PHARMACOLOGY AND MEDICOBOTANY OF ARISTOLOCHIA TAGALA
CHAM: A REVIEW
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ABSTRACT
Aristolochia tagala is a traditionally important and rare medicinal plant used in fever, stomachache, bilious disorders, swollen limbs, infantile tympanites, menstruation problem, rheumatoid pain, tumour and snake and poisonous bites. The plant is used as tonic, carminative and emmenagogue. Pharmacologically different parts of the plant act as antimicrobial, antiproliferative, cytotoxic, analgesic, antioxidant, antifertility, insecticidal and nephrotoxic agent. This review deals with a compilation of different reports on A. tagala incorporating reports on its distribution, morphotaxonomy, pharmacology, phytochemistry, tissue culture, chromosome study, ethnomedicobotany and plant-insect interaction.

Keywords: Aristolochia tagala, Pharmacology, Phytochemistry, Ethnomedicobotany, Review.

INTRODUCTION
Aristolochia tagala (Aristolochiaceae), a member of the bitter and poisonous Aristolochias is a rare medicinal herb reported to be used against snakebites and bowel complaints¹. The plant is commonly known as Oval leaf Dutchman’s pipe² and is distributed in the northeast and southern parts of India, China, South-East Asian countries and Australia. The major negative aspect of some of the aristolochic acids found in the members of Aristolochiaceae is nephro- toxicity which restricts its use³,². A significant amount of research have been reported involving different species of Aristolochia viz. A. indica⁴, A. elegans⁵, A. cucurbittifolia⁶, A. pubescens⁷, A. anguicida⁸, A. cymbifera⁹, A. chamissonis¹⁰, A. fimbriata¹¹, A. paucinervis¹², A. bracteolata¹³ etc.

This review compiles different aspect of the plant species emphasizing on its pharmacological and ethnomedicobotanical aspects.

Distribution:
Aristolochia contains many species from warm temperate to tropical regions throughout the world\cite{14}. *A. tagala* is distributed from India to Papua New Guinea\cite{15}. The plant is present in India, Sri Lanka, China, Malaysia, Burma, Java and Australia\cite{16}. The species was mentioned as an important member of rich biodiversity of Northeast India region\cite{17}. The plant is reported to be grown in the lower watershed zone of Naujan Lake National Park, Mindoro Oriental Province, Philippines\cite{18}. The species has been reported from Bangladesh\cite{19}. This glabrous climber was reported from Ramgarh Upazila of Khagrachhari District\cite{20} and Lawachara National Park, Bangladesh\cite{21}. In Peninsular Malaysia *A. tagala* is one of the five Aristolochiaceae species found. All of them have a very narrow distribution range except *A. tagala* which is widespread\cite{22}. The plant was conserved *ex-situ* at University of Agricultural Sciences, Bangalore, Karnataka\cite{23}. This 20m long twining climber was found at lowland forest of Pulau Tioman, Peninsular Malaysia\cite{24}. The species represents among the 850 species of medicinal plants found in Meghalaya, India\cite{25}. The plant was reported in tropical forests of southern Eastern Ghats, Tamil Nadu, peninsular India\cite{26}. It was reported from Thailand also\cite{27}.

**Conservation status:**

The plant has become rare due to indiscriminate harvesting\cite{28,16}. VU/R (Vulnerable/Rare) status was assigned to the species in a Red Data List of South Indian medicinal plants\cite{29}. Scanty endosperm restricts the seed viability of the species. Deforestation, *jhum* cultivation and over exploitation are the major causes of disappearance of this medicinal plant\cite{30}.

**Morphology and Taxonomy:**

The species is a climbing shrub\cite{16}. Diverse floral forms from radial to monosymmetric and a wide variety of insect pollinators are the characteristic features of the family\cite{31,11}. Flowers of *A. tagala* are produced in axillary cymes and are distinctly stalked, bisexual, zygomorphic having inferior ovary. Pollination biology, floral phenology and breeding system of the plant conserved *ex-situ* were reported. A Dipterean Chironomid fly was found to be the pollinator of *A. tagala*\cite{16}. Phylogeny of Aristolochiaceae on the basis of parsimony and likelihood was reported. Bayesian analyses of plastid *trn*L*-F* sequences was done to resolve position of Aristolochiaceae in Piperales\cite{32}. Molecular phylogeny of *Aristolochia sensu lato*
(aristolochiaceae) based on \( rbcL, \ matK, \) and \( phyA \) gene sequences and chromosome numbers have been discussed to clear the ambiguity and controversy of \textit{Aristolochia} classification. According to the authors \textit{A. tagala} was included in \textit{Aristolochia} L. subgenus \textit{Aristolochia}\textsuperscript{[14]}. Classification of \textit{Aristolochia} species on the basis of GC–MS and chemometric analyses of essential oils has been reported\textsuperscript{[31]}. Metabolic profiling by combined GC-MS and LC-MS involving aristolochic acid has been performed\textsuperscript{[34]}. The plant was mentioned in a cladistic analysis of \textit{Asarum} and was treated as an outgroup taxon\textsuperscript{[35]}. All members of Aristolochiaceae have anatropous, bitegmic, crassinucellate endostome ovules with a few exceptions\textsuperscript{[36]}. Identity of \textit{A. acuminata} Lam. and \textit{A. tagala} Cham. was discussed\textsuperscript{[37]}. 

