Barleria prionitis Linn.: A Review of its Traditional Uses, Phytochemistry, Pharmacology and Toxicity

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ABSTRACT

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, gastrointestinal disorders and as diuretic and tonic. A wide range of phytochemical constituents including balarenone, pipatpine prionisides, barlerinoside, verbascoside, shanzhiside methyl ester, barlerin, acetylbarlerin, lupuhniside, scutellarein have been isolated from the different parts of this plant. Extracts and isolated phytochemicals from this plant have been found to possess wide range of pharmacological include antimicrobial, antihelmintic, antifertility, antioxidant, anti diabetic, anti-inflammatory, anti-arthritis, cytoprotective, hepatoprotective, diuretic, anti diarrhoeal, enzyme inhibitory and anti-ociceptive activities without any toxic effects. So, in this review attempt has been made to highlight the traditional uses, phytochemistry, pharmacology and toxicity of this plant.

Key words: Barleria prionitis, traditional uses, phytochemistry, pharmacology and toxicity

INTRODUCTION

Medicinal plants are used worldwide in management of healthcare problems since time immemorial and approximately 60-80% of the world's population still depending on the traditional medicines (Dey et al., 2009; Ansari and Inamdar, 2010; Shafaei et al., 2011; Mengersi et al., 2011;Ramachandran et al., 2011; Kumar and Chandrashekar, 2011). Currently, the global demand of herbal medicines is increasing rapidly because of their higher safety margin and low cost (Musyimi et al., 2008). Medicinal plants are believed to be a potential source for the discovery of new drug candidates (Mohajer et al., 2006; Dey et al., 2010; Roy and Banerjee, 2010; Kayode and Kayode, 2011). Numbers of active compound classes like alkaloids, terpenes, flavonoids, glycosides, lignans, phenolics, saponins etc has been used in the modern system of medicines for their wide therapeutic activities (Saadabi et al., 2006; Mukherjee et al., 2009; Sohail et al., 2011; Agrawal et al., 2011; Gandait et al., 2011).

Ayurveda, a traditional systems medicine in India, have major treatment globally (Mukherjee et al., 2009; Bele et al., 2010). B. prionitis Linn. (family: Acanthaceae) is well-known
medicinal plant in ayurvedic system of medicine in India. The whole plant, root, leaves and bark of the plant occupy a significant place in the indigenous system of medicine of India for the treatment of various diseases like toothache, inflammations, boils, glandular swellings, catarrhal affections etc. (Khare, 2004, 2007; Daniel, 2006; Aneja et al., 2010). In India it has several vernacular names like In English-yellow nail-dye plant, porcupine flower; Sanskrit-vajradanti, kurantaka, koranta; Hindi-kala bans, katsareya, piabansa; Bengali-kantantijini, peetthani; Gujarati-kantashila; Kannada-karunta, mullugorante; Malayalam-chemmuli, varemutti; Marathi-kalsunda, kate koranti, kholeta, koranta, pivala-koranta; Odia-daskeranta; Tamil-kattu kanagaambaram, semmulli and in Telugu-mullugarinta chettu (Shendage and Yadav, 2010; Singh and Panda, 2006). In Indian traditional systems of medicine (Ayurveda) it is known as sahachara, baana, kurantaka, kuranta, koranda, korandaka, shairiya and pita-saireyaka. In folk medicine it is known as piyaabasaas, jhinti and katsaraiyas (Khare, 2007). Here, the attempt has been made to highlight its traditional uses, phytoconstituents, pharmacology and toxicity.

DISTRIBUTION

It is commonly found in tropical Asia include India, Malesia, Pakistan, Philippines, Sri Lanka and in tropical Africa and Yemen. This plant is distributed throughout the hotter parts of India and commonly grown in gardens as a hedge plant (Khare, 2007; Shendage and Yadav, 2010). It is commonly found in the states of India include Andaman and Nicobar Islands, Andhra Pradesh, Assam, Bihar, Chhattisgarh, Delhi, Diu and Daman, Goa, Gujarat, Jharkhand, Karnataka, Kerala, Laccadive and Maldives Islands, Madhya Pradesh, Maharashtra, Orissa, Puducherry, Rajasthan, Tamil Nadu, Uttar Pradesh and West Bengal (Shendage and Yadav, 2010).

