



The Potential Medicinal Value of *Barleria lupulina*: A Mini Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Medicinal plants are a major source of numerous valuable natural chemicals and medicines. Therefore, they have been in use for thousands of years against varying diseases, and even at present around 80% of the world population depends on plant derived medicines. *Barleria lupulina* Lindl. widely known as "Ranwan Katukarandu" in Sri Lanka is a plant which has been used widely in traditional plant derived medicines, as it includes numerous phytochemicals with potential biological properties. *B. lupulina* has been tested for its many phytochemical constituents such as, flavonoids, phenylethanoid glycosides, quinones, iridoids, immunostimulant proteins, antibiotics, alkaloids, starch, tannin, reducing sugars, protein, amino acids, glycosides, steroids etc; which have been found to possess antioxidant, antimicrobial, larvicidal, antidiabetic, immunomodulatory and antiarthritic properties. In future, extensive scientific research needs to be conducted on these phytochemicals to produce natural, effective and alternative medicines in place of synthetic medicines. This review gives a report on existing literature, phytochemistry and biological activity of the species *Barleria lupulina*.

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1. INTRODUCTION

Plant derived medicines are safe, widely available, less expensive, and rarely known to cause undesirable side effects. Further, the human immune system is known to have been improved by natural-biologically active phytochemical compounds. Owing to these reasons medicinal plants have played a vital role in meeting the global demand on therapeutics for thousands of years. Medicinal plants are used in various health systems around the world to treat various immunological disorders. *Barleria* spp. belongs to the family Acanthaceae and is a large, widespread, polymorphic, pantropical genus of herbs, shrubs and rarely climbers, including some 300 species. *Barleria* species exhibit several medicinal properties. *Barleria lupulina* widely known as "Ranwan Katukarandu" in Sri Lanka is one of the best-known species with medicinal properties. English name of the plant is Hophead "Philippine Violet" and "Cem Mulli" in tamil. It is known to possess a wide variety of phytochemicals with potential biological properties. The glycosides such as barlerin, shanzhiside, methyl ester, and a few others are restricted to the leaf and stem. *B. lupulina* has been used in folk medicine as an anti-diabetic [1], anti-inflammatory [2,3], analgesic [2], antibacterial [4], and anti-ulcerogenic agent [4]. The flowers, leaves, stems, roots and even seed extracts are rich in bioactive compounds and have been used widely in folk medicine to treat varying ailments and infections [5]. Traditionally the plant leaves have been used to treat snake bites, dog bites, cough, fever, body aches, eczema and itches and sexual disorders [6]. Due to its wide array of phytochemicals the herb can be used as a new lead for making novel drugs [6].

Constituents of *B. lupulina* have been tested for antitumor activity in different carcinogenic models. In addition to the above, *B. lupulina* has also been reported to possess antibacterial [7,8,9], antimicrobial [10], anticancer [11], antiarthritis [12], antiulcerogenic [13], neuropharmacological [14], acute and sub-chronic diuretic [15], as well as anti-viral [16] properties. However, little is known about the biochemical properties that bring out these therapeutic effects. This mini review includes the botanical description, taxonomic classification as well as biological activities, phytochemistry, pharmacological properties and distribution of the

phytochemicals extracted from *B. lupulina* which will continue to hold an important place in indigenous medicine.

2. TAXONOMY AND DESCRIPTION

2.1 Taxonomy [17]

Domain: Eukaryota
Kingdom: Plantae
Phylum: Spermatophyta
Subphylum: Angiospermae
Class: Dicotyledonae
Order: Scrophulariales
Family: Acanthaceae
Genus: *Barleria*
Species: *Barleria lupulina*

2.2 Botanical Description

B. lupulina is a 1.5 m tall, glabrous, branching shrub with axillary spines. Its leaves are linear-oblong, 3-9.5 cm long, with a cuneate base and an acute apex. The petiole is short and red. The inflorescence is a terminal spike with overlapping bracts that can be up to 9 cm long. The bracts are broadly ovate, 1.2 cm long, ciliate, purple-tinged, and on the back, they have cupular glands. The calyx lobes are broadly ovate, and pubescent, and the outer ones are about 10 mm long and the inner ones are about 8 mm long. The corolla tube is 3 cm long, bent. Approximately 3 cm of glabrous style. Fruits are ovoid and capsular whereas its seeds are flattened, and covered with matted hairs (Fig. 1) [18].

2.3 Distribution

Originally from Mauritius and eastern India, *B. lupulina* has spread rapidly throughout tropical and subtropical areas of the world. The greatest representation of this genus occurs in Africa and Asia, with its greatest center of diversity in tropical East Africa [19].

2.4 Phytochemistry

Phytochemicals are chemical substances, naturally produced by plants which may have significant biological activities. These are the secondary metabolites of the plant, and they can give desirable health benefits in addition to nutrition to reduce the risk of major diseases [20].



