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Review Article

Aristolochia bracteolata: An Overview on Pharmacognostical, Phytochemical and Pharmacological Properties.

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ABSTRACT

Aristolochia bracteolata is a shrub distributed throughout India, belongs to the family Aristolochiaceae. A.bracteolata commonly called as Worm killer in English and Aadutheendaapaalai in Tamil. It is used in traditional medicines as a gastric stimulant and in the treatment of cancer, lung inflammation, dysentery and snakebites. In the indigenous system of medicine, the plant was used as purgative, antipyretic & anti-inflammatory agents. The root part has antifungal and antibacterial activity and was used to treat syphilis, gonorrhoea, and skin diseases and also used during labours to increase uterine contraction. Its leaves are bitter and antihelmintic, antiulcer, antiplasmodial and are medicinally important. Almost every part of the plant has medicinal usage. A.bracteolata is proved to have antioxidant property and insecticidal properties. The plant contain Aristolochic acid, has many medicinal properties in various disease condition. The Phytochemical screening revealed the presence of alkaloids, triterpenoids, steroids and sterols, flavonoids, tannins and phenolic compounds and cardio glycosides. The present review is an attempt to provide an up-to-date and detailed survey of literature of Pharmacognostical, ethno botanical and traditional uses as well as Phytochemical and Pharmacological reports on A. bracteolata.

KEYWORDS: Aristolochia bracteolata, Aristolochiaceae, Ethno botanical.

INTRODUCTION

Medicinal plants have been an integral part of life in various regional communities for food and drug both. India has more than 3,000 years of medicinal heritage based on medicinal plants. Medicinal plants are largely used by all divisions of the population either directly as folk medications or indirectly in the preparation of recent pharmaceuticals ^[1]. Numerous plants synthesize substances that are useful in the maintenance of health in humans and animals^[2]. Plants are used medicinally

in different countries and are a source of many potent and powerful drugs ^[3]. The use of medicinal plants to treat human diseases has its roots in pre historical times. Medicinal plants are used by 80% of the world population as the only medicines especially available in developing countries ^[4]. The information of medicinal plants have been accumulated in the course of several centuries based on various medicinal systems such as Ayurveda, Homeopathy, Naturopathy, Amchi, Modern, Siddha

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and Unani. In India, it is declared that traditional healers use 2500 plant species and 100 species of plants serve as natural principles of medicine^[5]. With a view to increasing the wide range of medicinal usages, the present day entails new drugs with more potent and desired activity with less or no side effects against particular disease^[6].

Aristolochia is an important genus in the family of Aristolochiaceae. The genus Aristolochia consists of about 400 species of herbaceous perennials, under shrubs or shrubs bearing essential oils and is widespread across tropical Asia, Africa and South America^[7]. Aristolochia species has been used extensively in the traditional Chinese medicine. Its diverse biological functions include hypertension relief, enhancement, leukocyte rheumatism relief, edema therapy, as well as analgesic and diuretic effects [8-11]. Various Aristolochia species have been used in herbal medicines since antiquity in obstetrics and in treatment of snakebite ^[12], festering wounds, and tumours, and they remain in use particularly in Chinese herbal medicine [13, 14]

Aristolochia bracteolata Linn. (Aaduthinnapalai – Tamil; Worm killer -English; Gadaparku - Telugu; Bhringi-

Hindi), is a shrub distributed throughout belongs India. It to the family Aristolochiaceae. In the indigenous system of medicine, the plant was used for the treatment of skin diseases, inflammation and purgative ^{[15,} ^{16]}. Root extract was reported to have anti bacterial activity [17] and also Toxicity of A. bracteolata was reported [18]

This species which had been shown to be nephrotoxic, mutagenic and carcinogenic due to the cytotoxicity of the Aristolochic acid constituents. The leaves of the plant which are used by native tribal and the villagers. It is commonly called as "worm killer" in English and aadutheendapaalai in Tamil, due to supposed antihelminthic activity and trypanocidal effect ^[20]. It is used in traditional medicines as a gastric stimulant and in the treatment of cancer, lung inflammation, dysentery and snakebites. Methanolic extract of plant parts of A. bracteolata were the source of physiological active compounds. The use of plant as an anti malarial is not recommended in its crude form ^[19]. The whole plant was used as a purgative, anti pyretic and anti inflammatory. It also possess a potent anti allergic activity ^[21] and has pronounced antibacterial and antifungal activities^[22].