GENERAL BOTANICAL DESCRIPTION

B. priotis is a perennial, erect, bushy shrub grows up to 1-2 m high. They possess 2-4 sharp long axillary spines which about 11 mm long. The stems are terete, glabrous, much branched with cylindrical and tapering branchlet (Dassanayake, 1998; Kamble et al., 2007). Leaves are smooth, opposite, ovate-elliptic to obovate, acuminate, tapering to base, bristle-tipped and about 6.5-15 cm long and 4.6 cm wide. The petioles are about 0.5-3 cm long (Shendage and Yadav, 2010). The flowers are sessile, yellow in colour and often solitary in lower axils and spicate in the upper axils. Bracts are acute, linear-lanceolate, foliaceous, about 1.5 cm long and 0.2-0.8 cm wide with bristle tipped (Dassanayake, 1998; Shendage and Yadav, 2010). The bracteoles are long, narrowly linear-lanceolate, spinous-tipped, about 1.4 cm long and 0.15 cm wide. The calyx is two parted. The outer calyx-lobes are mucronate, ovate-oblong and inner lobes are mucronate, linear-lanceolate. The outer lobes are 1.5 cm long and 0.4 cm wide while the inner lobes are 13 mm long and 2 mm wide (Dassanayake, 1998; Kamble et al., 2007). The corolla is bright, golden yellow in colour with pubescent outside and glabrous inside and about 1.5 cm long. It is somewhat bilipped and lobes are oval-oblong, rounded and entire. The stamens include 2 fertile stamens and 2 staminoid stamens. The fertile stamens are exerted beyond the corolla tube while the staminoid stamens are very short. The filaments are hairy and about 2-2.5 cm long, glandular-pubescent and yellowish in colour. The yellow anthers are 3 mm long (Dassanayake, 1998; Kamble et al., 2007; Shendage and Yadav, 2010). The ovary is ovoid and sigma is long, linear, sticky and pinkish in colour. The fruit capsule is ovoid, 2 seeded and about 1.5-2 cm long and 0.6-0.8 cm wide. The seeds are oval-oblong,
covered with silky copper-brown appressed hairs and measuring about 7.4-8.5×6-8.8 mm (Dassanayake, 1998; Kamble et al., 2007; Shendage and Yadav, 2010).

USE IN TRADITIONAL MEDICINE

In indigenous system of medicine in India, the juice of B. prionitis leaves is used in stomach disorders, urinary affections, ulcer and fever (Khare, 2007). The leaf juice mixed with honey given to children in catarrhal affections and fever (Khare, 2007). Leaves are chewed to relieve from toothache. Some tribal communities are used leaves for the treatment of piles and reduce irritation (Aneja et al., 2010; Shukla et al., 2011). The leaf juice is applied externally in laerated soles of feet and pimples. The dried stem bark is used as an expectorant in whooping cough and diaphoretic (Khare, 2007; Aneja et al., 2010). The aerial parts of this plant are also used in inflammations and gastrointestinal disorders. The root paste is externally applied to disperse boils and glandular swellings (Aneja et al., 2010). The flowers are used internally for the treatment of migraine, internal abscesses, oedema, haemoptysis, urethral discharges, seminal disorders and reduce obesity (Khare, 2004). The whole plant is also used in stiffness of limbs, enlargement of scrotum and sciatica. The whole plant, specifically the roots are used as diuretic and tonic. It is also used in urinary infection, jaundice, hepatic obstruction and dropsy (Shukla et al., 2011; Khadse and Kakde, 2011). Ash of the whole plant with honey is given in bronchial asthma. The crude extract of this plant in oil is recommended in arresting the greying of hair, arthritis and gout (Khare, 2004, 2007). In South India, this plant is widely used in neurological disorders like paraplegia, sciatica, also in leprosy and other skin diseases (Khare, 2004). The plant formulation, available in over the counter is prescribed in dysurea, rheumatic affections, internal abscesses, nerve disorders and in chronic sinusitis (Khare, 2004).

