

# A Review on *Ajuga Bracteosa*, a Traditionally Important Medicinal Plant

<sup>1</sup>Anindita Deka\*, <sup>2</sup>Pori Deka

<sup>1</sup>Department of Zoology, Gauhati University, India

<sup>2</sup>Department of Bioengineering and Technology, Gauhati University, India

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## Abstract—

**W**ith the shifting of belief from chemically synthesized medicinal drugs associated with adverse side effects, to traditionally used safe medicinal herbs, there is a massive attempt in this field for identifying potent plants as a remedy against various ailments. *Ajuga bracteosa*, a low perennial herb is one such plant, known to have numerous medicinal properties against various ailments such as arthritis, gout, malaria, cancer etc. It is also a well known medicinal plant in Ayurveda. In his review, an attempt is made to highlight the pharmacological properties of *Ajuga bracteosa* along with the botanical description of the plant along and chemical compounds.

**Keywords—** *Ajuga bracteosa*, Ayurveda, arthritis, malaria, cancer

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## I. INTRODUCTION

*Ajuga bracteosa* is a low perennial herb known to have numerous medicinal properties for which it finds its application as a remedy against various ailments. Commonly known as Bracted bugleweed, Blue bugle, Bungle, Small-flowered bugleweed, it belongs to the family Lamiaceae which includes plants which are generally aromatic and widely used as culinary herbs and plays a very important role in the medicinal and Ayurvedic world. It acts as a natural astringent, febrifugal, stimulant, tonic, diuretic and having depurative properties, and is used for the treatment of gout and rheumatism, palsy, amenorrhoea and also for cancer treatment. It is used also to kill parasites like lice. The juice of the leaves is taken as a blood purifier and also to get relief from fevers. The powdered leaves are used for burns and boils.

## II. BOTANICAL DESCRIPTION

### A. Systematic Classification

Kingdom:	Plantae
Phyllum:	Angiosperms
Order:	Lamiales
Family:	Lamiaceae
Genus:	<i>Ajuga</i>
Species:	<i>A. bracteosa</i>

### B. Distribution

*Ajuga bracteosa* is usually found at an altitude of 2000 m. It is distributed from Kashmir to Nepal, in the sub-Himalayan tract, plains of Punjab and the upper Gangetic plain[1]. It is also found in Grassy slopes in Sichuan and Yunnan Provinces and found extending the Himalayas from Kashmir to Nepal and China.

### C. Habits and Relationships

*Ajuga bracteosa* usually grows well in moist ground and grassy slopes, often along the sides of tracks, at elevations of 700 - 4000 metres[2]. It is suitable for light (sandy), medium (loamy) and heavy (clay) soils and prefers well-drained soil with acidic, neutral or basic pH. It can grow in semi-shade (light woodland) or no shade.

Different types of bacteria are found which remain associated with the roots of *Ajuga bracteosa* that suggests a positive rhizosphere effect of the plant. A total of 123 morphologically different bacteria were isolated from the rhizospheric soil and roots of the plant. Majority of the rhizospheric soil isolates belonged to  $\alpha$ - and  $\gamma$ -Proteobacteria, with *Pseudomonas* constituting the most dominant species. Endophytic bacterial community, on other hand, consisted almost exclusively of Firmicutes. All of these contributed to enhance plant gross production (PGP) activity by producing siderophores and indole acetic acid. A significant proportion of isolates also demonstrated other ecologically important activities like phosphate solubilization, nitrogen fixation, and production of hydrolytic enzymes including amylase, protease, lipase, chitinase, cellulase, pectinase and phosphatase. Firmicutes were found to be metabolically the most versatile group and performed multiple enzyme activities[3].

### D. Description

Whole plant: *Ajuga bracteosa* is a low herb covered with soft hairs, with erect, ascending stems which arise from the rootstock. Branching is usually diffuse originating from the base and measuring 10 to 20 centimetres in length.

