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A Review on Ethnobotany, Phytochemistry and Pharmacology on *Ajuga Bracteosa*

[1]Dr.Chinu Kumari, [2]Dr.Dev Prakash Dahiya, [3]Pratibha Rana*

[4]Dinesh Kumar Thakur, 5Utsav Pathak, 6Anita kumari,7Munish Choudhary

Pharmacognosy,

Abhilashi University, Chailchowk, India

Abstract: *Ajuga bracteosa* is a member of the lamiaceae family, which is expanding over the Indian subcontinent, Bangladesh, Nepal, Sri Lanka, and South East Asia. It is a component of many traditional remedies that treat a range of illnesses. *A. bracteosa* have a variety of medicinal effects. Flavonoids, saponins, phenols, tannins, terpenoids, xanthoproteins, glycosides, and other compounds are among them. According to this review ethanol extract had the highest level of flavonoid concentration while chloroform-methanol extract had the highest level of radical scavenging ability. Its primary applications include hepatoprotective, antihypertensive, anticancer, antidiarrheal, antioxidant, and antibacterial properties. This review paper provides details on the many pharmacological actions of *A. bracteosa* , which could serve as a basis for more investigation.

Index Terms- Ajuga bracteosa, **traditional remedies, antihypertensive, pharmacological actions**

Introduction

Plants have been utilized for restorative purposes from 5000 BC with the rise of the Indus Valley Development. The native arrangement of medication, viz.- Ayurvedic, Siddha and Unani, have been in presence for a very long time[1]. The nation has 45,000 different plant species and 15000 restorative plants that incorporate 2000 plants utilized in Ayurveda, 700 in Unani, 600 in Siddha, 450 in Homeopathy and 30 in current medications. The medications are gotten either from the entire plant or from various parts like leaves, stem, bark, root, bloom, seed and so forth. A few medications are ready from excretory plant item like gum, pitches and plastic. [2,3]

Plants are straightforwardly utilized as drugs by a greater part of societies all over the planet, for instance Chinese medication and Indian medication. [4]

- Many food crops make restorative impacts, for instance garlic.
- Medicinal plants are assets of new medications. It is assessed there are more than 250, 000 blossom plant species. [5]

Thus concentrating on therapeutic plants assists with grasping plant harmfulness and safeguard human and creatures from regular toxic substances. Development and conservation of restorative plants safeguard natural variety, for instance metabolic designing of plants. [6,7]

As indicated by the WHO, 25% of present day meds are produced using plants initially utilized customarily[8]. One late model is the utilization of Artemisinin based drugs for getting intestinal sickness due the jungle fever parasite displaying drug protection from recently recommended drug treatments. Customary Chinese medication has been utilized to successfully treat jungle fever with developed Artemisia plants for over 2500 years. [9]

Diabetes is one more region where a great deal of examination is going on *Ajuga reptens* (the dynamicm rule is said to potentiate impacts of insulin), *Galagea officinalis* (galagine) [10], *Bougainvillea spectabilis* (pinitol) [11], *Momordica charantia* (chirantin), [12] *Gymnema sylvestre* (gymnemic corrosive) [13] are a few therapeutic spices that have shown viability in non-insulin subordinate diabetes. As of late concentrate of Tecoma stans has shown powerful enemy of diabetic movement. Alkaloid tecomonine is viewed as dynamic rule of the spice. [14]

Joint pain is another potential illness where no agreeable response is available in present day medication. *Commiphora mukul* (guggulsterones), [15] *Boswellia serrata* (boswellic corrosive), [16] *Withania somnifera* (withanolides), *Ruscus acueleatus* (ruscogenin) are unmistakable plants with against joint movement. [17]

Ajuga bracteosa is to be a highly important medicinal plant the majority of the natural population of the plant is currently under severe pressure due to high demand. This species is rapidly declining as a result of overexploitation. This herb is in high demand in the pharmaceutical industry at both the local and international levels. But the fact is that it is extremely endangered and, if it continues to be exploited at the current rate, will go extinct within the next few years [18]Therefore, long-term use of this incredibly healing species is required to preserve for its numerous known uses. This species has received a lot of attention in the last decade. A multifaceted strategy is necessary for maintenance, which could offer a solution to the current issue. This strategy comprises the selection of higher-quality genotypes, as well as ex-situ and in-situ conservation, followed by multiplication utilizing both conventional and biotechnology means[19]. Any medicinal plant's worth is based on the active components that are present in that species. Elite clone development would be desirable. Chemo-profiling and different molecular marker approaches can be used to find superior clones. Commercial plantations can be multiplied and grown for conservation using conventional propagation techniques as well as plant tissue culture procedures. To speed up the creation of favoured genotypes and commercial micro propagation, tissue culture can be employed as an alternative to traditional in vitro propagation techniques. Plant tissue culture techniques are now used for gene transfer, selection, and regeneration of transformants[20]. The Cell suspension culture, in addition to in vitro propagation, is useful for

