. Chemistry of *Heterodermia microphylla*, a lichen new to Sri Lanka. J Natn Sci Foundation Sri Lanka, 2008; 36(3):251-252.

Boom PVD, Elix J, Sipman H. New or interesting lichen records from Guatemala I. Willdenowia, 2007; 37:363-375.

Brisdelli F, Perilli M, Sellitri D, Piovano M, Garbarino JA, Nicoletti M, Bozzi A, Amicosante G, Celenza G. Cytotoxic activity and antioxidant capacity of purified lichen metabolites: an in vitro study. Phytother Res, 2013; 27(3):431-437.

Córdova MM, Martins DF, Silva MD, Baggio CH, Carbonero ER, Ruthes AC, Iacomini M, Santos AR. Polysaccharide glucomannan isolated from *Heterodermia obscurata* attenuates acute and chronic pain in mice. Carbohydr Polym, 2013; 92(2):2058-64.

Devkota A. Taxonomic study of lichens of Phulchowki hills, Lalitpur district (Kathmandu valley). Scientific World, 2008; 6(6):44-51.

Devkota S, Chaudhary RP, Werth S, Scheidegger C. Indigenous knowledge and use of lichens by the lichenophilic communities of the Nepal Himalaya. Journal of Ethnobiology and Ethnomedicine, 2017; 13(1):15.

Din LB, Zakaria Z, Samsudin MW, Elix JA. Chemical profile of compounds from lichens of Bukit Larut, Peninsular Malaysia. Sains Malaysiana, 2010; 39(6):901-908.

Fazio AT, Adler MT, Bertoni MD, Sepulveda CS, Damonte EB, Maier MS. lichen secondary metabolites from the cultured lichen mycobionts of *Teloschistes chrysophthalmus* and *Ramalina celastri* and their antiviral activities. Z Naturforsch, 2007; 62c:543-549.

Gunathilaka PADHN, Ranundeniya RMNS, Najim MMM, Seneviratne S. A determination of air pollution in Colombo and Kurunegala, Sri Lanka, using energy dispersive X-ray fluorescence spectrometry on *Heterodermia speciosa*. Turkish Journal of Botany, 2011; 35:439-446.

Gupta VK, Darokar MP, Saikia D, Pal A, Fatima A, Khanuja SPS. Antimycobacterial activity of lichens. Pharmaceutical Biology, 2007; 45(3):200-204.

Hengameh P, Rajkumar GH. Assessment of bactericidal activity of some lichen extracts by disc diffusion assay. Int J Drug Dev & Res, 2017; 9(1):9-19.

Hengameh P, Rashmi S, Rajkumar HG. In vitro inhibitory activity of some lichen extracts against α-amylase enzyme. European Journal of Biomedical and Pharmaceutical Sciences, 2016; 3(5):315-318.

Honda NK, Pavan FR, Coelho RG, Leite ASR, Micheletti AC, Lopes TIB, Misutsu MY, Beatriz A, Brum RI, Leite CQF. Antimycobacterial activity of lichen substances. Phytomedicine, 2010; 17:328-332.

Jha BN, Shrestha M, Pandey DP, Bhattarai T, Bhattarai HD, Paudel B. Investigation of antioxidant, antimicrobial and toxicity activities of lichens from high altitude regions of Nepal. BMC Complementary and Alternative Medicine, 2017; 17:282.

Joshi Y, Upadhyay S, Chandra K. *Heterodermia upretii*, a new species from India (Physciaceae, Ascomycota). Phytotaxa, 2014; 175(2):117-120.

Kambar Y, Vivek MN, Manasa M, Vinayaka KS, Mallikarjun N, Kekuda PTR. Antimicrobial activity of *Leptogium burnetiae*, *Ramalina hossei*, *Roccella montagnei* and *Heterodermia diademata*. International Journal of Pharmaceutical and Phytopharmacological Research, 2014; 4(3):164-168.

Karthik S, Nandini KC, Kekuda PTR, Vinayaka KS, Mukunda S. Total phenol content, insecticidal and amylase inhibitory efficacy of *Heterodermia leucomela* (L). Annals of Biological Research, 2011; 2(4):38-43.

Karunaratne V, Bombuwela K, kathirgamanathar S, Thadhani VM. Lichens: A chemically important biota. J Natn Sci Foundation Sri Lanka, 2005; 33(3):169-186.

Kathirgamanathar S, Ratnasooriya WD, Baekstrom P, Andersen RJ, Karunaratne V. Chemistry and bioactivity of Physciaceae lichens *Pyxine consocians* and *Heterodermia leucomelos*. Pharmaceutical Biology, 2006; 44(3):217-220.

