Minireview Article

The Potential Medicinal value of *Barlerialupulina*: A mini review

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ABSTRACT

Medicinal plants are amajor source of numerous valuable natural chemicals andmedicines. 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. *Barlerialupulina*Lindl. widely known as "RanwanKatukarandu" in Sri Lanka is a plant which has been used widely in traditionalplant derived medicines, as it includes numerousphytochemicals with potential biological properties. *B. lupulina* has been tested for its many phytochemical constituents such as, for example: flavonoids, phenylethanoid glycosides,quinones,iridoids, immunostimulant proteins, antibiotics, alkaloids, starch, tannin, reducing sugars, protein, amino acids, glycosides, steroids etc. to name a few, which have been found to have antioxidant, antimicrobial, larvicidal, antidiabetic, immunomodulatory and antiarthritic properties. In future, extensive scientific research needs to be performed on these phytochemicals to produce natural effective and alternative medicinesfor synthetic medicines. This review gives anextensive report on existing literature, regarding the phytochemistry and biological activity of the species*Barlerialupulina*Lindl.

Keywords: Barlerialupulina, Phytochemicals, Biological properties, Medicinal plants

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. Due to these reasons medicinal plants have played avital role in meeting the global demand on therapeutics for thousands of years. Medicinal plants are used in various medical 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. *Barlerialupulina*widely known as "RanwanKatukarandu" in Sri Lanka is one of thebetter-known species with medicinal properties. English name of the plant is Hophead Philippine Violet and Cem Mulli in tamil. It is known to include 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 traditionally 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 aliments and infection [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], antiartheritis[12], antiulcerogenic[13],neuropharmacological[14], acute and sub-chronic diuretic[15], as well asanti-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 asbiological 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: *Barlerialupulina*

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 (Figure 1)[18].

2.3 DISRTIBUTION

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].

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

2.4 PHYTOCHEMISRTY

Phytochemicals are chemical substances, naturally produced by plants which have biological activity. These arealso known as secondary metabolites, and they can give desirable health benefits in addition to nutrition to reduce the risk of major diseases [20]. According to 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,ipolamiidosideacetylshanzhiside methyl ester, and iridoid glucosides are found in the leaves of*B. lupulina*. Further, the presence of shanzhiside methyl ester, acetylbarlerinn and barlerincompounds havebeen 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 protein and reducing sugarand also lignin 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 astannins 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 phytochemicalcompounds that areactive against bacteria as well as cancer cells. *B. lupulina* consists of twelvephytochemical 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 concentration and microwave power. Four new Phenylethanoidglycoside compounds were identified in the species.

2.5 PHARMACEUTICAL PROPERTIES

The disc diffusion method has shown the anti-microbial 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 applied 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 the plants'above ground parts [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'sabove ground portions considerably decreased the amount of stomach juice, overall acid content, and ulcer index [33]. A significant defense was also provided 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 hasten 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 cells[34].Assesment of in vitro aldose reductase potential and anticataract activity of *Barleria lupulina* Lindl.are also documented [35]

2.6 ANTIOXIDANT ACTIVITY

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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 amount 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* with Minimum inhibition Concentration (MIC) of 0.125 mg/mL has been shown to have antibacterial activity by disc diffusion technique against *Escherichia coli* and *Staphylococcus aureus* [30]. The entire plant shows activity against bacteria with inhibition zones against *Bacillus subtilis* and *Staphylococcus aureus*. The traditional use of the above ground parts of *B. lupulina*have a few important bioactive compounds that prevent the growth of pathogenic microorganisms. viz., *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus*, and *Salmonella typhi* [7,8]. Further, it can also be concludedthat *B. lupulina* will be useful against many respiratory diseases [9].

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Pattanayakand 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* and the methanol extract of 200 mg/ ml was more effective than the 100 mg/ml concentration. Similarly,Kumari and Dubey [11] in another study state that the ethanol and aqueous extracts of *B. lupulina* leaf blade demonstrate activity against the bacteria *S. aureus*, *E. coli, P. aeruginosa, K. pneumonia*and *S. typhi*. Further, a study done byDoss *et al*. [30] revealed that the methanol extract showed inhibitory activity against *E. coli*and *S. aureus*but the aqueous extract did notdemonstrate anyactivity. 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 byJeyasankar *et al* [38],It is shown that *Baleria* sp.can be used as a potential biocontrol agent against *Culextritaeniorhynchus*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 above ground parts of *B. lupulina* extracted into methanol orally tested at doses of 100, 200 and 300 mg/kg showedhigh 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* Lindl. in streptozotocin-diabetic rats. The extract exhibited considerable (p 0.05) anti-hyperglycemic activity at all levels tested after 4 h of intake compared to the control, and the impact was also extended up to 12 h. The extract displayed greatest activity (p 0.001) 12 h after intake at dosages of 200 mg/kg body weight and over. The group given 300 mg/kg body weight had the highest significant action (15.35% blood glucose decrease) after 12 h hours of following delivery, and the usual medication glibenclamide (10 mg/kg) had the least [1].

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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, spleenic leukocytes count and also increase 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 carcarrageenin and serotonin-induced paw edema volumes [8, 4].

2.11 ANTIARTHRITIC ACTIVITY

B. lupulina leaves have been checked for their antiarthritic activity by several models such as, adjuvant inducedarthritis, monosodium iodoacetate induced osteoarthritis, formalininduced arthritis and collagen type II-induced arthritis. Results revealed that Methanol extracts of *B.lupulina* extracts demostrated significant inhibition (P<0.05 and P<0.001) of the edema formation and Myeloperoxidase (MPO) [12].

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2.12 ANTI-CANCEROUS ACTIVITY

The leaf extracts of *B. lupulina* have been reported to have anti-cancerous properties on Hep G2 cells. Hep G2 is a human liver cancer cell line [11]. Anti-cancerous potency of *B. lupulina* was evaluated using THP-1cell lines in vivo and invitro [33]. THP-1 cell line is a human monocytic cell line derived from an acute monocytic leukemia patient. 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 groundcomponents of*B. lupulina*activated the Nrf2 cell defense pathway in endothelial cells which agrees with its common use and ability to reduce inflammation. HPLC analysisshowed the presence of three alkyl catechols: 4-ethylcatechol, 4-methylcatechol and 4-vinylcatechol that are potent Nrf2 activators. Further, Wanikat and co-workes [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 phenylpropiolate (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 and these extracts significantly and dose-dependently inhibited edema formation in this modelat all time points (0, 15, 30, 60 and 120 minutes) examined.

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3.CONCLUSION

The types and number of phytochemical elements extracted from *B. lupulina* plants were different based on the method and solvent used during extraction. The methanol soluble leaf and stem extracts of *B. lupulina*Lindl. showedpotent 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 preventdifferent ailments such as autoimmune diseases. Blood glucose reducing and diabetes ameliorating 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 thespecies, *Barlerialupulina*Lindl.

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