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PHCOG REV.: PLANT REVIEW PHYTO-PHARMACOLOGY OF *BARLERIA PRIONITIS* LINN. - A REVIEW

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ABSTRACT

Plants have been one of the important sources of medicines since the beginning of human civilization. There is a growing demand for plant based Medicines, health products, Pharmaceuticals, Food supplements, Cosmetics etc. *Barleria prionitis* Linn belonging to Acanthaceae family is a small spiny shrub. It is an indigenous plant of South Asia and certain regions of Africa & India. Various parts of the plant such as leaves, roots, aerial parts, flowers & stems are used as an Antiarthritic, Antibacterial, Antifertility, Antioxidant, Antidiabetic, Antifungal, Antiviral, Hepatoprotective, Enzyme inhibitory, Anthelmintic & Anti-inflammatory agent. It is reported to certain flavonoids, saponins, glycosides, phytosterols & tannin. The plant contains some specific compounds such as barlenoside, barlerine, acetylbarlerine, balarenone & some common secondary metabolites. A review of chemical constituents present in various parts of *B. prionitis* & their Pharmacological actions is given in the present article.

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INTRODUCTION

Herbal medicines are also in great demand in the developed world for primary health care because of their efficacy, safety and lesser side effects. They also offer therapeutics for age-related disorders like memory loss, osteoporosis, immune disorders, etc. for which no modern medicine is available. India despite its rich traditional knowledge, heritage of herbal medicines and large biodiversity has a dismal share of the world market due to export of crude extracts and drugs. WHO too has not systematically evaluated traditional medicines despite the fact that it is used for primary health care by about 80% of the world Population. However, in 1991 WHO developed guidelines for the assessment of herbal medicine [1].

Herbal medicines are in great demand in both developed and developing countries as a source of primary health care owing to their attributes having wide biological and medicinal activities, high safety margins and lesser costs. Traditional use of medicine is recognized as a way to learn about potential future medicines. Researchers have identified number of Compounds used in mainstream medicine which were derived from "ethnomedical" plant sources. Plants are used medicinally in different countries and are a source of many potent and powerful drugs [2].

The genus *Barleria* Linn. (Acanthaceae) consists of 28 taxa including 26 species. It is an old world genus, with its greatest center of species diversity in tropical East Africa, followed by South Africa and Asia. Some of the species belong to genus Barleria are B. prionitis, B. acanthoides, B. aculeate, B. albostellata, B. buxifolia, B.cristata, B. greenii, B. lupulina, B. micans, B.observatrix, B. obtusa, B. opaca, B. popovii, B. longiflora, B. mysorensis, B. noctiflora, B. tomentosa, B. acuminate and B. strigosa etc [3]. It is widely used in traditional medicine to treat infection related ailments. It is mainly used for medicinal purpose. Plant pacifies vitiated vata, pitta and it has numerous medicinal properties including treating fever, respiratory diseases, toothache, joint pains, burns, dental caries, and nocturnal ejaculation and a variety of other ailments and it has several cosmetic uses [4]. It is widely used in urinary and paralytic affection, reuthmetic pain, and itch. A mouthwash made from root tissue is used to relieve toothache and treat bleeding gums. To increase sexual vigor, seed extract is administered daily once for a night. Seed paste is used for a toothache. Because of its antiseptic properties, extracts of the plant are incorporated into herbal cosmetic and hair products to promote skin and scalp health. Juice of leaf administered in a little honey or sugar in catarrhal affections of children, which is accompanied by fever and much phlegm [5-7]

Locally on skin o expel out spine from the skin, in acute stage of cyst in blood vessels, in glandular swellings, as diuretic, rich in potassium salts and in bronchial asthma etc [8]. The whole plant, root, leaves and bark of plant occupy a significant place in the indigenous system of medicine in India for the treatment of various disease like toothache, inflammations, boils, glandular swelling & catarrhal affections etc [9]. This review can be considered as a bird's eye view highlighting the current progress of *Barleria prionitis* in Pharmacological and Pharmacognostical field with its prominent folk uses.