**Leaves:** Leaves are oblanceolate or subspatulate, 2.5 to 10 centimeters long, and 1 to 3.5 centimeters wide. The lower leaves are stalked and the upper leaves are stalkless and sinuate-toothed or nearly entire.

**Flower:** The flowers are hermaphrodite (have both male and female organs) and are pollinated by insects. Calyx is hairy, with ovate-lanceolate teeth. Corolla is pale blue or white and hairy; the tube is rarely twice as long as the calyx; the upper lip is erect and 2-fid; the side lobes or lower lobes are oblong, and the midlobe is dilated and variable in length. Stamens protrude from the upper lip. Nutlets are ellipsoid and very small[4].

### E. Chemical constituents

*Ajuga bracteosa* is an endangered medicinal herb which contains several natural products of therapeutic importance like 20-hydroxyecdysone (20-HE), the accumulation of which increases during chilling cold conditions as a defense response [5]. A large number of compounds have been isolated from *Ajuga bracteosa* herb. Ajuganane, a new phenolic compound was isolated from *Ajuga bracteosa* Wall along with other three known compounds, 3,4'-dihydroxy-3,6,7-trimethoxyflavone, 7-hydroxy-3,6,3',4'-tetramethoxyflavone and ursolic acid[6]. Both clerodin- and dihydroclerodin-type diterpenes were obtained when dichloromethane extract of *Ajuga bracteosa* were subjected to "hydroxyl-free" purification conditions. Four new compounds, ajubractins A-D, along with clerodin, 3-epi-caryoptin, ajugapitin, 14,15-dihydroclerodin, 3-epi-14,15-dihydrocaryoptin, ivain II, and 14,15-dihydroajugapitin were isolated. When methanol-water mixtures were used for a C18 reversed-phase prepurification procedure and for semipreparative HPLC, the new ajubractin E was also isolated [7]. Bractin A (= (2S,3S,4R,5E)-2-[[ (2R)-2-hydroxydodecanoyl]amino]triacont-5-ene-1,3,4-triol and bractin B (= (2S,3S,4R,5E,8E)-2-[[ (2R)-2-hydroxyhexacosanoyl]amino]pentadeca-5,8-diene-3,4,15-triol 1-O-beta-D-glucopyranoside, new sphingolipids, and bractic acid (= (5Z,10Z,15Z)-2-decyl-4,7,8,12,13,17,18-heptahydroxy-20,23-dioxopentacos-5,10,15-trienoic acid, a long-chain polyhydroxy acid, were isolated from the whole plant *Ajuga bracteosa* along other diterpenoids[8]. Three new withanolides, bracteosin A (= (22R)-5beta,6beta : 22,26-diepoxy-4beta,28-dihydroxy-3beta-methoxyergost-24-ene-1,26-dione, bracteosin B (= (22R)-5beta,6beta : 22,26-diepoxy-4beta,28-dihydroxy-3beta-methoxy-1,26-dioxoergost-24-en-19-oic acid, and bracteosin C (= (22R)-22,26-epoxy-4beta,6beta,27-trihydroxy-3beta-methoxyergost-24-ene-1,26-dione, and Dihydroclerodin-1, clerodin A, lupulin A, and dihydroajugapitin were also isolated for the first time from the whole plants of *Ajuga bracteosa* [9]. From the hexane extract of the whole plant of *Ajuga bracteosa*, a new phthalic acid ester 1,2-benzenedicarboxylic acid bis(2S-methyl heptyl) ester was isolated. In addition, chloroform and methanol extracts yielded neo-clerodane diterpene ajugarin-I and two iridoid glycosides, reptoside and 8-O-acetyl harpagide. This plant is a new source of a valuable perfumery compound, linalyl acetate[10]. The whole plant of *Ajuga bracteosa* is a source of one new clerodane diterpenoid designated as Bracteonin-A. The other compounds identified were 14,15-dihydroajugapitin, 14-hydro-15-hydroxy ajugapitin, beta-sitosterol, and stigmaterol [11].