PHYTOCHEMISTRY

Preliminary phytochemical analysis of hydro-methanolic extract of B. prionitis whole plant indicated the presence of glycosides, saponins, flavonoids, steroids and tannins (Maji et al., 2011). The leaves and flowering tops were reported to rich in potassium salts (Khare, 2007). Several phytochemicals viz., balarenone (1), pipataline (2), lupeol (3), prioniside A (4), prioniside B (5) and prioniside C (6) has been isolated from the ethanolic extract of B. prionitis (Ata et al., 2007; Kosmulalage et al., 2007). Numbers of glycosides include barlerinoside (7), verbascoside (8), shanzhiside methyl ester (9), 6-O-trans-p coumaroyl-8-O-acetylshanzhiside methyl ester (10), barlerin (11), acetylbarlerin (12), 7-methoxydiderroside (13), lupulinoside (14) has been also isolated from the aerial parts (Taneja and Tiwari, 1975; Chen et al., 1998; Singh et al., 2005; Ata et al., 2009). 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 (Ganga Raju et al., 2002). The leaves were reported to contain seculellarin (15), melilotic acid (16), syringic acid (17), vanillic acid (18), p-hydroxybenzoic acid (19), 6-hydroxyflavones (20) (Daniel, 2006). Beside these phytochemicals, luteolin-7-O-β-D-glucoside (21), β-sitosterol (22), seculellarin 7-neochesperidoside (23), apigenin 7-O-glucoside (24), 13, 14-seco-stigmasta-5, 14-diene-3-a-ol (25) were also reported to present in B. prionitis (Harborne et al., 1971; Gupta and Saxena, 1984; Gupta et al., 2000; Khare, 2007; Kosmulalage et al., 2007). The structures of some phytochemicals are given in Fig. 1.
Fig. 1: Continued
Fig. 1: Structures of some selected phytochemical isolated from B. prionitis Linn.

PHARMACOLOGICAL ACTIVITY

**Antibacterial activity:** It has been reported that different solvent (ether, ethanol and chloroform) extracts of B. prionitis leaves and callus showed antibacterial activity against numbers of gram positive bacterial isolates while no or slight inhibitions were observed against the aqueous extracts. Among these extracts, the ether extract showed strongest antibacterial activity (Shukla et al., 2011). Some antibacterial phytochemicals include balarenone, pipataline and 13, 14-seco-stigmasta-5, 14-diene-3-a-ol have been isolated from the ethanolic extract of B. prionitis and these compounds showed strong antibacterial activity against Bacillus cereus and Pseudomonas aeruginosa (Kosmulalage et al., 2007). It was reported that the different solvent extracts of barks, leaves and stems showed potent antibacterial activity against oral pathogens Streptococcus mutans, Staphylococcus aureus, Pseudomonas aeruginosa and Bacillus cereus causing dental caries (Aneja et al., 2010). Among the extracts, the methanolic bark extract showed more potent inhibitory activity against all the oral pathogenic bacteria (Aneja et al., 2010). The antimicrobial activity of B. prionitis may be due to the presence of acetylbarlerin, barlerin, shanzhiside methyl ester, verbascoside, balarenone, pipataline, 13, 14-seco-stigmasta-5, 14-diene-3-a-ol and 6-O-acetyl shanzhiside methyl ester (Kosmulalage et al., 2007; Aneja et al., 2010).