GENERAL INFORMATION

Barleria prionitis Linn. (Family: Acanthaceae) is a well-known perennial, Ayurvedic herb distributed in the tropical Asia, Africa and Yemen. The whole plant or its specific parts (leaf, stem, root, bark and flower) has been utilized for treatment of toothache, catarrhal affections, whooping cough, inflammations, glandular swellings, urinary infection, jaundice, fever. Barleria contains about 250 species with about 70 species in Africa. it is commonly found in tropical Asia included India, Malesia, Pakistan, Philippines, Sri Lanka and Africa Barleria grows on a wide variety of soil types and seems to prefer well-drained soils. On the Australian mainland it grows well in tropical savanna country and along riverbanks. It is rugged limestone outcrops with little soil cover by clinging to the rocks and crevices with a network of roots. Barleria also grows well in disturbed areas such as roadsides or overgrazed pastures [10]. The whole plant or its specific parts (leaf, stem, root, bark and flower) has been utilized for treatment of various diseases.

Scientific name - *Barleria prionitis*

Common name - Porcupine flower

Figure. 1- Whole Plant of *Barleria Prionitis* (Left) and its Flowers & Leaves (Right).

HABITATE

Barleria prionitis is a branched annual shrub of about 1–3 feet height with flowering and spiny invader. The Shrub is armed with 5-20 mm long spines in leaf axils. Most often found on road sides. The *Barleria prionitis* is native to tropical areas of east Africa and Asia, but may be found throughout tropical Asia (India and Sri Lanka) and in South Africa also. The month of August to November is favourable for the flowering and fruiting within the plant. It has 3–5 sharp, pale-coloured spines 1–2 cm long, in each leaf axil. Branches are smooth, brown and roughly square in cross-section. Leaves are oval, 10–12 cm long, with a pointed tip ending in a short spine. Yellow, tubular flowers about 4 cm long with long projecting stamens occur in upright spikes at the top of the plant. Seed capsules are oval-shaped and about 18 mm long, tapering into a 6 mm long beak. Seeds are large (8 mm long and 5 mm wide), flat and covered in matted hairs. Root are central tap type with lateral roots branching in all direction [11]. gastrointestinal disorders and as diuretic and tonic. Taxonomical classification of *B. prionitis* is given in Table 1 [12].

Table 1: Taxonomical classification of *B. prionitis.*

Kingdom	Plantae
Sub kingdom	Tracheobionta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Asteridae
Order	Scrophulariales
Family	Acanthaceae
Genus	Barleria
Species	*Prionitis*

MEDICINAL USES

It has numerous medicinal properties including treating fever, respiratory diseases, toothache, joint pain and a variety of other ailments; and it has several cosmetic uses. A mouthwash made from root tissue is used to relieve toothache and treat bleeding gums. The whole plant leaves, and roots are used for a variety of purposes in traditional Indian medicine. For example, the leaves are used to promote healing of wounds and to relieve joint pains and toothache. Because of its antiseptic properties, extracts of the *Barleria prionitis* Linn are incorporated into herbal cosmetics and hair products to promote skin and scalp health [13,14].

TRADITIONAL USES OF *BARLERIA PRIONITIS* LINN.

Barleria prionitis is used in the treatment of catarrhal condition in children. The juice of the leaves mixed with the honey seems to be the remedy for this in the Indian society. The ash of the whole plant mixed with honey is remedy for bronchial asthma, the flower is given internally for the treatment of Haemoptysis [15-16]. Juice of leaves is applied to heels to prevent craking and laceration. The leaves are also a remedy for infected wounds, erysipelas and pimples. The oil extract of the plant is used to arrest greying of hair [17]. The leaves and flowering tops are considered as Diueretics and used to treat the various urinary affections [18]. The plant has been used in the treatment of paraplegia, stiffness of the limbs and sciatica. The herb extracted in oil is also to treat these neurological conditions, gout and arthritis by massaging the affected joints with it. Flower are given internally migraine. Paste form of root is directly applied in boils and glandular swellings whereas paste with goat milk is given in rheumatic fever [11]. Root extract is given locally on skin to expel out spine from the skin and its decoction is taken orally for treatment of snakebite [19]. In viral fever, flower is efficacious [20]. Paste form is taken daily once for edema [21]. In case of whooping cough, prepared tablets (burned in an airtight earthen pot, heated until fine powder is obtained and then mixed with garlic juice) from green shoots and even roots mixed with honey are given one per day [11].