## III. PHARMACOLOGICAL PROPERTIES

The various biological properties known traditionally have been proved by modern scientific procedures that have been highlighted in mainstream scientific literature. Some of these are stated below.

### A. Traditional Uses

Traditionally, *Ajuga bracteosa* is used to cure many ailments. The plant is aromatic, astringent and tonic [12]. It is useful in the treatment of agues. The juice of the root is used in the treatment of diarrhoea and dysentery. The leaves are used in the treatment of fevers as a substitute for quinine [12].

Crushed leaves are used as astringent to stop bleeding. Leaf decoction with honey and ginger juice is used for high fever and respiratory congestion[13]. In Taiwan, the entire plant of *Ajuga bracteosa* has been used to treat various inflammatory disorders, including hepatitis[14]. *Ajuga bracteosa* is also mentioned in Ayurveda for the treatment of rheumatism, gout, palsy and amenorrhoea [15]. It is also used traditionally as a remedy for malaria [16]. In Asian countries it is used as a folk medicine against gout, hepatitis, pneumonia, rheumatism, and various neuro-inflammatory disorders [17]. The decoction of the leaves, flowers, and barks is used in India for the treatment of cancer and other diseases like diabetes, malaria, and inflammation etc [18].

### B. Anti-arthritis activity

The traditional use of *Ajuga bracteosa* for rheumatism and other inflammatory diseases was proved by treating turpentine oil- and formaldehyde- induced acute non immunological and complete Freund's adjuvant (CFA)-induced chronic immunological arthritis in albino rats with 70% ethanolic extract of *Ajuga bracteosa* (EEAB). EEAB showed a significant ( $P < 0.05$ ) and dose dependent inhibitory effect against acute and chronic models of arthritis and the results were even better than the standard aspirin [15].

### C. Anti-inflammatory

Anti-inflammatory properties were studied by screening the inhibitory action of chloroform fraction of *Ajuga bracteosa* extract (ABCE) on lipopolysaccharide (LPS)-stimulated RAW264.7 cells and Kupffer cells and also on CCl<sub>4</sub> induced hepatic fibrosis. It was seen that ABCE could possibly block the production of NO and/or TNF- $\alpha$  and also inhibited the LPS-induced expression of NO synthase in LPS-stimulated RAW264.7 cells and Kupffer cells. ABCE also has the potential to inhibit the activation of NF- $\kappa$ B induced by LPS, associated with the abrogation of I $\kappa$ B $\alpha$  degradation, with a subsequent decrease in nuclear p65 and p50 protein levels. ABCE also can suppress the phosphorylation of MAPKs in

LPS-stimulated RAW264.7 cells. Animal studies showed ABE protects the liver from injury by reducing the activity of plasma aminotransferase, and by improving the histological architecture of the liver. RT-PCR analysis revealed that ABE inhibited the hepatic mRNA expression of LPS binding protein, CD14, TNF- $\alpha$ , collagen( $\alpha$ 1)(I), and  $\alpha$ -smooth actin. The reason for such alleviation of CCl<sub>4</sub>-induced liver fibrosis may be due to the suppression of macrophage activation [14].

The anti-inflammatory activity maybe possibly mediated through inhibition of COX-1 and COX-2 enzymes as shown by Gautam *et al.*, in 2011. They studied the effect of 70% ethanolic extract of *Ajuga bracteosa* in TPA-induced mouse ear edema assay and its effect on cyclooxygenase (COX)-1 and COX-2 inhibitory activity. The extract showed a strong *in vitro* COX-1 and COX-2 inhibitory activity at 25 and 50  $\mu$ g/mL concentrations. Among the various compounds isolated such as Aajugarin I, lupulin A, withaferin A, reptoside and 6-deoxyharpagide, 6-deoxyharpagide exhibited highest COX-2 inhibition as compared to others which showed moderate COX-1 and COX-2 inhibition at 30  $\mu$ M concentration. The 70% ethanol extract of whole plants of *Ajuga bracteosa* also exhibited a significant ( $p < 0.05$ ) and dose-dependent anti-inflammatory activity in an acute inflammation model at the dose of 0.5 and 1.0 mg/ear [15].