Figure 1- Morphology of Aristolochia bracteolata

The present paper aims to review its ethno medical, Pharmacognostical, Phytochemical, Pharmacological actions

Ethno Botanical Survey ^[23]

Synonym: Aristolochia bracteata Scientific classification Kingdom: Plantae Order: Piperales Family: Aristolochiaceae Subfamily: Aristolochioideae Genus: Aristolochia Species:Bracteolata **Synonyms** English: Bracteated birthwort Gujarat: Midmari Hindi: Kitamari,Kalipaad, Hukka-bel Kanada: Kattackiru banagida Orissa: Paniri Sanskrit: Keetamari Dhoomrapatra, Nakuli, kitamari, visanika. Tamil: Aaduthinnapalai, atutinnapalai. Telugu: Gadida gadapa, gadidhagadapaaku, kadapara, Thella esshvari. Marathi:Gandhari,Gindhaan

Ethno pharmacology Traditional uses:

The uses of different parts of *Aristolochia bracteolata* in traditional system of medicine (Table 1).

Plant parts	Traditional uses as/in
Whole plant	Dermatitis, allergic disorder, leprosy, jaundice ^[24] ,
	worms, fever ^[25] ,
	Mosquito repellent ^[26] ,
	Anodyne, purgative, emmenagogue ^[27, 28] .
Leaves	Anti-inflammatory ^[29] ,
	dermatitis, rashes ^[25] ,
	skin disease, for scorpion sting ^[25] ,
	Antipyretic, snake bite ^[30] ,
	Antiulcer, amenorrhoea, antihelmintic ^[5] ,
	Antiplasmodial ^[31,32]
Seeds	Antibacterial, anti inflammatory and analgesics, may toxic to goats ^[33,17]
Roots	Syphilis, gonorrhoea & skin diseases, eczema ^[5] .

Table 1. Ethnomedical uses of different parts of A. bracteolate

Macroscopy and Microscopy^[23]

Macroscopic description: Leaf, reniform, cordate or rounded, 3.8-7.5 cm long and as broad as long, obtuse, cordate at the base with a wide shallow sinus, entire, finely reticulately veined, tubescent beneath, glabrous above; petiole cylindrical, slightly grooved on upper surface 1.2-3.1cm long (Figure.1). It has bitter taste with characteristic odour. Fruits are oblong or ellipsoid capsules and seeds compressed with cordate base.

Microscopy: Transverse section of leaf passing through midrib is strongly convex below, slightly elevated above, conjoint, shows a collateral and meristele embedded in its parenchymatous ground tissue located at the basal region of the two laminar extensions; 5-6 rows of collenchymas lie under the upper epidermis, it being 2-3 in rows at lower side. Lamina dorsi ventral, shows a layer of palisade under the upper epidermis and 5-6 rows of spongy parenchyma traversed with

obliquely cut vascular bundles both the epidermis are covered with this cuticle,

traversed with stomata and bear simple, uniseriate, covering trichomes characterized by a straight or hook shaped terminal cell resting on a short rectangular cell with a balloon like extension.

Nodal Anatomy ^[34]: N.C.Nair *et al.*, has reported that in *A. bracteolata* the vascular system of the axis immediately below the node consists of nine large, widely separated collateral bundles. All of them enter the lamina to display the palmate venation characteristic. The leaves in *A.bracteolata* are cordate and they are palmately veined. The stomata are present only on the surface and they are of the Ranunculaceous type ^[35].