large-scale secondary metabolite production. Another factor that influences plant quality is post-harvest handling. Herbal material collectors pay less attention to material quality during harvesting, handling, and storage. Mycotoxin-producing fungi have been discovered in herbal drug samples that have been stored. Cultivation practices must be addressed as well. Wild harvested plants vary in consistency and quality due to genetic and environmental differences[21]. The efficacy of medicinal plants is also influenced by regional environmental conditions. Temperature, photoperiod, soil characteristics, and rainfall all have a significant impact on the production of active constituents. As a result, consistent efforts should be made at the community level to ensure the long-term management of medicinal plants. Shivanee et al reported that MS medium supplemented with IAA (2 mg/L) and BA (5 mg/L) induced 100 % shoot regeneration [22].. In this experiment leaf, petiole and root as an explants were selected. Leaf displayed quickest response followed by petiole while root was shown the slowest response. It was further experimentally proved that shoot induction is predominantly dependent on plant growth regulators added to the culture medium. Full- or half-strength Murashige and Skoog medium with or without auxin is used for in vitro rooting. An estimated survival rate of 82-100% was achieved when rooted shoots are acclimatized in the greenhouse[23]. Micropropagation is a key technique used in our previous work to conserve the plant.

Taxonomic Classification [24]

Kingdom - Plantae

Division - Tracheophyta

Class -Magnoliopsida

Order - Lamiales

Genus -*Ajuga bracteosa*

Family- Lamiaceae

Fig: Plant *Ajuga bracteosa*

Vernacular Name- *A .bracteosa* comes to the kingdom Planate of the Tracheophyta division, the Magnoliopsida class, the Lamiales order, and the Lamiaceae family. A. bracteosa is known by many different names. It's called "Bungle" in English, "Nilkanthi" in Sanskrit, and "Jan-i-adam" in Kashmiri, Kauri booti in Urdu. [26]

Morphological Characters

It is an aromatic medicinal, villous, soft, and decumbent herb that grows 15–30 cm tall. It is perennial evergreen plant with prolixly branching stems that stay flattened. The flowers are yellowish with axillary spirals. It has a woody rootstock, leaves that can grow to be up to 8.5 cm 3.5 cm in length and are usually much smaller with a more crenate to lobed margin, calyces that are 3.5–4.5 mm in length. [27]

Geographical Distribution

A.bracteosa is commonly known as Kauri booti and it belongs to family Lamiaceae . *A. bracteosa* is a prized medicinal, aromatic, soft and decumbent herb which is about 10-30 cm in height . It is well- settled on grassland, exposed slopes and open field in temperature and subtropical region of the world. At an elevation of 1300 to 2400m. [28]

Traditional Use

A. bracteosa is highly medicinal plant and it is the most valuable species among all the species of genus Ajuga. A. bracteosa is traditionally used to treat fever and phlegm in China. It is recommended in Ayurveda to treat gout, palsy, amenorrhea and rheumatism. Leaves of A. bracteosa are stimulant, diuretic and locally used to treat malaria. A. bracteosa is regarded an alternative to cinchona [29].

Compounds produced by A. bracteosa have a variety of medicinal goods. Flavonoids, saponins, phenols, tannins, terpenoids, xanthoprotein, glycosides, and other composites are among them. The ethanol excerpt had the loftiest position of flavonoid attention while chloroform – methanol excerpt had the loftiest position of radical scavenging capability. Polyphenols like pyrocatechol, gallic acid, resorcinol, catechin, chlorogenic acid, caffeic acid, syringic acid, ferulic acid, vanillic acid, coumarin, trans – cinnamic acid rutin, were verified using RP- HPLC – quantification . 6- deoxyharpagide and raptoside are iridoid glycosides present in the factory. These composites are optically active cyclopentonoids monoterpenes and could be used for defence action [31,32].

