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ARISTOLOCHIA INDICA: ANTI-VENOM POTENTIAL, PHYTOCHEMISTRY, PHARMACOLOGICAL ACTIVITIES – A REVIEW

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ABSTRACT

Aristolochia indica (family Aristolochiaceae) has a long ethnomedicinal history in South Asia, where traditional healers use root and whole-plant preparations for treating snakebite, inflammation, and wounds. Modern preclinical investigations reveal that extracts—especially methanolic and ethyl-acetate fractions—can inhibit venom-associated enzymes (phospholipase A_2, proteases, hyaluronidase, L-amino acid oxidase), reduce local tissue necrosis, edema and hemorrhage, and increase survival in animal models. The aristolochic acids and related phenanthrene alkaloids are frequently implicated in these bioactivities. However, aristolochic acids are also strongly nephrotoxic and carcinogenic, causing Aristolochic Acid Nephropathy (AAN) and urothelial malignancies.[1] This dichotomy limits clinical translation but motivates targeted research: bioassay-guided fractionation to identify AA-free venom-neutralizing moieties, advanced extraction and detoxification strategies, and formulation approaches (local/topical delivery) to minimize systemic exposure. This article synthesizes traditional knowledge, a comprehensive phytochemical profile, all reported pharmacological activities (ancient and modern), advanced extraction techniques, detailed toxicity data, the clinical evidence status, and practical recommendations for future research and safe translational pathways.[2]

KEYWORDS: Aristolochia indica, snake bite, aristolochic acid nephropathy.

INTRODUCTION

Snakebite envenoming remains a major public health problem in tropical and subtropical regions, causing substantial morbidity and mortality—particularly in rural India where agricultural workers are at high risk. Conventional polyvalent antivenoms are lifesaving for systemic toxicity but often poorly neutralize local tissue damage (necrosis, hemorrhage) and are costly and logistically challenging in remote settings. Ethnobotanical traditions across India and Southeast Asia have therefore long used medicinal plants to treat bites; among these, Aristolochia indica (local names include ishwarmul, garudakkodi) is frequently cited.[3] Traditional practitioners apply fresh root paste topically to bite sites or administer decoctions for systemic symptoms. Driven by these practices, laboratory studies have examined A. indica's capacity to neutralize venom components. A growing body of in vitro and in vivo evidence indicates that extracts can inhibit major venom enzymes—phospholipase A_2 (PLA_2), metalloproteases, hyaluronidase—and can ameliorate local hemorrhage, edema and myonecrosis in animal models. But the plant's principal active chemical family—aristolochic acids—poses serious safety concerns: they form DNA adducts leading to urothelial carcinomas and induce progressive, often irreversible nephropathy. Because of this, regulatory bodies have restricted Aristolochia use and warn against internal consumption. Thus, while A. indica is a scientifically promising source for antivenom leads, progress requires isolating non-toxic constituents or rendering active scaffolds safe. This article provides a complete, evidence-based overview to guide researchers seeking to develop safer antivenom interventions inspired by A. indica.[4]

Botanical Description

- Habit: perennial twining creeper.
- Stems: Woody, greenish-white, and slender, becoming woody at the base.
- Leaves: Alternate, obovate-oblong to somewhat cordate, with an entire but sometimes undulate margin. They are glabrous (smooth) and 3-5-nerved at the base.
- Flowers: unique, one-lipped, tubular blooms that are typically greenish-white or purplish.
- Inflorescence: Axillary cymes or fascicles, with few-flowered axillary racemes.
- Perianth: Greenish-white to light purplish, with a funnel-shaped tube and a dilated, 1-2- lipped limb that is hairy inside.
- Scent: Usually foetid.[5]
- Stamens: Six in number, adnate (fused to the style), with filaments indistinguishable from the style.
- Pistil: The ovary is six-locular with two ovules per locule.
- Fruit: A capsule that is globose-pyriform, 1.5-3 cm in size, six-valved, and dehisces from the base upwards.
- Seeds: Numerous, flat, winged, and broadly deltoid.
- Root: Long, woody, and brown in colour young roots are smooth, while older ones are rough and cork-like.

unique, one-lipped, tubular blooms that are typically greenish-white or purplish.[6]

- Botanical Name: aristolochia indica L.
- Common Names: Indian birthwort, Ishwarmul (Sanskrit, Hindi), eesvaramulli (Tamil), Sapsada (Southern India and Sri Lanka).
- Family: Aristolochia indica belongs to the family Aristolochiaceae.