PHYTOCHEMISTRY

Preliminary phytochemical analysis of hydro-methanolic extract of *B. prionitis* whole plant indicated the presence of glycosides, saponins, flavonoids, steroids and tannins. The leaves and flowering tops were reported to rich in potassium salts. Several phytochemicals viz., balarenone, pipataline, lupeol, prioniside A, prioniside B and prioniside C has been isolated from the ethanolic extract of *B. prionitis*.

Numbers of glycosides include barlerinoside, verbascoside, shanzhisidemethylester, 6-O-trans-p-coumaroyl-8-O-acetylshanzhiside-methylester, barlerin, acetylbarlerin, 7-methoxydiderroside, lupulinoside has been also isolated from the aerial parts.

Two anthraquinones derivatives has been also identified in this plant and their structures were characterized as 1,8, dihydroxy-2,7-dimethyl 3, 6-dimethoxy anthraquinone and 1,3,6,8-tetra methoxy-2,7-dimethyl anthraquinone. The leaves were reported to contain scutellarein, melilotic acid, syringic acid, vanillic acid, p-hydroxybenzoic acid, 6-hydroxyflavones. Beside these phytochemicals, luteolin-7-O-β-D-glucoside, β-sitosterol, scutellarein 7-neohesperidoside, apigenin 7-O-glucoside, 13, 14-seco-stigmasta-5, 14-diene-3-a-ol were also reported to present in *B. prionitis* [22]. A wide range of phytochemical constituents are Balarenone, Pipataline, Lupeol, Prioniside A, B and C, verbascoside, shanzhiside methyl ester, Barlerin, Acetyl barlerin, 7- methoxy diderroside, lupulinoside 1,8, dihydroxy-2,7-dimethyl 3,6- dimethoxy anthraquinone; 1,3,6,8- tetramethoxy- 2,7- dimethyl anthraquinone; 4- carbomethoxy, 5,6-dehydro,7,8- dihydroxy, 8- methyl-1b-D-glucopyranosidal iridoid, 13,14-seco-stigmasta-5,14-diene-3-ol have been isolated from the different part of plant.

Leaves contain Sutellarein, Shanzhiside, methyl ester, Melilotic acid, Syringic acid, Vanillic acid, p- hydroxybenzoic acid, 6-hydroxyflavones [23-25]. A brief summary of phytochemical constituents isolated from B. prionitis is given Table 2.

Table 2: Phytochemical constituents identified, isolated from Barleria prionitis Linn.

