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Barleria lupulina: A medicinal plant of Bangladesh: A review

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Abstract
Barleria lupulina Lind L. is a medicinal plant belonging to the Acanthaceae family found in Bangladesh in the wild and on fallow lands. Various folk medicinal uses of the plant include being used as tonic, and for treatment of dermatitis, sexual disorder, cough, fever, body ache, eczema, itches, and scabies. The plant contains a number of iridoid glucosides of possible therapeutic importance. Pharmacological studies indicate that the plant has anti-microbial, anti-oxidant, anti-viral, immunomodulatory, diabetic wound healing, anti-inflammatory, anti-amebic, anti-ulcer, and neuropharmacological properties. The presence of bioactive principles combined with the traditional uses and reported pharmacological properties of the plant indicate that the plant can be considered an important source for lead compounds and new drugs.

Keywords: *Barleria lupulina*, acanthaceae, glucosides, anti-microbial, anti-amebic

Introduction
Barleria lupulina Lindl. is a medicinal plant belonging to the Acanthaceae family found in Bangladesh in the wild and on fallow lands. In English it is known as 'Hophead Philippine violet' and in Bengali known as 'Lal-tarokh, Kali-chondal, or Rahu-chondal'. It is a branched evergreen perennial shrub and can grow up to 150 cm tall. The plant is considered a medicinal plant in traditional medicinal systems of Bangladesh and other countries. As the plant also has been reported to contain bioactive components of possible therapeutic values and further reported to exhibit important pharmacological activities, it was of interest to review the plant as a potential source of lead compounds and new drugs.

Taxonomic hierarchy of Barleria lupulina

Kingdom	Plantae
Sub-kingdom	Tracheobionta
Division	Magnoliophyta
Class	Magnoliopsida
Sub-class	Asteridae
Order	Scrophulariales
Family	Acanthaceae
Genus	*Barleria*
Species	*Barleria lupulina* Lindl.

Ethnomedicinal uses of the plant or plant parts
The various ethnomedicinal uses of the plant in Bangladesh are shown in Table 1 and compiled from sources as mentioned in the References section [1, 2].

Table 1: Ethnomedicinal uses of *Barleria lupulina* in Bangladesh.

Scientific and English names	Family	Local names (Bengali)	Parts used	Ailments treated/Uses
Barleria lupulina Lindl. English: Hophead Philippine violet	Acanthaceae	Lal-tarokh, Kali-chondal, Rahu-chondal	Whole plant, leaf, root	Tonic, dermatitis, sexual disorder, cough, fever, body ache, eczema, itches, scabies

The plant is also well known in Thai traditional medicine. The various applications include use as anti-inflammatory agent against insect and snake bites and for amebic diseases [3, 4]. Leaf juice is given to stop bleeding; leaf paste is used for alleviating pain and to treat acne [5]. The plant is also used in Thailand to treat swellings due to fall or boils [6]. In villages of upper northeastern Thailand, the plant is used against herpes [7]. In Ayurveda, the Sanskrit name of the plant is 'Bishalyakarani'. In India the plant is used for treatment of various ailments like mental illness, fever, pain, snake bite, rheumatoid arthritis, and diabetes, and as diuretic [8]. The Orang Asli people in Kampung Bawong, Perak, West Malaysia, use leaves of the plant to remove warts [9].

