Ethnopharmacology, Pharmacology and Phytochemistry of *Aristolochia bracteolata* Lam: A Review of an Antimalarial Plant

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**ABSTRACT**

Malaria remains one of the most common infectious diseases in the sub-Saharan African countries and other developing countries. Among the medicinal plants used in the endemic countries for the treatment of malaria is *Aristolochia bracteolata* Lam. due to its availability, accessibility, and traditional use. This study therefore reviewed the ethnomedicinal use, pharmacology, and the chemistry of *Aristolochia bracteolata*. Different electronic databases such as Medline/Pubmed, Cochrane Library, and Embase were searched to identify all published articles on *Aristolochia bracteolata* Lam. Key search words included ethnopharmacological use, pharmacological and phytochemical parameters of *A. bracteolata*. Retrieved articles were reviewed and synthesized. In addition, the reference list of retrieved articles was reviewed and articles which were not retrieved by previous search were hand searched. The review included original research articles that has investigated *Aristolochia bracteolata* Lam. of any study design. Only published original articles, any languages, any time of publish, and grey literature (Conference paper, theses both PhD. and Msc. technical report) were included. Those articles with full text not available, those without information of interest, e.g ethnopharmacology, pharmacology and phytochemistry of *A. bracteolata* were excluded. Despite having multiple use, the plant is mainly used in the treatment of malaria with a reported antiplasmodial activity. Aristolochic acids (AAs) were reported as the major and active ingredient among other components in the plant. The review revealed that *A. bracteolata* has various traditional use with promising pharmacological activity. However, information on its safety is limited.

**Keywords:** *Aristolochia bracteolata*, Ethnopharmacology, Pharmacology, Phytochemistry, South Sudan, Malaria, Aristolochic acids.

**INTRODUCTION**

Medicinal plants played a very important role in human life right from the ancient times till today. They comprise many chemical constituents with different pharmacological effects thereby regulating different biological mechanisms and treating different types of diseases. They have a vital role in treating and preventing various diseases. Some of these medicinal plants have been reported for their antimalarial activities and have been the source of new lead drugs including artemisinin, quinine, etc. In addition to antimalarial efficacy, some of these plants have been reported to exhibit antiidiuretic, anti-inflammatory, anti-analgesic, anticancer, antiviral, antibacterial and antifungal activities. The use of herbal medicine (HM) has become an alternative source of treatment over the past three decades to address the gap of...
high cost, resistance to conventional drugs and as alternative
drug for primary healthcare (PHC). Medicinal plants have
played important roles in drug discovery through
phytochemicals which can be directly used as medical
remedy, structural basis for chemical synthesis or act as
structural model for semi-synthetic drugs. Medicinal
plants are the richest bio-resource of drugs of traditional
systems of medicine, modern medicines, nutraceuticals,
food supplements, folk medicines, antimalarial drugs etc.
Many plants are useful to human lives as source of food,
supplement or therapeutic purpose, however, some
have been reported to have mutagenic and genotoxic effect
in vivo. Plant toxicity may arise from contaminants like
lead, mercury, arsenic and other that can be absorbed from
the soils or from the end products of plant metabolism.
Current studies have focused more on ethnomedicinal use,
pharmacology and phytochemistry of medicinal plants used
by humans. This is very significant in order to guarantee
the safety of the consumers of plant products. The plant toxicity
may originate from different contaminants which may be
chemical (organic pollutant, toxic metals or non-metals),
biological (parasitic or microbiological) or agrochemical
residues. A number of bioassays are used in research to
certainty toxicity level of medicinal plants or herbal extracts
which may be in vivo using laboratory animals or in vitro
using cell line cytotoxicity studies. Identification of
phytochemicals responsible either for biological activity or
 toxicity is important for enhancing the bioactive effect or
preventing the toxic effect. In malaria endemic countries,
medicinal plants are used as alternative for treatment of the
different ailments including malaria, and has remained a first
line source of novel drugs such as quinine, artemisinins etc.
Aristolochia bracteolata is used for the treatment of various
diseases in many countries including South Sudan but
review on its safety, phytochemistry and efficacy is limited.
This review synthesized information on ethnopharmacology, pharmacology and phytochemistry of
Aristolochia bracteolata Lam.