Phytoconstituents	Isolated from	Mol. Formula	Class	Possible activity	References
Barlerinoside	Aerial parts	$C_{42}H_{58}O_{23}$	Phenylethanoid glycoside	Glutathione S-transferase (GST) inhibitory activity	39
Balarenone	Aerial part	-	Terpenoid	Glutathione S-transferase and acetylcholinesterase inhibitory activity, antibacterial activity	36
7-Methoxydiderroside	Aerial parts	$C_{20}H_{30}O_{13}$	Secoiridoids	Antioxidant activity, antiviral activity	39
Melilotic acid	Leaves	$C_9H_{10}O_3$	Phenolic acid	Antioxidant activity, antiulcer activity	51
Vanillic acid	Leaves	$C_8H_8O_4$	Dihydroxybenzoic acid derivative	Anticancer activity, anti-inflammatory activity, antioxidant activity, antinociceptive activity	22
Syringic acid	Leaves	$C_9H_{10}O_5$	Phenolic acid	Antioxidant activity, anticancer activity, antimicrobial activity, antifungal activity, antidiabetic activity, hepatoprotective activity	22
β-sitosterol	Roots	$C_{29}H_{50}O$	Phytosterols	Anti-inflammatory activity, anticancer activity, anthelminthic activity, cytotoxic activity, antisteroidogenic activity, antifertility activity, antioxidant activity, antidiabetic activity	30
Scutellarin	Leaves	$C_{21}H_{18}O_{12}$	Flavone	Antioxidant activity, anti-inflammatory activity, cardioprotective activity, hepatoprotective activity, enzyme inhibitory activity	22
Barlerin	Aerial part	$C_{19}H_{28}O_{12}$	Iridoid glycosides	Antioxidant activity, antiviral activity, anticancer activity, enzyme inhibitory activity, antiinflammatory activity	41
Acetylbarlerin	Aerial part	$C_{21}H_{30}O_{13}$	Iridoid glycosides	Antioxidant activity, antiviral activity, anticancer activity, enzyme inhibitory activity, anti-inflammatory activity	41
Shanzhiside methyl ester	Aerial part	$C_{17}H_{26}O_{11}$	Iridoid glycosides	GST, AChE inhibitory activity, antioxidant activity	39
Pipataline	Aerial part	$C_{19}H_{28}O_2$	Terpenoid	Enzyme inhibitory activity, antioxidant activity	36

PHARMACOLOGICAL ACTIVITIES

The present review is focused on giving an overview of the pharmacological activities that have been reported on B. prionitis in the past and present.

Antifertility effect

The methanolic root extract of *B. prionitis* L. was given orally to male rats (100 mg/d). The duration of the study was 60 days, and the extract reduced the fertility of male rats by 100%. Antifertility effects of Barleria appeared to be arbitrated by conflicts in Leydig and Sertoli cells functions, resulting in the physiomorphological events of spermatogenesis [26]. Antispermatogenic activity is also shown by this [27-29]. In another study done by us, an active component β-sitosterol (BS) was isolated from the methanolic root extract of *B. Prionitis*, and its antifertility potential was evaluated in the male albino rats. The rats were orally administered olive oil (Group-I, control), BS at the dose level of 5 (Group II), 15 (Group III), and 25 mg/kg body weight (BW) (Group IV) for 60 days. BW was measured weekly. The results exhibited that BS from the roots of *B. prionitis* impairs spermatogenesis and fertility that recommends that BS from *B. prionitis* can be used for the development of the male contraceptive drug, which has very limited available options [30].

Antiarthritic activity

Anti-arthritic activity of ethylacetate fractions of chloroform extract from leaves of *Barleria prionitsis* was studied against formaldehyde-induced acute non immunological and Freund's Complete Adjuvant-induced chronic immunological arthritis in rats. Dose dependent and significant inhibition of edema was observed in both acute as well as chronic models. The extract showed most potent and significant paw edema inhibition which is supported by the results of body weight, biochemical parameters, motor in coordination and nociceptive threshold in Freund's Complete Adjuvant-induced arthritis model [31]. Ethyl acetate fraction (125 and 250 mg/kg) of leaf significantly suppressed the joint swelling after 8- 10 days administration in formaldehyde induced arthritis model and it also decreased significant level of arthritic score with weight gain in FCAinduced arthritis rat model [32].

Antibacterial activity

Prionitis bark extracts such as Acetone, methanol, ethanol, aqueous screened for in vitro antimicrobial activity against four oral bacteria Streptococcus mutans, Staphylococcus aureus, Pseudomonas sp., Bacillus sp.The antimicrobial potential of B.prionitis bark against Bacillus sp. was comparable with the standard antibiotic drug ciprofloxacin [33]. Ethanol, chloroform and petroleum ether extract of B. Prionitis showed comparative antibacterial activity on various bacterial species. The different extracts of the plant were first prepared on basis of various concentration levels and then extensively applied on selected bacterial culture media for determination of minimum inhibitory concentration and these extracts exhibited significant antibacterial activity [34]. Leaf juices of *Barleria prionitis* are used by rural people in the treatment of oral ailments such as dental troubles, gum ailments, pyorrhea, dental carries and mouth ulcers. Zone of inhibition and minimum inhibitory concentration all the extracts showed that ethanolic extract had more antimicrobial as compared to the aqueous extract [35].