Anatomy of reproductive shoot: It was found that the inflorescence is one or two flowered and secondary peduncle does not develop in *A.Bracteolata*. The single flower has a bract on the posterior side and is sessile, large, leafy and subreniform. The margins of the limb are revolute. Prominent multicellular hairs are present on the inner surface of perianth. They are very small in inflated region becoming larger towards the tip of the perianth. The tapetum is binucleate and glandular. When it disorganises globular oily depositions have been observed in *A.bracteolata*. The peduncle shows a ring of 8 in *A.bracteolata*.

In *A.bracteolata* the median gap shows two separate vascular strands at the nodal level and these at lower levels are related to two independent systems of vascular strands. This feature can be regarded as evidence against the telometheory as applied to the angiosperm leaf^[36].

Description of pollen type^[37]:

Aristolochia bracteolata has non aperture pollen with spheroidal shape. It has sexine thiner than nexine *A.bracteolata* tectum is rugulatefossulate or densely regulate and pollen diameter is 46-61 µm.

Phytochemistry

The Phytochemical screening revealed the presence of alkaloids, triterpenoids, steroids and sterols, flavonoids, saponin, Phytosterols, carbohydrates, proteins, phenolic compounds and cardio glycosides ^[19, 39].

Vaghasiya *et al.*, carried out the analysis of phytoconstituent of A.bracteata in different extracts. The total phenolics content in the methanolic extract and acetone extract was found to be $59.22 \pm 0.65 \& 39.67 \pm 0.92$ respectively, were as the total content of flavonoids were $36.06 \pm 0.17 \& 130.93 \pm 2.58$ in the methanolic and acetone extract respectively^[40].

Pharmacological activity of A. bracteolata

1. Anti Pyretic Activity: Pet. ether and acetone extracts of *A. bracteolata* was investigated for their anti pyretic activity

Pet ether and acetone extracts of the plant *A. bracteolata* were prepared using Soxhlet extraction. Pyrexia produced in rats by injecting 20ml/kg (s.c) of 20% aqueous suspension of brewer's yeast suspension. Extracts at 250 mg/kg exhibited significant anti pyretic activity. Aspirin (300mg/kg) was used as standard for which Pet. Ether extracts was found to be more effective than acetone extract ^[41].

2. Anti allergic activity: Antiallergic activity of A. bracteolata was evaluated by using compound 48/80 induced anaphylaxis, dermatitis rhinitis and pruritis, as a preclinical model for acute phase of hypersensitivity reactions. The hypersensitivity phase late was evidenced by considering toluidine induced volume diisocynate of bronchoalveolar fluid secretion and its inhibition. The possible antiallergic mechanism was evaluated by using compound 48/80 induced mast cell activation and estimated serum nitric oxide (NO), rat peritoneal fluid NO, bronchoalveolar fluid NO and blood histamine levels. It has been reported that the chloroform extract of A. bracteolata had potent and significant inhibitory effect on compound 48/80 induced pruritis and dermatitis activity in Swiss albino mice. It showed significant effect in toluidine diisocvnate induced rhinitis in Swiss albino mice. membrane stabilization Mast cell activity was also observed in compound 48/80 induced mast cell activation. A significant reduction was observed in serum nitrate levels, rat peritoneal fluid nitrate levels and BAL nitrate levels. The extract was also found to posses' significant inhibitory effect on blood histamine levels. It could be concluded that the chloroform extract posses potent antiallergic activity, possibly through

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mast cell membrane stabilization, inhibiting NO and histamine pathway [21].

3. Anti-inflammatory activity: The ethanollic extract of the shade dried leaves of A. bracteolata was evaluated anti inflammatory activities in wistar rats by using the carrageeenan induced left hind paw edema method. Significant reduction of edema volume was observed in the drug treated group when compared with the standard and un treated control. Antioxidant investigation of the ethanol extract along with its two successive fractions using nitric oxide and 1,1-diphenyl-2 picryl hydrazyl (DPPH)-induced free radical assay methods showed good free radical scavenging activity, thereby supporting its anti inflammatory properties^[42].