#### D. Anti-plasmodial

Antiplasmodial efficacy of *Ajuga bracteosa* was screened and it was found to possess significant *in vitro* antiplasmodial efficacy with an IC<sub>50</sub> of 10.0  $\mu$ g/ml. *In vivo* schizontocidal activity and efficacy in terms of survival time in *Plasmodium berghei* infected BALB/c mice was also carried out. The extract at 250, 500, and 750 mg/kg/day showed significant ( $p < 0.0001$ ) blood schizontocidal activity during established infection with enhanced mean survival time comparable to that of standard drug chloroquine [19]. The ethanolic leaves extract of *A. bracteosa* (250, 500 and 750 mg/kg/day) demonstrated a dose-dependent chemosuppression during early and in established infections, along with significant ( $P < 0.05$ ) repository activity in *Plasmodium berghei* infected BALB/c mice [16]

#### E. Immunoregulatory

*Ajuga bracteosa* has immunoadjuvant potential. The immunoregulatory effects of the ethanolic extract of *Ajuga bracteosa* (ABEE) was studied on systemic Th1/Th2 immunity in SRBC immunized Balb/C mice. Treatment with ABEE showed significant biphasic immunostimulation of effector T-helper immunity. ABEE at 50 mg/kg dose caused maximal activation and proliferation of T and B lymphocytes as evident by increase in antibody titers, DTH responses and CD4<sup>+</sup>/CD8<sup>+</sup> T-cell percentages. It also exhibited maximal up regulation of LPS and CON A stimulated splenocyte proliferation and also maximal up-regulation of both Th1 (IL-2, IFN- $\gamma$ ) and Th2 (IL-4) cytokines which suggest its mixed Th1/Th2 immunostimulatory activity. However, at higher doses (100 mg/kg), significant down regulation of all these effector T-helper (Th) immune responses was observed. The study therefore suggests mixed biphasic immunostimulatory Th1/Th2 activity of ABEE [17].

#### F. Anti-cancer

Petroleum ether, methanolic and water extracts of *Ajuga bracteosa* were tested against human breast adenocarcinoma (MCF-7) and larynx carcinoma (Hep-2) tumor cell lines. It was found that the methanolic fraction of *Ajuga bracteosa* was effective against MCF-7 and Hep-2 tumor cell lines. The methanolic, petroleum ether and aqueous extract from *Ajuga bracteosa*, presented an IC<sub>50</sub> value at 24 h of 10, 65, 70  $\mu$ g/ml and 5, 30, 15  $\mu$ g/ml on MCF-7 and Hep-2 cells, respectively [18].

#### G. Nervous disorders

The cholinesterase inhibitory potential along with calcium antagonistic ability and safe profile in human neutrophil viability assay could make compounds such as Bractin A, Bractin B and Bratic acid, isolated from *Ajuga bracteosa*, possible drug candidates for further study to treat Alzheimer's disease and associated problems [8].

#### H. Insecticidal

Crude methanolic extracts of all *Ajuga* plants, showed considerable efficacy against larvae of two exopterygota (sucking insect) species i.e. *Dysdercus cingulatus* F and *Acyrtosiphon pisum* (Harris) [20].

### IV. CONCLUSIONS

From the above discussion it is found that the traditional beliefs of the medicinal property of *Ajuga bracteosa*, are confirmed by recent scientific techniques. But, more exploration of this holistic plant needs to be done for reaping out the maximum benefits. Active compounds contributing to such medicinal property needs to be isolated that could be further tried clinically for best results with minimal side effects.

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