Conditions	Methods of applications[33]
Headache	Paste of the leaves is applied to cure headache
Abdominal pain	Powder of the whole plant is given to treat abdominal pain
Indigestion	Powder of whole plant is also used to treat indigestion
Astringent	Whole plant is used as astringent
Bladder disease	Plant extract is used is used to treat this.
Eye trouble	Plant extract is used is used to cure eye trouble
Bites of insects	Plant extract is used is used to cure bites of insects
Tonic	Whole plant is also used as tonic
Internal colic	Whole plant is used to treat internal colic
Pimples	Barks juice is used to treat pimples
Jaundice	Leaves extracts are used to treat jaundice

Hypertension	Whole plant is used to treat hypertension
Sore throat	Whole plant is used to sore throat
Cold	Decoction of root is taken
Leprosy	Root powder ingested
Blood purification	Leaves extract is used for blood purification
Diabetes	Decoction of leaves is used to treat the diabetes
Fever	Decoction of leaves is used to treat the fever
Swollen wounds	Plant extract is used is used to cure swollen wounds

Ethnomedical Significance[34,35,36]

1. Drug powder:

It has shown hypoglycemic activit. A decoction of the leaves of the herb is usedin the traditional medicine for diabetes and a number of diseases including hypertension, fever, malaria and stomach pain.

2. An alcoholic fraction of leaves:

It had shown Cardiotonic action on frog heart, rabbit auricle and rat ventricle. An alkaloidal fraction showed stimulant action on the perfused frog heart. The alkaloidal fraction obtained from the plant showed a positive inotropic action on the frog heart, isolated rabbit auricle and electrically driven rat ventricle.

3. Ethanolic ext. of plant:

It has been shown as spasmolytic and anticancer. Ethanolic extract of the plant in a preliminary biological screening showed effect on guinea pig ileum and Anticancer activity in sarcoma 180 in mouse and HS human sarcoma in the embryonated egg.

4. The aqueous extract of Plant:

A dose of 2.4 g/kg in normal saline administered intra-gastrically, showed protection against carbon tetrachloride-induced liver damage as Hepatoprotective.

5. The juice of the root:

It is also used in the treatment of diarrhoea and dysentery. According to Asia Pacific Medicinal Plant Database, the leaves are regarded as stimulant, diuretic and tonic. Juice of the plant (about 3 teaspoons twice a day) is given to treat troubles of the bile duct. Leaf powder is given to cure ulcer of mouth. Decoction of leaves (3–4 drops) is given thrice a day to small children (4 months old) who have breathing problems and also to cure internal sores.

Phytoconstituents[37,38]

Phytochemically, A. bracteosa contains various compounds such as neo-clerodane diterpenoids, flavonol glycosides, iridoid glycosides, ergosterol-5,8-endoperoxide and phytoecdysones. These chemical compounds were either synthesized or isolated from the plant. Cytotoxicity level was evaluated using skin carcinoma cell line and it was found that ergosterol-5,8-endoperoxide and neo-clerodane diterpenoids were not cytotoxic at higher concentration used for antiplasmodial activity. Compounds produced by *A. bracteosa* have a variety of medicinal effects. Flavonoids, saponins, phenols, tannins, terpenoids, xanthoproteins, glycosides, and other compounds are among them. According to Zahra et al., ethanol extract had the highest level of flavonoid concentration while chloroform-methanol extract had the highest level of radical scavenging ability. Polyphenols like pyrocatechol, gallic acid, resorcinol, catechin, chlorogenic acid, caffeic acid, syringic acid, p-coumaric acid, ferulic acid, vanillic acid, coumarin, sinapinic acid, trans-cinnamic acid, rutin, and kaempferol were confirmed using RP-HPLC-based quantification . 6-deoxyharpagide and raptoside are iridoid glycosides present in the plant . These compounds are optically active cyclopentonoids monoterpenes and could be used for defence action . Ajuga bracteosa has a rich phenolic content and is hence a superior choice for phenolic-guided pharmacological activities. According to studies, the constituent 20-hydroxyecdysone is present but its concentration varies depending on where it is found due to the action of various exogenous factors. One such exogenous factor, cold temperature, is ideally suited for consistent 20-hydroxyecdysone synthesis. Studies have also suggested that this steroid might also have therapeutic benefits for a number of respiratory illnesses as well as cardiometabolic and neuromuscular problems. Lactone steroids withanoloide, which serve as cholinesterase inhibitors, is also present in the plant. Dichloromethane extract of whole plant of A. bracteosa produced a variety of clerodane and neoclerodane diterpenoids. Neoclerodane diterpenoids have been shown to be effective as an anti-bacterial in tests. As per report analysis the antimicrobial activity and insect anti-feedent activity can also be correlate Ajuga bracteosa. There are several other biologically active compounds were isolated and identified from the methanol extract of aerial part of Ajuga which are showing anti-mutagenic activity.