**Antifungal activity:** The acetone, methanol and ethanol extracts of B. prionitis bark showed antifungal activity against oral pathogenic fungus Saccharomyces cerevisiae and two strains of Candida albicans. Among the extracts, methanolic extract was more potent against all the fungal isolates (Aneja et al., 2010). Amoo et al. (2011) reported that the petroleum ether, dichloromethane and ethanol extract of stem and root showed fungistatic and fungicidal activities against C. albicans.

**Antiviral activity:** Chen et al. (1998) isolated two iridoid glycosides viz. 6-O-trans-p-coumaroyl-8-O-acetylshanzhiside methyl ester and its cis isomer from B. prionitis. In vitro study showed that
these two glycosides possess potent antiviral activity against Respiratory Syncytial Virus (RSV) with EC$_{50}$ and IC$_{50}$ values of 2.48 and 42.2 µg mL$^{-1}$, respectively (Chen et al., 1998).

**Anthelmintic activity:** The whole plant extract of *B. prionitis* was reported have anthelmintic activity (Chavan et al., 2010a). *In vitro* study showed that aqueous and ethanolic extracts were significantly paralyzed the *Pheretima posthumna* worms at lower doses (50, 75 and 100 mg mL$^{-1}$) and caused death over 100 mg mL$^{-1}$ dose concentration in compare to standard drug albendazole (Chavan et al., 2010b).

**Antifertility activity:** The antifertility activity of *B. prionitis* roots was reported by Gupta et al. (2000). Oral administration of methanolic root extract (100 mgrat/day) reduced the spermatogenesis in male albino rats (Gupta et al., 2000; Verma et al., 2005). It was observed that the root extract decreased the production of round spermatids, sperm motility, spermatogonia, preleptotene spermatocytes population and mature leydig cells. Biochemical investigation revealed that the root extract was also reduced the total protein, glyocgen, sialic acid contents of the testes, testicular glycojen contents, epididymides, ventral prostate and seminal vesicle (Gupta et al., 2000; Verma et al., 2005). The antifertility effect of root extract may be due to the presence of iridoid glycosides barlerin and acetyl barlerin via affecting the function of testicular somatic cells (Gupta et al., 2000).

**Antioxidant activity:** The whole plant extract of *B. prionitis* was reported to show potent antioxidant activity (Chhetan et al., 2011). *In vitro* study showed that the ethanol and aqueous extracts of whole plant possess significant antioxidant activity against 1, 1-diphenyl-2-picrylhydrazyl (DPPH), 2, 2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) (ABTS), nitric oxide and hydroxyl radical scavenging assay and Fe$^{3+}$ reduction assay (Chhetan et al., 2011). In compare to antioxidant potency, the ethanol extract was more potent than aqueous extract and its antioxidant potency showed sharp co-relation with the phenolic content of the extract (Chhetan et al., 2011). Amoo et al. (2011) reported that the methanolic extract of roots, leaves and stems showed significant antioxidant property. It was observed that the leaves showed higher degree antioxidant potential and high phenolic content in comparison to flower and stem (Jaiswal et al., 2010a). Some glycosides have been isolated from the aerial parts of *B. prionitis* namely barlerinoside, shanzhiside methyl ester, 6-O-trans-p-coumaroyl-8-O-acethylshanzhiside methyl ester, barlerin, acetylbarlerin, 7-methoxydideroside and lupulinoside showed antioxidant activity. Among the isolated glycosides, only barlerinoside showed higher potential of antioxidant property with an IC$_{50}$ value of 0.41 mg mL$^{-1}$ (Ata et al., 2009).

**Antidiabetic activity:** Dheer and Bhatnagar (2010) revealed that the alcoholic extract of *B. prionitis* leaves showed antidiabetic activity. Oral administration of alcoholic extract at dose concentration 200 mg kg$^{-1}$ body weight significantly decreased the blood glucose, glycosylated hemoglobin level and increased serum insulin and liver glycogen level in diabetic rats. The extract also arrested the diabetes mediated weight loss (Dheer and Bhatnagar, 2010).