METHOIDS

| TABLE 1. Classification of Aristolochia bracteolata Lam. |
|------------------------|---------------------------------|
| **Family** | **Aristolochiaceae** |
| **Genus** | Aristolochia |
| **Species** | A. bracteolata |
| **Scientific name** | Aristolochia bracteolata Lam. |
| **Synonyms** | Aristolochia bracteata Retz., Aristolochia benadirana Flori., Aristolochia abyssinica Klotzch., Aristolochia mauritiana Pers. Aristolochia crenata Ehreb ex.Duch. |
| **Common names** | Wormkiller, Dikeritimelo. Morodi. |
| **Habit** | Climbing herb |
| **Habitat** | Dry areas, black cotton soil, riverbanks, bush lands, desert grassland and sandy soil. |
| **Propagation** | Seed |

Different electronic databases searches were performed in
Medline/Pubmed, Cochrane Library, Google scholar, proquest library and Embase to identify all published articles
on Aristolochia bracteolata. The key words included
ethnopharmacological use, pharmacological and
phytochemical parameters of Aristolochia bracteolata. In
addition, the reference list of retrieved articles was reviewed
and articles which were not retrieved by previous search
were hand searched. The review included original research
articles that has investigated Aristolochia bracteolata Lam.
of any study design. Only published original articles, any
languages, any time of publish, and grey literature
(Conference paper, theses both PhD. and MSc., technical
report) were included. Full text not available, those without
information of interest, e.g. ethnopharmacology,
pharmacology and phytochemistry of A. bracteolata were
excluded.

RESULTS

Search results

After searching the data bases and hand searching a total of
215 articles were obtained. After reviewing articles for
relevance, 73 were excluded. Since 23 full text were not
available, 5 were reviewed articles, and the remaining does
not have the information of interest. Therefore, 42 articles
were finally included in this review.

Botany of Aristolochia bracteolata Lam.

The Plant A. bracteolata Lam. belongs to the family
Aristolochiaceae. The genus aristolochia has over 500
species, but those reported to be found in Africa includes; A.
elegans, A. chilenis, A. clematis A. albida, A. baetica. A.
embergeri, A. heppi, A. hockii, A. fontanesii, A. paucinervis,
A. pistolochia, A. rigida, A. sempervires and A.
bracteolata. Aristolochia bracteolata is a climbing
perennial plant with corolate leaves and dark–purple colour
tubular flowers widely distributed in tropical Asia, Africa
and South America. It is commonly known as worm killer
and classification details are provided in Table 1.
Ethnopharmacology of Aristolochia bracteolata Lam.

Aristolochia bracteolata Lam. was the leading antimalarial plant reported in the list of medicinal plants in South Sudan. Other various plants that are used for the treatment of malaria include Gardenia thunbergia, Cucumis dipsaceus, Tamarindus indica, Balanites aegyptiaca, and cassia nigricans. Apart from treating malaria, A. bracteolata is also used for treatment of various diseases and ailments in South Sudan traditional health system. These uses include dysentery, headache, fever, general body pain, snake bites, scorpion bites, high blood pressure, diabetes, diarrhea and stomach ache. The whole plant has been reported to be of medicinal importance. The plant A. bracteolata Lam. is the most commonly used as an antimalarial plant and sold in the markets as a source of income for the local inhabitants in South Sudan. The whole plant is either administered fresh or after sun dried. For the topical use, the plant paste is applied in the affected area and seeds are swallowed for the treatment of malaria and other stomach conditions. Its root is also powdered, infused in water and administered orally for the treatment of malaria, fever, headache, general body pain, stomachache, diarrhea and flu. Table 2 depicts ethnopharmacological uses of different parts of A. bracteolata.