**Pharmacology:**

Pharmacognostical studies on the root of \textit{A. tagala} were performed\textsuperscript{[11]}. Extract of leaves of the plant collected from Western Ghats, India was assayed \textit{in vitro} by microtitre-plate resazurin reduction method against 4 bacterial strains namely \textit{Staphylococcus aureus}, \textit{Pseudomonos aeruginosa}, \textit{Bascillus subtilis} and \textit{Escherischia coli} indicated no antibacterial activity\textsuperscript{[38]}. Petroleum ether, Chloroform and Ethyl acetate extracts of the plant collected from Coimbatore, India were tested for antioxidant properties. Ammonium thiocyanate assay, DPPH (\( \alpha,\alpha^-\)-Diphenyl-\( \beta\)-picryl-hydrazyl) radical scavenging activity, reducing power activity and total poly phenols were measured during the experiments\textsuperscript{[39]}. Anticancer efficacy of the plant taken from Western Ghats, India was assayed. Leaf and stem extracts were screened for antiproliferative activity by MTT assay and cytotoxic activity by Clonogenic assay\textsuperscript{[40]}. Potential of \textit{A. tagala} in dermatology was noted\textsuperscript{[41]}. Analgesic and antimicrobial activity of the dried leaves' extracts of the plant were reported\textsuperscript{[42]}.

Chronic interstitial nephropathies in Indians were mentioned to be associated with \textit{Aristolochia} sp.\textsuperscript{[43]}. This species was treated among known or suspected botanicals to contain aristolochic acid\textsuperscript{[2]}. Aristolochic acid was isolated from \textit{A. tagala} and its toxicity was tested\textsuperscript{[44]}.

Antifertility activity of \textit{A. tagala} leaf extracted in ethanol in female Wister rats was reported when administered orally. Treated rats showed decreased number of corpora
lutea and implantation sites. The plant extract was found to be an abortifacient also\[45\]. Anti-fertility activity of the dried leaves extracts was also found\[46\].

Morphogenetic effects and antifeedant properties of *A. tagala* have been recorded\[47\]. The plant species from Philippines was found to have anti insecticidal property against the diamondback moth (DBM) *Plutella xylostella* L (Lepidoptera: Yponomeutidae), an important insect pest of crucifers throughout Southeast Asia\[48\]. The species was found to have repellant and antifeedant activities against the common cutworm, *Spodoptera litura* (Fabr.). (Lepidoptera: Noctuidae) Pronounced effects in the larval, pupal, and adult stages were noted\[49\]. Asiatic corn borer, *Ostrinia furnacalis* (Guenée) was also affected by the plant’s crude extracts\[50\]. *A. tagala* extracts on the diamond-back moth *Plutella xylostella* (L.) was reported to be toxic\[51\]. Bioefficacy of leaf and root extracts the plant was tested against *Spodoptera litura* Fab. 5.0% ethyl acetate leaf extract has showed antifeedant activity, lethal concentration for feeding inhibition, larvicidal, pupicidal, total mortality and prolonged larval–pupal duration\[52\].

**Phytochemistry:**

Chemical constituents of *A. tagala* were reported\[53\]. As contents of total aristolochic acids in the roots and rhizomes of different *Aristolochia* species vary greatly, the morphological and histological differences of different species including *A. tagala* were elucidated\[54\]. Poly cis-prenols of 10, 11 and 12 chain length was found in the plant collected from north and central Vietnam\[55\]. *Krai-krue*, a crude drug commonly used in Thai traditional herbal medicine was analyzed to explore its botanical identity. Two *Aristolochia* species were compared namely *A. pierrei* Lec. and *A. tagala*. Morphology, histology and TLC (Thin Layer Chromatography) data supported the drug to be *A. pierrei*\[56\].