Kekuda PTR, Raghavendra HL, Vinayaka KS. Antimicrobial activity of *Heterodermia incana* (Stirt.) D.D. Awasthi. International Journal of Green Pharmacy, 2017; 11(Suppl 3):S568-S574.

Kekuda PTR, Ranjitha MC, Firdose G, Vidya P, Vinayaka KS. Antimicrobial activity of selected corticolous lichens. Science, Technology and Arts Research Journal, 2015; 4(3):169-174.

Kekuda PTR, Vinayaka KS. In vitro anticaries activity of some macrolichens of Karnataka, India. International Journal of Pharma Research and Health Sciences, 2016; 4(3):1244-1248.

Kumar B. Assessment of lichen species in a temperate region of Garhwal Himalaya, India. The Journal of American Science, 2009; 5(4):107-112.

Londoño-Castañeda PA, Buril MLL, Rego-Cunha IP, Silva NH, Honda NK, Pereira EC, Andrade LHC. Lichens used in the traditional medicine by the Pankararu Indigenous community, Pernambuco-Brazil. Global Journal of Science Frontier Research: C Biological Science, 2017; 17(4):15-22.

Luckling R, del Prado R, Lumbsch TH, Will-Wolf S, Aptroot A, Sipman HJM, Umana L, Chaves JL. Phylogenetic patterns of morphological and chemical characters and reproductive mode in the *Heterodermia obscurata* group in Costa Rica (Ascomycota, Physciaceae). Systematics and Biodiversity, 2008; 6(1):31-41.

Molnár K, Farkas E. Current results on biological activities of lichen secondary metabolites: a review. Z Naturforsch C, 2010; 65(3-4):157-173.

Müller K. Pharmaceutically relevant metabolites from lichens. Appl Microbiol Biotechnol, 2001; 56(1-2):9-16.

Musharraf SG, Kanwal N, Thadhani VM, Choudhary IM. Rapid identification of lichen compounds based on the structure–fragmentation relationship using ESI-MS/MS analysis. Anal Methods, 2015; 7:6066-6076.

Nguyen KH, Chollet-Krugler M, Gouault N, Tomasi S. UV-protectant metabolites from lichens and their symbiotic partners. Nat Prod Rep, 2013; 30(12):1490-1508.

Oksanen I. Ecological and biotechnological aspects of lichens. Appl Microbiol Biotechnol, 2006; 73:723-734.

Parizadeh H, Garampalli RH. Evaluation of some lichen extracts for β-Glucosidase inhibitory as a possible source of herbal anti-diabetic drugs. American Journal of Biochemistry, 2016; 6(2):46-50.

Paudel B, Bhattarai HD, Pandey DP, Hur JS, Hong SG, Kim I, Yim JH. Antioxidant, antibacterial activity and brine shrimp toxicity test of some mountainous lichens from Nepal. Biol Res, 2012; 45:387-391.

Pereira MI, Ruthes AC, Carbonero ER, Marcon R, Baggio CH, Freitas CS, Santos AR, Eliasaro S, Sassaki GL, Gorin PA, Iacomini M. Chemical structure and selected biological properties of a glucomannan from the lichenized fungus *Heterodermia obscurata*. Phytochemistry, 2010; 71(17-18):2132-2139.

Pinokiyo A, Singh KP, Singh JS. Leaf-colonizing lichens: their diversity, ecology and future prospects. Current Science, 2006; 90(4):509-518.

Prabhu SS, Sudha SS. Evaluation of the antibacterial properties of some lichen species against human pathogens. International Journal of Advanced Research in Biological Sciences, 2015; 2(4):177-181.

Prabhu SS, Sudha SS. In vitro study on anthelmintic activity of *Heterodermia boryi* macrolichen collected from the Nilgiris, Tamilnadu, India. Int J Curr Microbiol App Sci, 2016; 5(9):764-768.

Rawat S. North West region of Nanda Devi biosphere reserves, Garhwal Himalaya with unexplored lichen wealth and its medicinal lichen distribution in different aspect. New York Science Journal, 2016; 9(9):28-40.

Reddy RG, Veeraval L, Maitra S, Chollet-Krugler M, Tomasi S, Dévéhat FL, Boustie J, Chakravarty S. Lichen-derived compounds show potential for central nervous system therapeutics. Phytomedicine, 2016; 23(12):1527-1534.

Rodríguez AOE, Andrade BW, Díaz LF, Celis C, Ortiz-Ardila A. Quantification of heavy metals in lichens from the upper basin of the river Bogotá. Pharmacologyonline, 2016; 2:21-27.

Russo A, Caggia S, Piovano M, Garbarino J, Cardile V. Effect of vicanicin and protolichesterinic acid on human prostate cancer cells: role of Hsp70 protein. Chem Biol Interact, 2012; 195(1):1-10.