4. Anti-arthritis Activity: Anti arthritic activity was demonstrated using Freund's complete adjuvant in rats. The results shows that, regular treatment of adjuvant induced arthritic rats with A. bracteolata extracts improves ESR, Hb value and also restores body weight. Significant (P<0.01) inhibitory effect was observed with A. bracteolata extract on Freund's complete adjuvant induced paw edema throughout the study (P<0.001). The latency to thermal stimuli and inhibitory effect on xylene induced ear edema was significantly (P < 0.05) affected by oral treatment of A. bracteolata, irrespective of solvent used for extraction. Treatment of FCA induced rats with A. bracteolata extracts shown (P<0.05) increase in pain weight bearing threshold. ability. ambulation and also decline in scratching, defecation and urination, were observed as a sign of improvement in behavioural condition^[43].

5. Antiulcer Activity: The aqueous extract of leaves of *A. bracteolata*

exhibited antiulcer activity in rats. The antiulcer activity of *A. bracteolata* was evaluated against ethanol induced and pylorus ligation induced models, at two different dose levels of 400 and 800 mg/kg/body wt/day. The activity was compared with standard drug Ranitidine. Pre-treatment with the extract resulted in a significant decrease of the ulcerated area. The volume and acidity of the gastric juice decreased in the pre-treated rats. Among the two dose assessed, 800 mg/kg was found to have the significant activity than the lower dose^[44].

Antibacterial 6. **Activity:** Α. bracteolata leaves were subjected to antibacterial activity on disc diffusion against bacillus subtilus. method lactobacillus plantarum, Escherichia staphylococcus coli. aureus. streptococcus faecalis and pseudomonas aeruginosa. The leaves of Aristolochia bracteolata Retz were extracted with petroleum ether, chloroform and alcohol. Alcoholic extract showed significant antibacterial activity as compared to that of other extracts ^[45].

Negi PS et al investigated the antibacterial activity of Aristolochia bracteolata root extracts. Powdered Roots of A. bracteolata were extracted with ethyl acetate, acetone, methanol, and water for 8 hours each using a Soxhlet extractor. Antibacterial activity of dried ex- tracts was evaluated by the pour-plate method against a few Grampositive and Gram-negative bacteria. All the crude extracts showed a broad spectrum of antibacterial activity among which ethyl acetate extract was found to be the most effective. This study shows the potential for replacement of synthetic preservatives by the use of natural extracts^[46]

According to another study ^[22], the different extracts (Aqueous,

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methanol and chloroform) of this plant were effective against the bacterial strains Escherichia coli, Bacillus subtilis, Staphylococcus aureus. Klebsiella pneumoniae, Pseudomonas fluorescens, Shigella flexneri, Proteus vulgaris and the fungal strains like Aspergillus Niger, Aspergillus terreus, Penicillium notatum and Rhizopus stolonifer. Among the three extracts, methanol extract was found to have the significant activity followed by the chloroform extract against certain bacteria. Water extract did not have any activity against bacteria. Antifungal activity assessment indicated that the tested fungal strains are more susceptible to aqueous extract followed by methanol extract and chloroform extract.

7. Antifungal Activity: the ethanolic extracts of *A. bracteolata* was studied Antifungal activity using disc diffusion method and was found to have highest activity at minimum concentration. The study justify that the bioactive principles present in the extracts may be responsible in the treatment of ringworm infection. It was reported that Ethanolic extract effective against *Trichiophyton rubrum* and *Microsporum canis*^[47].

8. Antiplasmodial activity: Invitro antiplasmodial activity against Plasmodium falciparum 3D7 (chloroquine sensitive) Dd2 and (chloroquine resistant and pyrimethamine sensitive) investigated was bv Ramasubramania raja R et al. It was found that extract of A.bracteolata exerted activity on P. falciparum strain 3D7 with an IC₅₀ less than $5 \mu g/mL$. Phytochemical analysis indicated that the most active phase contained terpenoids and tannins and was devoid of alkaloids and saponins. The effect of plant extracts on lymphocyte proliferation showed low toxicity to the human cells^[31].