**Enzyme inhibitory effects:** The extracts from the different parts and isolated phytochemicals of *B. prionitis* reported to inhibit the clinically significant enzymes, Acetylcholinesterase (AChE) and
glutathione S-transferase (GST). Kosmulalage et al. (2007), Ata et al. (2007, 2009), Amoo et al. (2009, 2011) reported that the methanolic extracts of leaf, stem and root exhibited AChE inhibitory activities and the leaf and stem extracts exhibited higher potency of inhibition in compare the root extract. Several glycosides include barlerinoside, shanzhiside methyl ester, 6-O-trans-p-coumaroyl-8-O-acetylshanzhiside methyl ester, barlerin, acetylbarlerin, pataline, lupeol, 7-methoxydideroside, 13, 14-seco-stigmasta-5, 14-diene-3-a-d and lupulinoside have been isolated from the aerial parts of _B. prionitis_ and these compounds showed different levels of AChE inhibitory activity (Kosmulalage et al., 2007; Ata et al., 2009). All these compounds and prionside B and prionside C also showed GST inhibitory activity of which prionside B and prionside C were more potential GST inhibitors (Kosmulalage et al., 2007; Ata et al., 2007, 2009).

**Anti-inflammatory activity:** Several reports demonstrated the usage of _B. prionitis_ in the treatment of inflammations. The anti-inflammatory activity of _B. prionitis_ was evaluated through _in vitro_ enzyme based cyclooxygenase (COX-1 and COX-2) assays. It was found that the dichloromethane, petroleum ether and ethanol extracts of leaves, stems and roots exhibited significant inhibition of COX-1 and COX-2 with subsequent inhibition of prostaglandin synthesis that are involved in pain sensation (Amoo et al., 2009). The Aqueous Fraction (TAF) of hydromethanolic extract of _B. prionitis_ whole plant reported to have significant anti-inflammatory activity against the acute inflammation induced by carrageenan, histamine and dextran in rats (Singh et al., 2003). The anti-inflammatory activity of the TAF may be due to the presence of iridoid glucosides, shanzhiside methyl ester, acetyl barlerin and barlelin (Singh et al., 2003). Another study revealed that the aqueous extract fractions (FR-III and FR-IV) of root significantly inhibited the carragennan induced rat paw edema (Khadse and Kakde, 2011). The FR-III and FR-IV at oral dose concentration of 400 mg kg⁻¹ body weight inhibited the paw edema by 50.64 and 55.76%, respectively and the results were comparable with the reference standard drug indomethacin with a 60.25% of inhibition (Khadse and Kakde, 2011). The ethanolic extract of flowers also exhibited anti-inflammatory activity in rats (Jaiswal et al., 2010b). Oral administration of flower extract (200 mg kg⁻¹ body weight) showed significant dose-dependent reduction in carrageenan induced swelling and cotton pellet granuloma weight that were equivalent to 48.6 and 38.4% protection (Jaiswal et al., 2010b).

**Anti-arthritic activity:** The TAF fraction was reported to have anti-arthritic property in _Mycobacterium tuberculosis_ induced adjuvant arthritis rats model (Singh et al., 2003). The TAF at oral dose range of 12.5-100 mg kg⁻¹ significantly inhibited leucocytes migration and lowered the Erythrocyte Sedimentation Rate (ESR) and exudate volume in pleural cavity which indicated the inhibition of vascular permeability in arthritis-induced rats (Singh et al., 2003).

**Cytoprotective activity:** Mast cells play an important role in inflammatory responses and release histamine upon their degranulation to produce various allergic reactions (Manek et al., 2011). Maji et al. (2011) reported that the hydro-methanolic extract of whole plant showed dose-dependent mast cells and erythrocyte membrane protection activity in response to the toxic chemicals. The extract inhibited the Compound 48/80 induced mast cells degranulation up to 64.91% at dose concentration 10 μg mL⁻¹ and the result was comparable with the reference standard disodium cromoglycate (10 μg mL⁻¹) with 19.32% protection (Maji et al., 2011). The extract (10 μg mL⁻¹) provided significant erythrocyte membrane protection (27.10%) against hypotonicity haemolysis.
and the result was comparable with reference standard indomethacin (10 µg mL⁻¹) with 61.29% protection (Maji et al., 2011).