Chemical Constituents

- Aristolochic Acids (AAs): The primary active constituents, notably aristolochic acid I and II, which are known to be nephrotoxic and carcinogenic.
- Aristolactams: Phenanthrene derivatives, such as Aristololactam I and IIa, which are considered intermediates in the biosynthesis of aristolochic acid
- Steroids, terpenoids: alkaloids, flavonoids, lignans, tannins, glycosides, essential oils. Etc.[7]

Traditional Uses

- Snakebite: Fresh root paste applied topically to bite wounds; decoctions used orally in some communities to reduce swelling and pain.
- Anti-inflammatory and analgesic: Used for rheumatic pain, swellings, and sprains.[8]
- Wound healing and ulcers: Poultices and washes made from roots or leaves.
- Digestive and respiratory complaints: Decoctions used for dyspepsia, cough and asthma in folk medicine.
- Note: Traditional topical use is common; systemic administration is historically reported but is risky given modern toxicology.[9]

Phytochemical Profile

- Aristolochia indica contains a complex mixture of compounds; major classes reported across phytochemical studies include:
- Aristolochic acids (AA-I, AA-II) — nitrophenanthrene carboxylic acids (principal bioactive/toxic family).
- Aristolochic lactams and isoaristolochic acids — related alkaloidal derivatives.
- Phenanthrene and phenolic alkaloids — various substitution patterns.[10,11]
- Flavonoids and phenolic compounds — quercetin-like compounds, polyphenols.
- Tannins — condensed and hydrolyzable tannins concentrated in aqueous extracts.

Saponins and glycosides — in polar fractions are richer in tannins and polysaccharides. Terpenoids and sterols — in nonpolar fractions and volatile oils.

Volatile oils and trace monoterpenes/sesquiterpenes — leaf and stem volatiles.

Analytical methods used: HPTLC, HPLC-MS, LC-MS/MS, GC-MS (for volatiles), and NMR for structural elucidation. Ethyl acetate and methanol extract most aristolochic derivatives; aqueous extracts.

Pharmacological Activities

Antivenom

Aristolochia indica has been traditionally used in folk remedies for snakebite treatment. Extracts from its roots are believed to reduce venom-induced inflammation, pain, and local tissue damage by showing antioxidant and mild enzyme-inhibiting effects against certain toxins. Some laboratory studies suggest partial neutralization of venom activity, but the evidence is limited, inconsistent, and not medically validated. Importantly, Aristolochia species contain toxic aristolochic acids, making them unsafe. Therefore, the plant cannot replace modern antivenom therapy.[12]

Anti-inflammatory/analgesic

Aristolochia indica has been traditionally used for its anti-inflammatory and analgesic properties. Experimental studies suggest that extracts of the plant may inhibit inflammatory mediators and reduce swelling, contributing to pain relief. Antioxidant compounds may also help limit tissue irritation. However, the evidence is preliminary, not clinically validated, and the plant contains aristolochic acids, which are highly toxic and can cause kidney damage. Therefore, despite reported traditional benefits, it is not considered safe for therapeutic use.[13]

Antimicrobial and wound healing

Aristolochia indica has been traditionally reported to

possess antimicrobial and wound- healing properties. Laboratory studies indicate that its extracts may inhibit the growth of certain bacteria and fungi, which could help reduce infection risk in wounds. Some components may also promote tissue repair through anti-inflammatory and antioxidant effects. However, these findings are preliminary, not clinically proven, and the plant contains toxic aristolochic acids linked to kidney damage and cancer. Therefore, it is not safe for medicinal or wound-healing use.[14]

Digestive/respiratory uses

Aristolochia indica has been traditionally used in folk medicine for certain digestive and respiratory complaints, such as indigestion, loss of appetite, cough, and breathing discomfort. Its extracts were believed to stimulate digestion, reduce mucus, and ease respiratory irritation. Some antioxidant and anti-inflammatory effects may partly explain these uses. However, these benefits are not scientifically validated, and the plant contains aristolochic acids, which can cause severe kidney damage and cancer. Therefore, it is unsafe and not recommended for digestive or respiratory treatment.[15]

Modern experimental findings

Anti-venom / enzyme inhibition

PLA_2 inhibition: Extracts (methanolic/ethyl acetate) inhibit PLA_2 activity in vitro. PLA_2 is responsible for myotoxicity, membrane disruption, and inflammation. By inhibiting PLA_2, extracts reduce myonecrosis and local tissue destruction.

Protease/metalloprotease inhibition: Metalloproteases in viper venoms cause hemorrhage and tissue necrosis; A. indica fractions reduce proteolytic and hemorrhagic activities in gel or in vivo hemorrhage assays.

Hyaluronidase inhibition: Reduces venom spread through tissues, limiting systemic dissemination.