Phytochemicals reported for Barleria lupulina

Iridoid glucosides including lupulinoside [8-*O*-acetyl-2′-*O*-(beta-glucopyranosyl) mussaenoside, acetylbarlerin, ipolamiidoside, 6-*O*-acetylshanzhiside methyl ester, barlerin, shanzhiside methyl ester, mussaenosidic acid, 8-*O*-acetyl shanzhiside, and shanzhiside have been isolated from flowers. Ipolamiidoside exhibited anti-herpes simplex type 1 activity [10]. Shanzhiside, isolated from fruits of *Gardenia jasminoides* has been shown to possess immunosuppressive effects as demonstrated by inhibition of interleukin-2 (IL-2) secretion induced by phorbol myristate acetate and anti-CD28 monoclonal antibody co-stimulated activation of human peripheral blood T cells [11]. From the aerial parts of the plant iridoid glucosides have also been isolated, which included saletpangponosides A-C, 8-*O*-acetyl-6-*O*-*trans*-*p*-coumaroylshanzhiside, 8-*O*-acetyl mussaenoside, shanzhiside methyl ester, 8-*O*-acetylshanzhiside methyl ester (barlerin), 6-*O*-acetylshanzhiside methyl ester, 6,8-*O*,*O*-diacetylshanzhiside methyl ester (acetylbarlerin), ipolamiide, ipolamiidoside, and phlorigidoside, as well as phenylpropanoid glycosides – forsythoside, verbascoside, and poliumoside, lignan glucoside – (+)-lyoniresinol 3a-*O*-beta-glucopyranoside, aliphatic glycoside – (3*R*)-1-octen-3-yl-beta-primeveroside, and a benzyl alcohol glycoside – benzyl alcohol beta-(2′-*O*-beta-xylopyranosyl) glucopyranoside [3]. Other iridoid glucosides (not reported before) isolated from the plant included 8-O-acetylipolamiidic acid, 8-O-acetyl-6-O-(p-methoxy-cis-cinnamoyl) shanzhiside, and 8-O-acetyl-6-O-(p-methoxy-trans-cinnamoyl) shanzhiside, and ten other known iridoid glucosides, of which ipolamiide showed alkaline phosphatase enhancing activity [12]. Eighteen iridoid glycosides including four new compounds have been reported from extracts of aerial parts of the plant; two of them showed weak antioxidant activity. The four new compounds were barlupulin A, barlupulin B, barlupulin C, and barlupulin D, while the fourteen other compounds were [6-*O*-*p*-methoxy-*trans*-cinnamoyl-8-*O*-acetylshanzhiside methyl ester], [6-*O*-*p*-methoxy-*cis*-cinnamoyl-8-*O*-acetylshanzhiside methyl ester], [6-*O*-*p*-methoxy-*trans*-cinnamoyl-8-*O*-acetylshanzhiside], [6-*O*-*p*-methoxy-*cis*-cinnamoyl-8-*O*-acetylshanzhiside], [6-*O*-*p*-*trans*-coumaroyl-8-*O*-acetylshanzhiside methyl ester], [6-*O*-*p*-*cis*-coumaroyl-8-*O*-acetylshanzhiside methyl ester], [acetylbarlerin], [barlerin], [ipolamiidoside], [8-O-acetylshanzhiside], [6-*O*-acetylshanzhiside methyl ester], [shanzhiside], and [mussaenosidic acid] [13]. Two novel 4,8,8-trimethylcyclooct-2-enone derivatives, chakyunglupulins A and B, together with six known lignans have been reported from the aerial part of *Barleria lupulina*; however, any pharmacological studies were not conducted with the lignans [14]. Some of the component structures are shown in Figure 1.

Pharmacological activity studies

Virucidal effect of organic extract of the plant has been reported against five clinical herpes simplex virus -2 (HSV-2) isolates [15]. Anti-microbial effect of crude extract of the plant has been demonstrated by disc diffusion method with inhibition of the pus forming bacteria *Propionibacterium acnes*, which triggers an inflammation in acne [5]. Acquired immuno-deficiency syndrome (AIDS) patients in southern Thailand use the plant as a therapeutic measure against the disease; although any anti-AIDS activity is yet to be reported, anti-amoebic activity against *Entamoeba histolytica* has been shown with chloroform extracts of the plant [4]. Methanol soluble leaf extract reportedly inhibited the growth of pathogenic bacteria like *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Salmonella typhi* [16].

Anti-inflammatory activities of extract of this plant have been studied using two neutrophil-dependent acute inflammatory models – carrageenan-induced paw edema and ethyl phenylpropiolate-induced ear edema in rats. Myeloperoxidase (MPO) activity was assayed as an indicator of neutrophil migration. The results demonstrated strong anti-inflammatory properties of the extract. Inhibitory effects were seen in both models of edema, and there was a significant inhibition of MPO activity in the inflamed tissue suggesting that the anti-inflammatory effect is associated with reduced neutrophil migration [17]. Anti-inflammatory, analgesic and anti-peroxidative efficacy of methanol extract of aerial parts of the plant have also been reported. Administration of extract significantly reduced carrageenin and serotonin-induced paw edema volumes in albino rats. There was also a significant reduction in granuloma weight in the cotton pellet induced granuloma model, comparable to that of the standard drug, indomethacin. The extract also demonstrated protection against carbon tetrachloride-induced lipid peroxidation and acetic acid-induced writhing [18]. Hot aqueous extract of the plant demonstrated antiinflamatory activity and reduced vascular pathology associated with diabetes. The active compounds responsible for these activities were identified to be alkyl catechols, namely 4-ethylcatechol, 4-vinylcatechol, and 4-methylcatechol. The extract and the catechols activated the Nrf2 (nuclear factor erythroid 2–related factor 2) cell defense pathway, organized cortical actin, reduced stress fibers, and improved cell junctions in microvascular endothelial cells [19]. Notably, activation of Nrf2 would induce expression of an array of antioxidant response element–dependent genes [20] and so can alleviate inflammation through reducing oxidative stress.

Other pharmacological activities reported for the plant include anti-ulcer and anti-diabetic activities. Methanol extract of aerial parts of the plant significantly reduced the volume of gastric juice, total acidity and ulcer index in pylorus ligated rats. There was also significant protection against alcohol and indomethacin-induced ulcer as well as stree induced ulceration. Thiobarbituric acid reacting substances (TBARS) were also reduced in the stomach of indomethacin treated rats. Additionally, the extract also gave protection against duodenal ulcers [21]. Methanol extract of aerial parts of the plant also showed pronounced anti-hyperglycemic activity in streptozotocin (STZ)-diabetic rats [22, 23]. Diabetic wound healing may also be expedited by two compounds present in hot water extracts of the plant through activation of Nrf2; the two compounds are 4-ethyl catechol and 4-vinyl catechol [24].