**Hepatoprotective activity:** The iridoid glycosides enriched fraction from hyrdoethanolic extract of leaves and stems of *B. prionitis* was reported to show significant hepatoprotection against carbon tetrachloride, galactosamine and paracetamol induced hepatotoxicity in mice and rats (Singh et al., 2005). The oral administration of iridoid fraction significantly reduced the hepatotoxin induced elevated levels of serum alanine aminotransferase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), bilirubin and triglycerides in a dose dependent manner. The fraction was also increased the hepatic glutathione content and reduced the hepatic lipid peroxidation in response to the hepatotoxicity in mice and rats (Singh et al., 2005).

**Diuretic effect:** The diuretic property of *B. prionitis* flower extract was performed by Musale et al. (2011). The oral administration of aqueous flower extract (200 mg kg⁻¹) was significantly increased the urination (diuresis) and sodium elimination but not potassium in rats. The diuretic effect of flower extract (200 mg kg⁻¹) was comparable and statistically significant with the reference drug furosemide (20 mg kg⁻¹) (Musale et al., 2011).

**Anti-nociceptive activity:** The analgesic activity of *B. prionitis* flowers was evaluated using an Ugo Basile Analgesy meter induced artificial pain and acetic acid induced writhing models (Jaiswal et al., 2010b). *In vivo* study showed that the flower extract dose dependently provided a significant increase in the analgesio-meter-induced force and exhibited significant resistance against pain in mice (Jaiswal et al., 2010b). The flower extract was also provided dose dependent significant reduction in writhing characterizes by the reduction in acetic acid induced abdominal cramping and abdominal cramping. At a dose concentration of 50 mg kg⁻¹ body weight, the extract provided statistically significant reduction of writhing by 5.24% (Jaiswal et al., 2010b).

**Anti-diarrheal activity:** Jaiswal et al. (2010c) reported the anti-diarrheal potential of butanol fraction of *B. prionitis* leaves. *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 (Jaiswal et al., 2010c).

**TOXICITY**

The toxicity study with the alcoholic extract of roots and leaves of *B. prionitis* did not showed any toxic effects in adult albino rats (Dheer and Bhatnagar, 2010). No death was observed up to the oral administration of extract dose concentration 2.5 g kg⁻¹ body weight during the 14 days of study period Dheer and Bhatnagar (2010). Singh et al. (2005) reported that the iridoid glucosides rich aqueous fraction *B. prionitis* did not produced any signs of abnormalities or any mortality up to the single oral administration of 3000 mg kg⁻¹ dose in mice during the 15 days of study period. However, the intraperitoneal LD₅₀ was determined as 2500 mg kg⁻¹ for the aqueous fraction in mice (Singh et al., 2005).

**CONCLUSION**

*B. prionitis* occupy a significant place in the Ayurvedic medicine in India. The detailed information as provided in this review on its traditional uses, phytochemistry, pharmacology and
toxicity of the extracts of different parts might be added value in the scientific evaluation of medicinal use of this plant. Extensive literature survey revealed the promising pharmacological includes antimicrobial, anhelminthic, antifertility, antioxidant, antidiabetic, anti-inflammatory, anti-arthritis, cytoprotective, hepatoprotective, anti-diarrhoeal, enzyme inhibitory, diuretic and anti-nociceptive activities of the extract and isolated molecules of this plant without any toxic effects. In future study, the conversion of these pharmacological activities in to the modern drugs, proper scientific evaluation includes isolation of responsible phytochemicals, their mechanism of actions, toxicity and proper standardization need to be explored.

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