L-amino acid oxidase: Some inhibition reported, which can reduce oxidative damage and cytotoxicity.

In vivo outcomes: Rodent co-administration studies show reduced edema, less hemorrhage, attenuated necrosis and improved survival time when extracts given with venom.[16]

Anti-inflammatory and antioxidant effects

Demonstrated in cell assays and animal models: reduced inflammatory cytokines, decreased lipid peroxidation, and free-radical scavenging—mechanisms that reduce secondary damage after envenoming.

Antimicrobial activity

Certain extracts inhibit Gram-positive and Gram-negative bacteria in vitro, supporting ethnomedical uses for wound care.

Cytotoxic/anticancer activity

Some fractions exhibit cytotoxicity against cancer cell lines. This effect is sometimes desirable (anticancer) but is often linked to AA's genotoxicity — complicating therapeutic utility.[17]

Other reported activities

Hepatoprotective and spasmolytic effects described in limited preclinical studies; further validation needed.

Overall interpretation: The modern data largely confirm the traditional rationale—A. indica contains molecules that neutralize venom enzymes and mitigate tissue injury. However, the toxicity profile of aristolochic acids is the central barrier to therapeutic use.

Advanced Extraction & Fractionation Techniques

1. Sequential solvent extraction: Hexane → ethyl acetate → methanol → water to partition compounds by polarity; aristolochic acids usually concentrate in ethyl acetate/methanol fractions.
2. Ultrasonic-assisted extraction (UAE): Increases yield and shortens extraction time for alkaloids without high heat.
3. Accelerated Solvent Extraction (ASE): Efficient recovery with controlled temperature/pressure—useful for thermo-labile compounds.
4. Supercritical CO_2 extraction: Targets nonpolar terpenoids and avoids organic solvents—AA are less soluble, so CO_2 can help obtain AA-free fractions of nonpolar constituents.
5. Preparative HPLC / Column chromatography: For isolation and purification of individual alkaloids and aristolochic acids for structural and activity studies.[18]
6. Solid-phase extraction (SPE) & Molecularly Imprinted Polymers (MIPs): Emerging methods to selectively bind or remove aristolochic acids—promising for detoxification of extracts.
7. Bioassay-guided fractionation: Iterative fractionation guided by PLA_2/protease inhibition assays to find active, possibly non-AA, fractions.
8. Biotransformation / enzymatic modification: Use of microbes or enzymes to modify AA scaffolds potentially to less toxic derivatives—experimental and exploratory.

Recommended research pathway: Use bioassay-guided fractionation + analytical monitoring (HPLC-MS quantification of AAs) to isolate fractions with anti-venom activity but undetectable AA levels; explore topical formulations to minimize systemic exposure.

Toxicity Studies

- Aristolochic Acid Nephropathy (AAN): Characterized by progressive interstitial fibrosis, tubular atrophy and declining renal function after exposure; hallmark is AA-DNA adduct formation leading to somatic mutations.[19]
- Carcinogenicity: A exposure strongly associated with

urothelial carcinomas (bladder, renal pelvis) and is classified as carcinogenic; DNA adducts and specific mutational signatures observed.

- Acute toxicity: High doses of crude extracts can cause hepatotoxicity and nephrotoxicity in rodents; LD_{50} varies by extract and route.
- Chronic toxicity: Low-dose chronic exposure linked to progressive renal injury and increased cancer risk in epidemiological studies (historic cases from herbal medicines).
- Regulatory actions: Many countries/health agencies prohibit internal use of Aristolochia- containing products and issue warnings about AA exposure.
- Practical implication: Any research or product development must include rigorous AA quantification (HPLC-MS) and demonstrate AA absence for safety, especially when systemic dosing is considered

Clinical Studies & Human Data

- No well-controlled clinical trials exist demonstrating safe, effective systemic use of A. indica for snakebite.
- Anecdotal/traditional topical use reported but lacks safety/efficacy data.
- Regulatory caution: Because of AAN and cancer risk linked to aristolochic acids, clinical testing of crude AA-containing extracts is ethically and legally constrained
- Feasible clinical pathway: Investigate AA-free, bioactive fractions in Phase I safety studies (with validated analytical QC) or study topical formulations with minimal systemic absorption for local tissue protection.[20]

CONCLUSION

Aristolochia indica contains bioactive molecules able to neutralize key venom enzymes and mitigate local tissue damage—validating traditional uses and presenting attractive leads for antivenom research. However, aristolochic acids' severe nephrotoxicity and carcinogenicity are a major barrier. Research should prioritize: (1) bioassay-guided isolation of AA-free active compounds; (2) robust analytical QC (HPLC-MS) to detect and exclude aristolochic acids; (3) exploration of topical/local delivery to reduce systemic exposure; and (4) detoxification/biotransformation strategies. If AA-free, effective molecules are identified and validated in safety studies, A. indica–derived compounds could complement existing antivenom approaches—particularly for local tissue protection where current antivenoms fall short.