Sanders WB. Lichens: The interphase between Mycology and Plant morphology. BioScience, 2001; 51(12):1025-1036.

Shah NC. Lichens of commercial importance in India. The Scitech Journal, 2014; 1(2):32-36.

Shahi SK, Shukla AC, Dikshit A, Upreti DK. Broad spectrum antifungal properties of the lichen Heterodermia leucomela. The Lichenologist, 2001; 33:177-179.

Shivanna R, Garampalli RH. Investigation of macrolichens for antifungal potentiality against phytopathogens. Indo American Journal of Pharmaceutical Research, 2016; 6(4):5290-5296.

Shivanna R, Parizadeh H, Garampalli RH. Invitro anti-obesity effect of macrolichens *Heterodermia leucomelos* and *Ramalina celastri* by pancreatic lipase inhibitory assay, Int J Pharm Pharm Sci, 2017; 9(5):137-140.

Singh S, Upreti DK, Lehri A, Paliwal AK. Quantification of lichens commercially used in traditional perfumery industries of Uttar Pradesh, India. Indian Journal of Plant Sciences, 2015; 4(1):29-33.

Spribille T, Thor G, Bunnell FL, Goward T, Bjork CR. Lichens on dead wood: species-substrate relationships in the epiphytic lichen floras of the Pacific Northwest and Fennoscandia. Ecography, 2008; 31:741-750.

Stocker-Wörgötter E. Metabolic diversity of lichen-forming ascomycetous fungi: culturing, polyketide and shikimate metabolite production, and PKS genes. Nat Prod Rep, 2008; 25(1):188-200.

Thadhani VM, Choudhary IM, Khan S, Karunaratne V. Antimicrobial and toxicological activities of some depsides and depsidones. J Natn Sci Foundation Sri Lanka, 2012; 40(1):43-48.

Thadhani VM, Choudhary MI, Ali S, Omar I, Siddique H, Karunaratne V. Antioxidant activity of some lichen metabolites. Nat Prod Res, 2011; 25(19):1827-1837.

Thadhani VM, Mesaik AM, Asif M, Karunaratne V, Choudhary IM. Immunomodulatory activities of some common lichen metabolites. Int J Pharm Pharm Sci, 2015; 7(11):144-147.

Thadhani VM, Naaz Q, Choudhary IM, Mesaik AM, Karunaratne V. Enzyme inhibitory and immunomodulatory activities of the depsidone lobaric acid extracted from the lichen *Heterodermia* sp. J Natn Sci Foundation Sri Lanka, 2014; 42(2):193-196.

Tiwari P, Rai H, Upreti DK, Trivedi S, Shukla P. Assessment of antifungal activity of some Himalayan foliose lichens against plant pathogenic fungi. American Journal of Plant Sciences, 2011; 2:841-846.

Upreti DK, Divakar PK, Nayaka S. Commercial and ethnic use of lichens in India. Economic Botany, 2005; 59(3):269-273.

Verma N, Behera BC, Makhija U. Antioxidant and hepatoprotective activity of a lichen *Usnea ghattensis* in vitro. Appl Biochem Biotechnol, 2008a; 151(2-3):167-181.

Verma N, Behera BC, Sonone A, Makhija U. Lipid peroxidation and tyrosinase inhibition by lichen symbionts grown in vitro. African Journal of Biochemistry Research, 2008b; 2(12):225-231.

Vinayaka KS, Krishnamurty YL. Ethno-lichenological studies of Shimoga and Mysore districts, Karnataka, India. Advances in Plant Sciences, 2012; 25(1):265-267.

Wang XY, Hur H, Lee YM, Koh YJ, Hur J. First Report of *Heterodermia squamulosa* (Lichenized Ascomycota, Physciaceae) in South Korea. Mycobiology, 2008; 36(3):190-192.

Weerakoon G, Aptroot A. Over 200 new lichen records from Sri Lanka, with three new species to science. Cryptogamie, Mycologie, 2014; 35(1):51-62.

Wei XL, Luo H, Koh YJ, Hur JS. A taxonomic study of *Heterodermia* (Lecanorales, Ascomycota) in South Korea based on phenotypic and phylogenetic analysis. Mycotaxon, 2008; 105:65-78.

White PAS, Oliveira RCM, Oliveira AP, Serafini MR, Araujo AAS, Gelain DP, Moreira JCF, Almeida JRGS, Quintans JSS, Quintans-Junior LJ, Santos MRV. Antioxidant activity and mechanisms of action of natural compounds isolated from lichens: A systematic review. Molecules, 2014; 19:14496-14527.

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