### Table 2. Ethnopharmacological uses of different parts of Aristolochia bracteolata Lam.

| Plant part     | Used                                                                 | Reference |
|---------------|----------------------------------------------------------------------|-----------|
| Whole Plant   | Is crushed, soaked in water taken orally as gastric stimulant treatment, cancer, lungs inflammation dysentery, and snake bite | 14        |
| Whole Plant   | For treatment of Malaria, convulsions, abdominal pain, scorpion stings, flu, vomiting, pneumonia, polymeorhrea and edema | 15        |
| Root          | Root paste as vulnerary agent: 100g of fresh roots taken processed and ground to paste. It is mixed with 1 spoonful of turmeric powder, warmed and applied on wounds | 16        |
| Root and Leaf | Roots used for Scorpion stings and anti-inflammatory, leaves for malaria | 17        |
| The Whole Plant | For the treatment of malaria and other conditions like, fever, headache, general body pain, stomachache, diarrhea and flu. | 13        |

Pharmacological activity of Aristolochia bracteolata Lam.

Aristolochia bracteolae Lam. has been reported to have antibacterial, antifungal, anti-arthritis, hypotensive, hypothermia, antioxidant, anti-inflammatory, antihyperglycemic and antihyperlipidemic activities. Hexane extract of A. bracteolata showed in vitro antimalarial activity on chloroquine sensitive P. falciparum MRC-2 strain with IC50 of 16 μg/mL. In another study, methanol extract of seed and root of A. bracteolata showed in vitro antiplasmodial activity on chloroquine resistant and pyrimethamine sensitive strain with IC50 less than 5 μg/mL. Likewise, petroleum ether/chloroform extract of whole plant of A. bracteolata showed in vitro antimalarial activity of 100% inhibition against P. falciparum at 50 μg/mL concentration. This confirms local community claim that the plant has effect on malaria parasite. Antimicrobial activity, anti-arthritis activity, anti-allergic activity and anti-oxidant property were also exhibited by the plant. The ethyl acetate, acetone and methanol extracts of the root showed promising antibacterial activity on Gram positive and Gram negative bacteria, with ethyl acetate extract being the most effective. Aristolochia bracteolata showed a promising hyperuricemia in a metabolic arthritis rat model and showed a potent in vitro wound healing action through anti-inflammatory and proliferative effect on human dermal fibroblasts and keratinocytes.

Phytochemistry of Aristolochia bracteolata Lam.

 Phytochemical screening of Aristolochia bracteolata Lam. showed that it contains presence of alkaloids, saponins, flavonoid, phenol and tannin. Methanol extract of A. bracteolata subjected to phytochemical screening has shown the presence of phenolic compounds, flavonoids, triterpenoids, alkaloids, steroids, cardiac glycosides, saponins and aristolochic acids A-D. The stem and the root were reported to contain the alkaloid and aristolochic acids. The chief active principle of the drug is aristolochic acid, though aristolic and p-coumaric acids also appear to contribute to the activities of the drug. Aristolochic acid is 8-methoxy-3; 4-methylenedioxy – 10 – nitrophenanthrene – 1–carboxylic acid. It is intensely bitter and is optically inactive. It is the same as iso-aristolochic acid, aristolochia yellow, aristinic and aristolochic acids, but is different from aristolochine now identified as 1-curine. The aristolochic acids were host of phenanthrene derived metabolites in which the aristolactams also possessed the similar skeleton. Both aristolochic acids (AAs) I and II are the major components of the plant in aristolochia genus. Phytochemical screening
Ethnopharmacology of *Aristolochia bracteolata* Lam

of *A. bracteolata* using different solvents is presented in *Figures 1* and *2* and *Table 3* depict structures of aristolochic acid I and II respectively. However, in another study, methanolic extract of *A. bracteolata* Lam was purified and toxic compounds identified as AAs were isolated using different purification techniques. It was noted in previous studies that the whole plant (200g) was defatted to produce dark green oily residue (5.35%). High performance liquid chromatography (HPLC) data also showed that AA-II was represented in a higher calculated quantity of 49.03 g/kg compared to AA-I (12.98 g/kg) in *A. bracteolata* L. whole plant.\textsuperscript{31,32} Although evidence of the presence of aristolochic I and II in *A. bracteolata* Lam. is reported by Achenbach and Fischer\textsuperscript{33}, Kumar\textsuperscript{34,35} reported absence of Aristolochic II in this plant. Variation in their results may be explained by the different techniques and methods of analysis used.