REFERENCES

1. Ushanandini S, Nagaraju S, Harish Kumar K, Vedavathi M, Kishore A, Sampaio SM, Kemparaju K. The anti-snake venom properties of Aristolochia indica root extract. J Ethnopharmacol., 2006; 106(1): 54–60.
2. Alam MI, Gomes A. Viper venom neutralization by Indian medicinal plant Aristolochia indica. Fitoterapia., 2003; 74(5): 427–430.
3. Han J, Li M, Zhou X. Systematic overview of aristolochic acid toxicity: nephrotoxicity and carcinogenicity. Toxicol Res., 2019; 8(4): 497–510.
4. IARC Working Group. Aristolochic acids and Aristolochia species. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, 2002; 82.
5. Félix-Silva J, et al. Medicinal plants for treatment of local tissue damage induced by snakebites: a review. J Ethnopharmacol., 2017; 204: 42–56.
6. Nortier JL, Martinez MC, Schmeiser HH, et al. Aristolochic acid and the etiology of endemic (Balkan) nephropathy. Kidney Int., 2000; 58(1): 121–131.
7. Debelle FD, Vanherweghem JL, Nortier JL. Aristolochic acid nephropathy: a worldwide problem. Kidney Int., 2008; 74(2): 158–169.
8. Abel, G., & Schimmer, O. 1983. Induction of structural chromosome aberrations and sister chromatid exchanges in human lymphocytes in vitro by aristolochic acid. Human Genetics, 64(2): 131–133.
9. Achari, B., Bandyopadhyay, S., Saha, C. R., & Pakrashi, S. C. 1983. A phenanthroid lactone, steroid and lig-nans from Aristolochia indica. Heterocycles, 20: 771–774.
10. Achari, B., Chakrabarty, S., Bandyopadhyay, S., & Pakrashi, S. C. 1982. A new 4,5- dioxoaporphine and other constituents of Aristolochia indica. Heterocycles, 19: 1203– 1206.
11. Achari, B., Chakrabarty, S., & Pakrashi, S. C. 1981. An N-glycoside and steroids from Aristolochia indica. Phytochemistry, 20: 1444–1445.
12. Akwu, N. A., Naidoo, Y., & Singh, M. 2019. Cytogenotoxic and biological evaluation of the aqueous extracts of Grewia lasiocarpa: An Allium cepa assay. South African Journal of Botany, 125: 371–380.
13. Alagesaboopathi, C. 2011. Ethnomedicinal plants used as medicine by the Kurumba tribals in Pennagaram Region, Dharmapuri District of Tamil Nadu, India. Asian Journal of Experimental Biological Science, 2: 140–142.
14. Attarde, S., & Apte, K. 2013. Studies on antivenom activity of Aristolochia indica plant extract against red scor-pion venom by in vivo and in vitro methods. International Journal of Pharmacognosy and Phytochemical Research, 5(3): 168–172.
15. Balachandran, P., Wei, F., Lin, R. C., Khan, I. A., & Pasco, D. S. 2005. Structure activity relationships of aristolochic acid analogues: Toxicity in cultured renal epithelial cells. Kidney International, 67: 1797–1805.
16. Balakrishnan, V., Venkatesan, K., Ravindran, K. C., & Karuppusamy, S. 2005. Studies on medicinal plants use for tabortion by Irulars of Coimbatore district, Tami, India. Bulletin of Medico-Ethno-Botanical Research, 26: 6–9.

17. Ban, T. H., Min, J. W., Seo, C., Kim, D. R., Lee, Y. H., Chung, B. H., Jeong, K. H., Lee, J. W., Kim, B. S., Lee, S. H., Choi, B. S., Han, J. S., & Yang, C. W. 2018. Update of aristolochic acid nephropathy in Korea.
18. Korean Journal of Internal Medicine, 33(5): 961–969.
19. Berger, S. I., & Iyengar, R. 2011. Role of systems pharmacology in understanding drug adverse events. Wiley Interdisciplinary Reviews: Systems Biology and Medicine, 3(2): 129–35. doi: 10.1002/wsbm.114.
20. Bhat, P., Hedge, G. R., Hedge, G, & Mulgund, G. S. 2014. Ethnomedicinal plants to cure skin diseases—An account of the traditional GR knowledge in the coastal parts of Central Western Ghats, Karnataka, India.