Enzyme inhibitory activity

A new compound, balarenone, along with three known compounds, pipataline, lupeol, and 13,14-seco-stigmasta-5,14-diene-3-α-ol was isolated from the ethanolic extract of *B. prionitis* of Sri Lankan origin. All four of these expressed moderate inhibitory activity against the enzyme glutathione S-transferase and acetylcholinesterase [36].

Antifungal activity

Antifungal activity of *B. prionitis* bark studied on two Candida albicans strains and Saccharomyces cerevisiae, involved in oral diseases of human. Acetone, methanol, ethanol, aqueous (hot and cold) extracts of *Barleria prionitis* bark were screened for in vitro activity against four three oral fungi C.albicansstrain 1, 2 and S.cerevisiae. Methanolic extract of *B.prionitis* bark showed much more potent activity against all the tested oral fungi than the standard drug amphotericin-B thus having a great potential to control candidiasis and other oral fungal infections [37]. Petroleum ether, dichloromethane, ethanol and methanol extract of different parts of Barleria prionitis, Barleria greenii and Barleria albostellata studied for its antifungal activity. All the extracts demonstrated both fungi static and fungicidal activities [38].

Antioxidant activity

Antioxidant potential of medicinal plant *Barleria prionitis* was studied by using DPPH assay. The ethylacetate soluble fractions have showed the maximum activity. Aerial parts of Barleria prionitis contain chemical constituent's phenylethanoid glycoside, barlerinoside, iridoid glycosides, shanzhiside methyl ester, 6-o-trans-p-coumaroyl-8-oacetylshanzhiside methyl ester, barlerin, acetylbarlerin, 7-methoxydiderroside and lupulinoside exhibited different free radical Scavenging activities [39]. The antioxidant activity of different extracts of *Barleria prionitis* leaf and stem was studied. The total phenolic contents were determined by Folin-ciocalteu method. The antioxidant potential and reducing power of all the prepared extracts were measured against DPPH as compared to standard ascorbic acid, and BHA respectively. The result indicated that the phenolic contents were higher in methanolic extracts of leaf and stem [40].

Antiviral activity

Two new iridoid glycosides were isolated from *Barleria prionitis*. The antiviral activity and cytotoxic effects of the isolated compound and control antiviral compound were determined by using viral cytopathic effect inhibition assay. 6-o-trans-p-coumaroyl-8-o-acetylshanzhiside methyl ester and 6-o-cis-p-coumaroyl-8-o-acetylshanzhiside metyl ester showed potent in vitro activity against respiratory syncytial virus [41].

Anthelmintic activity

Aqueous and ethanolic extract of the whole plant of *B. prionitis* exhibited anthelmintic activity using Pheretima posthuma worms in a dose-dependent manner giving the shortest time of paralysis (P) at 50, 75 mg/ml and death (D) with 100 mg/ml concentration when compared to standard anthelmintic drug albendazole [42,43].

Antidiabetic activity

Alcoholic extract of leaf (200 mg/kg) increased insulin (130%) and liver glycogen (96.68%) and decreased glycosylated hemoglobin (22%) in alloxan-induced diabetic rats. Alcoholic extract of root at same dose increased insulin (30%) and liver glycogen (46.40%) whereas decreased glycosylated hemoglobin (11%) in same rat model [44]. Alcoholic, aqueous extracts of leaf (200 mg/kg) and chlorpropamide (100 mg/kg) reduced blood glucose level as 82.39±0.95 and 92.52±2.88 and 73.68±1.83 mg/100 ml after 7 days treatment where initial values were 299.72±3.97, 233.59±3.49 and 274.93±6.7 mg / 100 ml in alloxan induced diabetic rat model. Aqueous and alcoholic extracts of root reduced as 94.56±2.04 and 74.12±1.13 mg/100 ml after 7 days treatment where initial values were 240.59±1.62 and 247.68±4.83 mg/100 ml in same rat model [45].