**Tissue culture:**

*In vitro* regeneration of the plant by direct organogenesis was reported. BAP (6-Benzylaminopurine) among cytokinins was found to be most effective for induction of shoots at a concentration of 3.0 mg/l. Multiplication of axillary buds was found to be most suitable in a combination of BAP and NAA (1-naphthaleneacetic acid). As the number of subculture increased, the number of shoot per culture was found to be increased. MS (Murashige and Skoog) medium supplemented with 0.5 mg/l IBA (Indole-
3-butyric acid) was found to be the most effective for rooting\cite{30}. Best multiple shoot organogenesis was observed on 1.0 mg/l BAP supplemented MS medium. MS medium containing IBA at 3.0 mg/l showed maximum rooting response\cite{57}.

**Chromosome study:**

2n=12\sup{58,14}.

**Medicobotany:**

The plant was reported to be among the folk plants for the treatment of snakebites in Southern part of Tamilnadu, India\sup{59}. Ethno-medico-botanical studies of Ayurvedic drug Valiya arayan (A. tagala) was reported by indigenous groups Kani\sup{60}. Flower decoction is taken to in menstrual disorders by the Kani in Agasthiyamalai Biosphere Reserve, South India\sup{61}. The plant is reported to be used by the Khasis (Hynniew Treps) of Meghalaya, India\sup{62}. The plant species along with some other plants is used against poisonous bites by the tribes of Tirunelveli hills, Tamil Nadu\sup{63}. Leaves, fruits, roots, juice and paste are said to be used in fever, dysentery, snakebite and malaria by the tribes of Chittagong Hill tracts, Bangladesh. Root decoction is used as tonic, carminative and emmenagogue\sup{64}. Abdominal pain, rheumatic pain and tumour are treated with different preparations of the plant by the Chakma tribe in Hill tracts districts of Bangladesh\sup{65}. Fresh grounded leaves and roots are used in stomachache and poisonous bites respectively by the Kurichyas, Kannur district, Western Ghats, Kerala\sup{66}. The plant was mentioned in a report on Medico-botany of Andaman and Nicobar Islands\sup{67}. Irula tribes of Chengal Combai, the Nilgiris, Tamilnadu, India use the plant\sup{68}. Malaywali tribals of Kollihills of Tamil Nadu, India have been found to use it\sup{69}. In Indonesia, the plant is used in swollen limbs and bilious disorders. In Malaysia, it is used in fever. In the Philippines, the species is used in infantile tympanites and to promote digestion and menses\sup{15}.

**Insect Plant interaction:**

Cecidomyii induced gall on A. tagala was reported\sup{70}. Biology of Pachliopta aristolochiae aristolochiae on its host plant A. tagala was also studied\sup{71}. A. tagala and A. schlechteri (natural host) were compared in terms of duration of different stages of Ornithoptera alexandrae of Rhopalocera\sup{72}. Sequestration of Aristolochic acid from A.
tagala by the insect *Troides helena* was undetected\(^7^{33}\) although in some other reports the species was found to contain aristolochic acid\(^7^{44}\).

**CONCLUSION**

Due to indiscriminate use of the roots and presence of scanty endosperm, the species has become rare in natural habitat. Alternative propagation techniques can be used to save the rare medicinal plant from extinction. The plant is a natural host of different insects. Sequestration of Aristolochic acid and other metabolites can be an exciting aspect of research. The plant was found to have a significant role in traditional medicine especially in South India. Like other aristolochias, this species is prescribed in snake and other poisonous bites by the tribal people. Anti snake venom efficacy of the species must be exploited carefully due to the presence of aristolochic acid which is a potent nephrotoxic agent. Therefore its widespread ethnic use should be restricted. Pharmacological investigations carried out in the plant makes it antimicrobial, antiproliferative, cytotoxic, analgesic, antioxidant, antifertility, insecticidal and nephrotoxic agent. The species can be used as an alternative to chemical insecticides. The antifertility effect can be exploited to develop herbal contraceptives which might prove useful to control population especially in the third world countries. Reports on phytochemical investigations of this species are rare. Modern analytical methods like HPLC (High Performance Liquid Chromatography), HPTLC (High Performance Thin Layer Chromatography), NMR (Nuclear Magnetic Resonance) etc. can be applied for qualitative and quantitative estimation of its active constituents. Pharmacological investigations carried out the rare medicinal plant species must be extended further to clinical trial to generate standard drugs.

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