Neuropharmacological experiments with methanol extracts of

aerial parts of the plant in mice and rats showed reduction in general behavioral pattern (spontaneous activity, alertness, awareness, pain response and touch response), and a significant reduction of the exploratory behavioral profile (Y-maze test, head dip test) and conditioned avoidance response. There was also significant motor in-coordination and muscle relaxant activity. The extract also potentiated phenobarbitone sodium-induced sleeping time. Taken together, the results suggest presence of phytochemicals in aerial parts of the plant, which possess significant psychopharmacological activity [25].

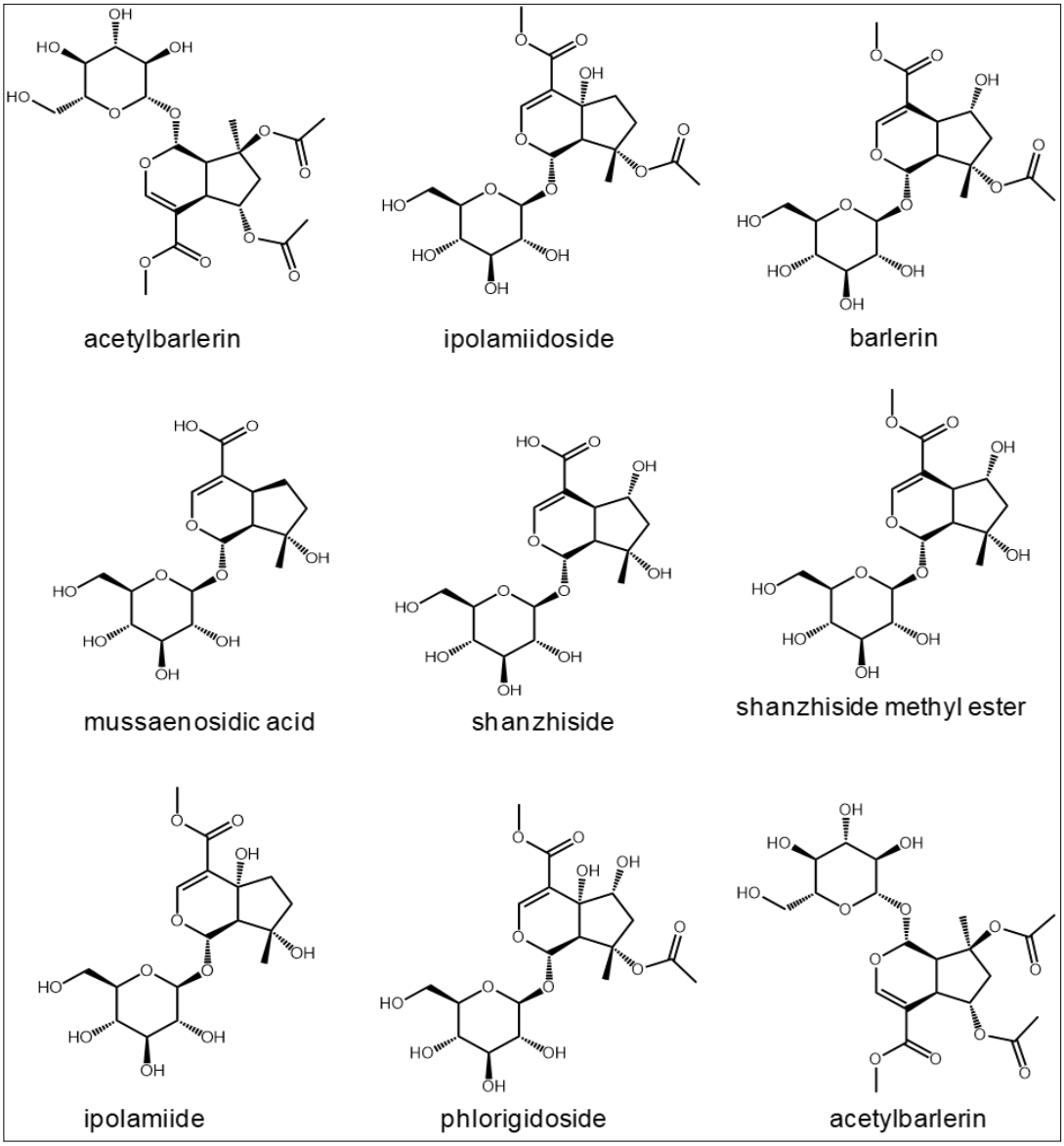

Fig 1: Some iridoid glycosides isolated from various parts of *Barleria lupulina*

Conclusion

Taken together, the plant can prove to be an important plant in the quest for lead compounds and newer drugs. The modern era is witnessing the emergence of antibiotic-resistant microorganisms and new viral diseases like Ebola, Nipah, bird flu, and MERS. New antibiotics and drugs against the resistant microorganisms and emerging viral diseases is a major necessity. At the same time, diabetes is rapidly turning into almost an epidemic. The plant can also prove useful in finding out new compounds which can reduce blood glucose and ameliorate diabetes-induced complications in diabetic patients.

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