Phytoconstituents present in species Ajuga[39,40]**:**

Ajugapitin	Ajugamarin
Dihydroajugapitin Chamaepitys	Deacetylajugarin
Ajugamarin	Ajugamarin
Dihydroajugamarin	Ajugacumbin
Ajugamarin chlorohydrin	Ajugachin A
Desrhamnosylverbascoside	Ajugachin B
2-O-(p-Coumaroyl)-	Ajugacumbin E
Decumbeside	Ajugavensin
Ajugavensin B	3β- Hydroxyajugavensin B
Ajugavensin C	3α-Hydroxyajugamerin
Ajureptoside C	Areptin B
22-Oxocyasterone	Ajugin
Ajugamacrin A	Ajugin A
22-Dehydro-12 Hydroxycyasterone	Ajugin
Ajugacumbin G	Ajugin
Deoxyajugarin-1	Ajugin D
Ajugarin-1 chlorohydrin	Cyasterone
Reptansterone	Withanolides
28-Epi-sengosterone	Neo-clerodane diterpenes)
Ajugavensin B	Ajugarin 1 -

Pharmacological Activities[41]

A. bracteosa has been evaluated exhaustively both in vitro and in vivo for diverse therapeutic claims. Previous studies explored that *Ajuga bracteosa* possessed numerous pharmacological activities due to its composition of secondary metabolite like diterpenoid, steroids and flavonoids etc. Studies on the therapeutic profile of these secondary metabolites focused on their immune system, anti-insect, anti-carcinogenic, anti-inflammatory, anti-arthritic, anti-malarial, and anti-carcinogenic properties

Antitumor/ anticancer/ antimutagenic activity: Cancer is still one of the world's deadliest conditions, and India is no exception. shops have long been crucial sources of effective anticancer drugs counting for further than 60 of all presently used anticancer medicines In this trial the author used the excrescence cell lines MCF-7 and Hep- 2. The methanol excerpt showed the maximum anticancer exertion rather than its petroleum ether and waterless excerpt. Whereas the traditional approaches support its decoction as anticancer eventuality .

The eventuality of the methanol excerpt is farther estimated for its antimutagenic exertion. In- vivo antimutagenic study was done in mice model convinced by Ethylmethanesulfonate. There are several composites were insulated and quantified by HPLC system. Among those, emulsion 14,15- dihydroajugapitin showed maximum reduction (85) of micronuclei followed by the emulsion β- Sitosterol and 8- O-acetylharpagide [42,43].

Antimalarial activity: Malaria is a dreadful complaint that's presently being treated and controlled by using a variety of shops. The appearance of germicide- resistant mosquito vectors and medicine- resistant spongers has made malaria control decreasingly gruelling. These are important way toward making herbal drugs more accessible and harmonious. The characterization of phytochemical substances lays the root for the creation of new ones. Ethanol splint excerpt inhibit content of sponger in blood in BALB/ c mice model and mean survival time is increased in cure dependent manner . piecemeal from these studies several other studies also reported for anti-parasitic exertion against Leishmania tropica. In the same study the author also reveals the maximum eventuality with n- hexane excerpt along with its insecticidal, anti-Alzheimer exertion[44,45].

Anti-inflammatory activity: Inflammation though it's part of the body's Défense medium but it includes a vast array of diseases and conditions that are characterized by inflammation including antipathetic response to autoimmune diseases or differently any visceral organ inflammation or indeed in case of graft rejection. 70 alcoholic extracts of Ajuga bracteosa showed anti-inflammatory exertion by the inhibition of Cyclooxygenase- I and Cyclooxygenase- 2. The finding proved the active phytoconstituents (lupulin A, ajugarin I, deoxyharpagide withaferin A, and reptoside) might be responsible for anti-inflammatory property. similar disquisition also supports the folk uses of Ajuga bracteosa for seditious complaint [45,46].

Analgesic activity: Significant and cure dependent analgesic exertion was estimated using the acetic acid convinced writhing inhibition and tail system on mice. The medium of action assumed to inhibition of lipoxygenase and/ or cyclooxygenase in peripheral tissue [47,48].