Antiulcer activity (Gastroprotective activity)

Gastoprotective activity of chloroform extract of leaves of *B. prionitis* was studied by using experimental in-vivo models. Ulcer was induced by non-steroidal anti-inflammatory drugs and pylorus ligation. Parameters of gastric secretion (volume, pH, total protein, free and total acidity) were determined by pylorus ligation model. The result showed that the chloroform extract and ethyl acetate fraction prevented the gastric ulceration caused by indomethacin. Ethyl acetate fraction inhibited gastric secretion in pylorus ligated rats. The result showed that chloroform extract of leaves of *Barleria prionitis* leaves possess antiulcer activity and thus supports the traditional use of this plant in treatment of gastric ulcer [46].

Hepatoprotective activity

Iridoid enriched fraction from the ethanol-water extract of leaves and stem of *B. prionitis* was found to be significant hepatoprotection against carbon tetrachloride, galactosamine and paracetamol induced hepatotoxicity. Silymarin was used as standard drug. Iridoid enriched fraction showed significant and concentration dependent hepatoprotective potential it reversed the majority of the altered hepatic parameters in experimental liver damage in rodents [47].

Antinociceptive activity

One study was undertaken to evaluate the antinociceptive activity of 50% ethanolic extract of the flower of *B. prionitis* in experimental animals. The analgesic effect of the extract tested in mice of either sex, using an Ugo Basile Analgesio meter. A significant increase was measured in the analgesio-meter-induced force ($p<0.01$- <0.001) at the dose level of 50,100 and 200mg/kg *B.prionitis* extract and exhibited resistant against pain after 30 min equivalent to 26.3-48.23% protection [48].

Antiinflammation activity

Ethanol extract of flower and phenylbutazone showed 48.6 and 57.5% inhibition in carrageenin-induced paw edema in rat model. Extarct at 50, 100 and 200 mg/kg decreased granuloma weight from 15.32 to 36.4% gradually where phenylbutazone exposed 36.1% inhibition in cotton pellet granuloma rat model. Aqueous extract of root showed significant percentage inhibition of rat paw edema (52.56% & 55.76%) at a dose of 200 & 400 mg/kg respectively after 4 hr treatment. Hydroalcoholic extract whole plant (10 µg/ml) reduced rat mesenteric mast cells degranulation up to 64.91% and prevented hypotonic solution induced hemolysis of rat erythrocytes by 27.10% [49].

Antidiarrheal activity

Butanol fraction of *B. prionitis* leaves showed significant anti-diarrheal activity. In vivo study showed that the butanol fraction dose dependently inhibited the castor oil induced diarrhea and PGE2 induced enteropooling in sprague-dawley rats. The butanol fraction also reduced the gastrointestinal motility in response to charcoal-induced gut transit changes [50].

CONCLUSION

According to ethnomedical study, *B. prionits* is very effective and safe for medicinal uses. The qualitative and quantitative analysis reported the presence of many bioactive constituents. Currently, some of the phytoconstituents have been isolated and identified from *B. prionits.* These compounds and crude extracts have been screened for pharmacological activities by *in vivo* and *in vitro* models. From this review it is conspicuous that several portions of *Barleria prionitis* individually or jointly administered successfully by traditional practitioners specifically against fever, severe pain, asthma, ulcer etc. Moreover, pharmacological assays identify its dominant role as anti-microbial, free radical scavenging, gastro- liver protective agent. But as an established medicinal plant, it is still underutilized and its huge potentials are still uncovered but significant presence of several new secondary metabolites strengthen the demand of further research based on its phytotherapeutical importance. With the availability of primary information, further studies can be carried out like phyto-pharmacology of different extracts, standardization of the extracts, identification and isolation of active principles and pharmacological studies of isolated compound. These may be followed by development of lead molecules as well as it may serve for the purpose of use of specific extract in specific herbal formulation.

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CONSENT
It is not applicable.

ETHICAL APPROVAL
It is not applicable.

CONFLICST OF INTEREST
The author declare that there is no conflict of interest to reveal.

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