**FIGURE 1:** $C_{17}H_{11}NO_{7}$, Relative molecular mass: 341.27

![Figure 1](image1)

**FIGURE 2:** $C_{16}H_{9}NO_{6}$, Relative molecular mass: 311.25

![Figure 2](image2)
TABLE 3. Phytochemical screening of Aristolochia bracteolata Lam. using different solvents

| Plant Part Used | Extract Solvents | Phytochemicals | Reference |
|-----------------|------------------|----------------|-----------|
| Whole Plant     | Methanol Extract | Presence of alkaloids, triterpenoids, glycosides, steroids, tannins, phenolic compounds, flavonoids and cardio glycosides | 27 |
| Whole Plant     | Methanol         | phenolic compounds, flavonoids, triterpenoids, alkaloids, steroids, cardiac glycosides, saponins and aristolochi acid-A, and aristolochic acid-D | 24 |
| Leaf Part       | Methanol & ethyl acetate | Presence of alkaloids, glycosides, phytosterol, saponins, tannins, phenol, carbohydrates | 28 |
| Leaf            | Increasing order of polarity from petroleum ether to benzene, chloroform, acetone and alcohol extract | Presence of alkaloids, saponin, glycosides, steroids, tannins, phenolic compounds, flavonoids | 29 |
| Leaf            | Methanol extract | Presence of alkaloids, saponin, steroids, tannins, terpenoids, flavonoids and glycosides | 30 |
| Leaf            | Aqueous extract  | Presence of alkaloids, saponin, steroids, tannins, phenol flavonoids, carbohydrates and glycosides | 28 |

Toxicity of Aristolochia bracteolata Lam.

Most of the plant family Aristolochiaceae are said to contain aristolochic acids (AAs)\(^{15}\). Pure AAs from A. bracteolata plant has been reported for nephrotoxic, mutagenic and carcinogenic in the tested animals after a prolong administration. In experimental animals, high doses of aristolochic acids administered either orally or intravenously caused severe necrosis of the renal tubules\(^{36}\). However, there is limited evidence in human on the carcinogenicity of the plant. The acute oral toxicity study on A. bracteolata extract showed no mortality and any sign of toxicity after dosing at 2000 mg/kg\(^{7}\). In a similar study, the ethanol extract of A. bracteolata administered orally at 1000, 2000, 3000, 4000, and 8000 mg/kg did not produce any sign of toxicity and mortality in rats when observed for 14 days post-administration, which could be safety-acutely.

Aristolochic acid administered orally on rats at 50 mg/kg for three days neoplastic lession on the kidneys were reported\(^{41}\). In another study, aristolochic acids administered through intraperitoneal injection on rabbits at 0.1 mg/kg for 17-21 months reported kidney tumors, ulcers, and peritoneal cavity\(^{34}\). However, it is important to recognize that safety concerns must be incorporated into a general ‘risk-benefit’ analysis and that toxicity of a drug does not necessarily mean that it should not be developed or approved. The aminoglycoside antibiotics, the cancer drug cisplatin and the antiviral tenofovir were some of the few mentioned examples of drugs which are proved to be nephrotoxic but efficacious in terms of treatment\(^{42}\).

CONCLUSION

This review study has shown that Aristolochia bracteolata Lam. is used as remedy for different ailment and unlike pure aristolochic acids which is toxic, the extracts did not show any sign of toxicity from the literature. The plants have also shown a promising antiplasmodial activity which could be recommended for antimalarial study in vivo. It could be concluded that the plant contains different chemical constituents with aristolochic acids being the marker which is reported for a degenerative effect on the organs. This plant however has shown a promising pharmacology which could be explored in the development of future drugs development.
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