Cardioprotective activity: As per WHO cardiovascular conditions are getting critical issues leading to death). One cannot put cutlet in one reason. Cardiovascular complaint (CVD) is a class of conditions that associated with either heart or blood vessels or both. CVD includes coronary artery disease (angina, myocardial contravention), stroke, hypertensive heart complaint, cardiac myopathy, cardiac arrhythmia, congestive heart failure etc. The underpinning multiple mechanisms vary depending upon the state of the complaint. Atherosclerosis is one of the main reasons for coronary artery disease, stroke and supplemental *Ajuga bracteosa* This may be caused by hypertension, obesity, high blood cholesterol, diabetes etc. On the frog heart and rat ventricle, an alkaloid bit of *Ajuga bracteosa* demonstrated cardio goad exertion. The bioactivity was inhibited by dichloroisoprenaline which didn't do in reserpine- treated hearT. Report also supported the activation of mamas 1 receptor 20- hydroxy which may contribute to similar exertion. Antioxidant and anti-inflammatory & antihypertensive action of the medicine could also be a strong reason for cardioprotective exertion. Shaukat et al further confirm the antihypertensive efficacity which strengthens the cardio-defensive exertion of the factory[49,50,51].

Antioxidant activity: ROS assault and beget oxidative damage to a variety of biomolecules, including DNA. In habitual diseases similar as diabetes, cerebrovascular complaint, rheumatism, cancer, and cardiovascular complaint, this damage is critical. Current remedial procedures are known to beget acute vulnerable responses and cytotoxicity in normal cells. Antioxidants are necessary for the prevention of habitual diseases. Antioxidants are substances that help to help and minimize oxidation. Antioxidants can cover cells from free revolutionary- convinced oxidative damage. They're used to treat heart complaint, cancer, arteriosclerosis, cerebrovascular conditions, and other illness. A wide range of medicinal species contain antioxidant chemicals known for their free revolutionary scavenging capacities. Antioxidant exertion may be intermediated by phenolic composites. There's a strong relationship between antioxidant exertion and phenolic chemicals produced in plants. Antioxidants can scavenge reactive oxygen species and hence may be profitable in the prophylaxis and treatment of conditions similar as Alzheimer's complaint, stroke, diabetes, cancer, inflammation, and arteriosclerosis. The antioxidant exertion of *A. bracteosa* oil painting was set up to be 78 percent, which is advanced than ascorbic acid's strong antioxidant exertion. The antioxidant exertion of the canvases was assessed using the 2,2- Diphenyl-1-picrylhydrazl stable free revolutionary as a standard. Upstanding and root corridor of the factory was also reported for flavonoid and phenolic contents. Studies supported for its antioxidant exertion of methanol excerpt of the factory. The author also revealed the anti-inflammatory, analgesic, antidepressant and anticoagulant conditioning of the extract [53,54,55]

Antiarthritic activity: There are several studies that supported the relationship of total phenolics and total flavonoid with anti-arthritic, anti-inflammatory, antioxidant activity. The anti-arthritic effect of Ajuga bracteosa showed the inhibition of cyclooxygenase –I and cyclooxygenase-II. The isolated active compounds, 6-deoxyharpagide, withaferin A, lupulin A, reptoside, and ajugarin I, are responsible for antiarthritic effects. [56,57,58]

Others activity: Methanol extract of *A. bracteosa* also shows activity against Hepatitis C Virus.antibacterial, antihemolytic, cytotoxic, anticancer, and leishmanial activity. the synergistic antibacterial activity of the plant when formulated as Silver Nanoparticles[59]. The author supported the volatile oil constituents obtained from leaf as antimicrobial against Staphylococcus aureas, E. coli etc. The author also claimed the presence of Limonene, α-humulene, β-Myrcene, Elemol, Camphene, β-Caryophellene, αphellendrene[60] by gas chromatography might be act as antimicrobial. Kokab Hafeez et al reported α-glucosidase inhibitory activities of several nonpolar and polar extracts of A. bracteosa. The author postulated such α-glucosidase inhibitory activity may also useful as hypoglycemic agents in the management of postprandial hyperglycemia. [61]

Conclusion

A thorough review of the literature showed that *A. bracteosa* is a significant medicinal plant with a wide range of pharmacological effects. It is discovered that more research on the traditional Ayurvedic uses of plants by humans can help locate cutting-edge medications. Any one of the *A. bracteosa* plants is frequently employed in Ayurvedic medicine. A variety of components have been identified in crude extracts from different parts of the *A. bracteosa* have a variety of medicinal effects. Flavonoids, saponins, phenols, tannins, terpenoids, xanthoproteins, glycosides, and other compounds are among them. According to this review ethanol extract had the highest level of flavonoid concentration while chloroform-methanol extract had the highest level of radical scavenging ability. Its primary applications include hepatoprotective, antihypertensive, anticancer,

antidiarrheal, antioxidant, and antibacterial properties. This review paper provides details on the many pharmacological actions of *A. bracteosa.* Additionally, the plant is used to cure piles, constipation, and stomach ulcers. As a result, this plant plays a vital part in both illness treatment and prevention.

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