Another studies ^[32], shows that the plant extract of A.bracteolata has potent antimalarial activity(*in vitro*) against schizonts maturation of Plasmodium falciparum, the major human malaria parasite. The whole plant extracts of Aristolochia bracteolata produced 100% inhibition of the parasite growth at concentration $\leq 50 \ \mu g/ml.$ The two most active plants showed the presence of sterols, alkaloids and tannins.

10. Antioxidant properties: Α. bracteolata Retz was investigated antioxidant 2. 2-diphenyl and picrylhydrazyl (DPPH) radical scavenging activities, reducing powers, and the amount of total phenolic compounds of the extracts were studied [48]

The antioxidant activity was determined by ammonium thiocyanate assay ^[51]. 2, 2-Diphenyl picrylhydrazyl (DPPH) free radicals scavenging activity was assessed according to Blois (1958) ^[52], with a slight weight modification. Absorbance was measured at 700 nm. Ascorbic acid solution was used for comparison. Increased absorbance of the reaction mixture indicated increased reducing power.

The antioxidative effect is mainly due to phenolic components, such as phenolic acids, and phenolic diterpenes ^[49]. The antioxidant activity of phenolic compounds is mainly due to their redox properties, which can play an important role in absorbing and neutralizing free radicals, quenching singlet and triplet oxygen, or decomposing peroxides ^[50].

11. Antimicrobial Activity: The antimicrobial activity of *A.bracteolata* was investigated by Parekh *et al.* The antimicrobial assay was done by both the agar disc and agar well diffusion method against six medically important

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microorganisms viz. Bacillus subtilis, Staphylococcus subfava, Alcaligenes fecalis, Proteus mirabilis, P. aeruginosa and Candida tropicalis. According to the study, the methanol extract was found to be more effective than the aqueous extract^[53].

It has been found that the aristolochic acid from the root of Aristolochia bracteolata posses significant antimicrobial activity. Aristolochic acid I was isolated from the methanolic & ethyl extract extracts of Aristolochia bracteolata and conformed through IR, NMR & MS. The percentage purity of aristolochic acid I was determined by UV & HPLC method. Antibacterial activity of extracts of A. bracteolata and the isolated compound was determined by disc diffusion method. Microbial assay of isolated compound (Aristolochic acid I) from ethyl acetate & ethanol extracts were shown good antimicrobial activity and the zone of inhibition of both at higher concentration 50ug/ml was similar with the standard aristolochic acid^[54].

12. Wound healing activity: The ethno botanical knowledge base for treatment of cuts and wounds which includes a usage of plants/plant extracts/decoctions or pastes, methods employed by tribals and folklore practices prevailing in India have been analysed ^[55].

The ethanol extract of the leaves of *Aristolochia bracteolata Lam.* was studied for its effect on wound healing in rats, using incision, excision and deadspace wound models, at two different dose levels of 400 and 800 mg/kg/body wt /day. The plant showed a definite, positive effect on wound healing, with a significant increase of the level of two powerful antioxidant enzymes, super oxide dismutase and catalase, in the granuloma tissue^[56].

13. Anti angiogenetic activity: petroleum ether extract of Aristolochia bracteolata Lam (Aristolochiaceae) roots was screened for the activity against cutaneous melanoma using Chicken Chorioallantoic Membrane (CAM) Assav has been studied. Angiogenesis and melanoma cell survival were visualized and recorded using dissecting microscope and imaging system. Concentrations of the extracts ranging from 10mg to 50mg were screened. Chemical tests of the extract revealed the presence of alkaloids, triterpenes and steroids. It was observed that 30mg dose notably reduced the proliferation of blood vessels and reduced survival rate of melanoma cells in CAM. Cultured melanoma cell lines were obtained from cancer research centre, Hyderabad.

It was concluded that the root extract of *Aristolochia bracteolata* possess inhibitory effect on proliferation of melanoma cells and its topical application may be more advantageous to treat cutaneous melanoma, since topical treatments have advantages for rapid, effective and natural healing of cancers targeting the cancer site with much higher doses than could ever be achieved with oral treatments alone ^[57].