Fig. 1. Habit of *Barleria lupulina* (L.) [Source: NParks Floral&Faunaweb]

According to reported studies, the bioactive substances identified from *Barleria* species, such as phenylethanoid glycosides, quinones, flavonoids, iridoids, antibiotics and immunostimulant protein, cause the aforementioned biological activities [4]. In preliminary studies, nine iridoid glucosides have been isolated from *B. lupulina* [21,22,23], such as Acetylbarlerin, Ipolamiidoside, Shanzhiside methyl ester, Shanzhiside, barlerin, 6-O-acetylshanzhiside, 6-O-acetylmussaenoside, Saletpangponosides A-C, and Lupulinoside. Lans and co-workers [24] stated that acetylbarlerin, barlerin, ipolamiidoside acetylshanzhiside methyl ester, and iridoid glucosides are found in the leaves of *B. lupulina*. Further, the presence of shanzhiside methyl ester, acetylbarlerin and barlerin compounds have been isolated from methanolic extracts of *B. lupulina* whole plant [25]. The methanolic extract of root, stem and leaf of *B. lupulina* are reported to contain starch, tannins, alkaloids, flavonoids, amino acids as well as proteins and reducing sugars and also lignins as the important phytochemical groups [17].

For the pharmacognostic evaluation of medicinal plants, the chemical analysis is of vital importance [26,27,28]. Sur and Co-workers [29] report terpenoids, steroids, flavonoids,

glycosides, carbohydrates as well as tannins in the ethanolic extract of *B. lupulina*. Further, Doss et al. [30] state that the dried material of this plant contains flavonoids and steroids. Kumari and Dubey [11] state that *B. lupulina* extracted from ethanol contains large quantities of phytochemical compounds that are active against bacteria as well as cancer cells. *B. lupulina* consists of twelve phytochemical compounds according to the result of GC-MS analysis. Out of them hexadecanoic acid, benzofuranon, ethyl 9,12,15-octadecatrienoate, and 3,7,11,15-tetramethyl-2-hexadecanoic acid were the most abundant. Ismail-Suhaimy and coworkers [31] attempted to optimize conditions for extracting biologically active compounds from leaves of *B. lupulina* using microwave assisted extraction method. The extraction efficiency varied depending on extraction time, ethanol volume and microwave power. Four new Phenylethanoidglycoside compounds were identified in the species.

2.5 Pharmaceutical Properties

The disc diffusion method has shown the antimicrobial efficacy of the plant's crude extract by inhibiting the *Propionibacterium acnes* bacteria, which causes an inflammation in acne [17]. Two neutrophil-dependent acute inflammatory

models, carrageenan-induced paw edema and ethyl phenyl propionate-induced ear edema in rats, were used to study the anti-inflammatory properties of this plant's extract. Anti-inflammatory, analgesic, and anti-peroxidative effectiveness have also been documented in the methanolic extracts of aerial parts of the plant [2]. The plant's hot aqueous extract showed anti-inflammatory action and decreased diabetes-related vascular pathology [17].

Alkyl catechols, specifically 4-ethylcatechol, 4-vinylcatechol, and 4-methyl catechol, were found to be the active substances which activate nuclear factor erythroid 2-related factor 2 (Nrf2) cell defense pathway [32]. The plant has both ulcer- and diabetes-preventive properties. In pylorus-ligated rats, the methanolic extract from the plant's aerial parts considerably decreased the amount of stomach juice, overall acid content, and ulcer index [33]. A significant defense has been reported against ulceration caused by alcohol, indomethacin, and other drugs [13]. Two substances, 4-ethyl catechol and 4-vinyl catechol, which are found in hot water extracts of the plant, may also speed-up the healing of diabetic wounds by activating Nrf2 [32]. The aqueous, ethanolic and methanolic extracts of *B. lupulina* were non-toxic or had low toxicity to normal cell lines and human red blood cells [34]. Assessment of *in vitro* aldose reductase potential and anticataract activity of *Barleria lupulina* are also documented [35]

2.6 Antioxidant Activity

Substances that significantly prolong or prevent the oxidation of a substrate in an organism are known as antioxidants. Oxidative stress is a main factor causing numerous chronic diseases [36]. *B. lupulina* might be a valuable source of bioactive compounds having diverse activities [8]. Antioxidant activity was highest in the methanolic stem extract (MSE) of *B. lupulina*. Additionally, MSE contained more phenol than gallic acid [8]. The highest number of phenols was found in the *B. lupulina* ethyl acetate fraction, next was the methanol soluble extract and the acetone soluble fraction with the highest level of phenolic and flavonoid compounds, which provide plants their antioxidant properties [8].

2.7 Antimicrobial Activity

The methanol-soluble extract of *B. lupulina* has been shown to have antibacterial activity by disc diffusion technique against *Escherichia coli* and *Staphylococcus aureus* [30]. The entire plant

shows activity against *Bacillus subtilis* and *Staphylococcus aureus*. The traditional use of the aerial parts of *B. lupulina* have a few important bioactive compounds that prevent the growth of pathogenic microorganisms. such as, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Salmonella typhi* [7,8]. Further, it has also been reported that *B. lupulina* has potential to fight against many respiratory tract pathogens [9].

Pattanayak and co-workers [10] stated that the methanol as well as the fresh extract of *B. lupulina* show antimicrobial activity against *E. coli*, *S. enteritides*, and *S. aureus*. Similarly, Kumari and Dubey [11] in another study state that the ethanol and aqueous extracts of *B. lupulina* leaves demonstrate activity against the bacteria *S. aureus*, *E. coli*, *P. aeruginosa*, *K. pneumonia* and *S. typhi*. Further, a study done by Doss et al. [30] revealed that the methanol extract showed inhibitory activity against *E. coli* and *S. aureus* but the aqueous extract did not demonstrate any activity. In contrast, a study done by Dey et al. [37] stated that the methanolic and aqueous extracts both were effective against *S. aureus* while being ineffective for *E. coli*.

2.8 Larvicidal Activity

No documented direct evidence is available for the larvicidal activity of *B. lupulina*. However, in work performed by Jeyasankar et al [38], It is shown that *Baleria* sp. can be used as a potential biocontrol agent against *Culex tritaeniorhynchus* because of its larvicidal effect. Mosquitoes acting as vectors for many communicable diseases could be controlled with the extract or isolated bioactive compounds applied into water bodies. However, field trails and further studies to fully ascertain the active principals and its method of action are needed before it can be recommended as an anti-mosquito product used against mosquitoes in a vector control program [38].

2.9 Antidiabetic Activity

The aerial parts of *B. lupulina* extracted into methanol showed high antihyperglycemic effect in streptozotocin-induced hyperglycemia in rats [1]. Based on folklore, Suba and colleagues [1] conducted trials to investigate the anti-hyperglycemic action of a methanol extract of aerial portions of *B. lupulina* in streptozotocin-diabetic rats. The extract exhibited considerable anti-hyperglycemic activity.

2.10 Immunomodulatory Activity

Mazumder and co-workers [12] state that the immunomodulatory activity of the *B. lupulina* leaf extract has increased leukocyte count in the blood, weight of spleen, splenic leukocytes count and also increased in paw volume on delayed type hypersensitivity footpad thickness suggesting an uplift of immune status. Methanol extract of *B. lupulina* aerial parts demonstrate anti-inflammatory effectiveness in acute and subacute inflammation models in albino rats. When compared to the untreated (control) group, the methanolic extract showed significant suppression of carrageenin and serotonin-induced paw edema volumes [8,4].

2.11 Antiarthritic Activity

B. lupulina leaves have been tested for their antiarthritic activity by several models such as, adjuvant induced arthritis, monosodium iodoacetate induced osteoarthritis, formalin induced arthritis and collagen type II-induced arthritis. Results revealed that methanol extracts of *B. lupulina* extracts demonstrated significant inhibition of the edema formation and myeloperoxidase (MPO) [12].

2.12 Anti-Cancer Activity

The leaf extracts of *B. lupulina* have been reported to show anti-cancer properties on Hep G2 cells. [11]. Anti-cancer potency of *B. lupulina* was evaluated using THP-1 cell lines in vivo and invitro [33]. The ethanolic extract showed significant cytotoxicity against THP-1 cell line at concentrations of 1 mg/ mL confirming that it can be used as an alternate drug to fight carcinogenic activity [39].

2.13 Anti-inflammatory Activity

Senger and co-workers [32] report that the hot aqueous extracts of the above ground components of *B. lupulina* activated the Nrf2 cell defense pathway in endothelial cells which agrees with its common use and ability to reduce inflammation. HPLC analysis showed the presence of three alkyl catechols: 4-ethylcatechol, 4-methylcatechol and 4-vinylcatechol that are potent Nrf2 activators. Further, Wanikat and co-workers [3] studied the methanolic crude extracts of leaves and twigs of *B. lupulina* for their anti-inflammatory activities in models of carrageenan-induced paw oedema and Ethyl phenyl propiolate (EPP)-induced ear edema in the rat. The results revealed that EPP-

induced ear edema as a suitable indicator for the screening of anti-inflammatory agents.

3. CONCLUSION

The types and number of phytochemical elements extracted from *B. lupulina* plants varies based on the method and solvent used during extraction. The methanol soluble leaf and stem extracts of *B. lupulina* showed potent immunostimulant activities where the specific and non-specific immune mechanisms were both stimulated. Antioxidant and antibacterial properties were also seen in the phytochemical compounds. These extracts with antibacterial, antioxidant and immuno-modulatory properties can be used to prevent different ailments such as autoimmune diseases. Blood glucose reducing and diabetes regulating compounds can also be extracted from this plant. The medicinal application of *B. lupulina* deserves further investigation to reveal its promising pharmacological including antimicrobial, cytopathic, antioxidant, antidiabetic, anti-inflammatory activities and antiarthritic activity of the extract and isolated molecules. The value of this species as a medicinal plant and a possible source of new and beneficial medications will therefore be better understood with more study regarding active biological substances and pharmacological compounds in the species, *Barleria lupulina*.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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