14. Trypansocidal effect: Aristolochia bracteolata was evaluated for its in vivo activity against trypanosome evansi infection in the rats. Six groups of 10 rats each aged 5-7 weeks, average weight 150grams were used. Both the chloroformic and methanolic extract of the plant extract was administered orally at dose rates of 250 and 500mg/kgBW. activity was compared The to cymelarsan which was given at a dose rate of 2.5mg/kg BW subcutaneously.

Results showed that plant extract gave a promising trypansocidal effect. The chloroformic extract gave better result than that of the methanolic extract with both doses ^[20].

15. Anti implantation & Abortifaciant activity: Ethyl acetate soluble fraction of the ethanolic extract of Aristolochia bracteolata was tested for precoital & postcoital anti implantation test & abortifacient activities in female albino rats. In the precoital study, the treatment at 20 & 40 mg/kg body weight showed significant & dose related anti implantation & abortifaciant properties. In the post coital study of 20, 30 & 40 mg/kg body weight doses similar results were observed. The total anti fertility activity of 40 mg/kg body weight was found to be comparable to the standard ethinyl oestradiol given for the similar period^[58].

Toxicity and Side Effects:

In goats: Diarrhea, dyspnea, tympany, arching of the back, loss of condition, and loss of hair from the back were the prominent signs when Aristolochia bracteolata was given orally to goats. The main lesions were hemorrhages in the lungs, heart, and kidneys, fatty change and congestion in the liver. mucoid abomasitis and enteritis and straw-colored fluid in serous cavities. An increase in aspartate aminotransferase activity, ammonia and urea concentradecrease and in tions а the concentrations of total protein and magnesium were detected in the serum

Rats: Swiss albino rats were used to study the toxicological effect of methanolic and chlorformic extract of *Aristolochia bracteolata*. Methanolic and chloroformic extracts were given at doses of 250 and 500 mg/kg BW to Swiss albino rats. Oral administration of the extract caused symptoms such as depression, arching of the back and tremors. Serum analysis indicated increase in the activity of Aspartate aminotransferease (AST), Alanine amino (ALT) transferase and alkaline phosphatase (ALP). The concentration of urea, creatinine, and ammonia were also increased and the concentration of total protein decreased. The main lesions found were haemorrhage in the kidney and congestion of the liver. It has been reported that chloroformic extract at the rate of 500 mg/kg was more toxic than all the treatments ^[60]

In chicks: A.bracteolata is used in Sudanese folkloric medicine for the improvement of health by increasing body weight and treatment of various disorders. bovans-type chicks were fed 10% A.bracteolata seed and 5% mixture A.bracteolata and Astragalus of gummifer of standard diet for two weeks. The given concentration mixture of the plants were toxic but not lethal to chicks and caused reduced body weight gain. was observed in te Mild diarrhoea chicks on the 5% mixture of two plants. Alteration of serum AST and ALT activities and total protein, albumin, globulin, cholesterol and uric acid were correlated with changes in haematology and pathological effects on vital organs [61]

CONCLUSION

Medicinal plants have been used as an exemplary source for centuries as an alternative remedy for treating human disease because they contain numerous active constituents of therapeutics value. In recent years, ethnobotanical and traditional uses of natural compounds especially of plant origin received much attention as generally believed to be safe for human use. Through screening of literature available on *A.Bracteata*

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depicted the fact that it is a popular remedy among the various ethnic groups. It is interesting to note that crude extract and aqueous extracts of root and leaf of A.bracteata have been screened for some pharmacological activities and anti-angeogenic, analgesic, antiinflammatory antioxidant, and antibacterial. antiplasmodial, antimicrobial activity and trypansocidal activity. Presently there is an increasing interest worldwide in herbal medicines accompanied by increased laboratory investigation into the pharmacological properties of the bioactive ingredients and their ability to treat various diseases. In future study the isolated principle needs to be evaluated in scientifically animal model and clinical trial to understand the molecular mechanism of action, in search of lead molecules from natural resources. As the global scenario is now changing towards the use of nontoxic plant product having traditional medicine use, development of modern drug from A.bracteolata should be emphasized for the control of various diseases.

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