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Review Article

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Medicinal Uses, Phytochemistry and Pharmacological Activities of *Antigonon leptopus* Hook. and Arn. (Polygonaceae): A Review

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ABSTRACT

Antigonon leptopus Hook. & Arn., belonging to the family Polygonaceae, is an invasive evergreen, woody liana. It is native to Mexico and is distributed in various parts of the world including India. In the present review, an extensive literature survey was carried out to update information available on the medicinal uses, phytochemistry and pharmacological activities of A. leptopus. The plant is shown to possess a wide range of phytochemicals. Alkaloids, phenolic compounds, saponins, triterpenoids and glycosides are detected in different parts of the plant. Compounds such as trihydroxy benzaldehyde, ferulic acid, quercetin-3-rhamnoside, anthraquinones, b-sitosterol and kaempherol-3-glucoside have been identified in the plant. The plant is used ethnomedicinally in various parts of the world for treating various ailments such as pain, cough, diabetes, dermatological problems, flu and stomachache. Different parts of the plant are investigated for pharmacological properties. The plant is reported to possess various bioactivities such as antimicrobial, antioxidant, hepatoprotective, analgesic, anti-inflammatory, cytotoxic and antidiabetic activities. Nanoparticles synthesized using A. leptopus were shown to exhibit bioactivities such as antimicrobial, antioxidant and cytotoxic activity. Information gathered from this extensive literature survey indicates the potential ethnomedicinal applications of A. leptopus and the possible utilization of the plant to develop pharmaceutical agents for disease therapy.

Keywords: *Antigonon leptopus* hook & Arn.; Polygonaceae; Phytochemicals; Ethnomedicine; Pharmacological activities

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INTRODUCTION

The genera belonging to the family Polygonaceae includes herbs, shrubs, trees and lianas of which majority are herbaceous plants. *Antigonon leptopus* Hook. & Arn., (Corallita, Honolulu creeper, coral vine, coral creeper, queen's wreath, Mexican creeper, railway creeper, bee bush) belonging to the botanical family Polygonaceae (buckwheat family), is an invasive, fast growing, evergreen, perennial woody liana native to Mexico. The plant is naturalized in India. Like many other members of Polygonaceae, *A. leptopus* is considered as an invasive species of natural areas. The plant grows commonly along roadsides and hedges. The plant flourishes at lowlands, beside streams and gullies as well as on dry and sandy heaps along the coast. It is often cultivated as an ornamental plant due to beautiful flowers. The flowers of *A. leptopus* are visited by a tremendous variety of insects (flies, butterflies, honey bees etc.) and birds like humming bird which facilitates its sexual reproduction outside of its natural range. It is a climber and it climbs on supporting materials with the help of tendrils. The plant grows in any type of soil and persists vegetatively by means of production of numerous tubers. The plant prefers full sunlight but can grow in partial sunlight also. Propagation is mainly by seeds. Caterpillars seem to be pests for the plant. In several parts of the world, the tubers (looks like small sized eggs) and flowers are consumed as food. The fried flour-coated leaves

and flowers of are served with noodles in Thailand. The flowers are used in the preparation of omelets and the hot tea prepared from the aerial portion is used as a treatment for cough and throat constriction in Jamaica [1-6]. In the present review, an extensive literature survey is carried out to compile data available on the medicinal uses, chemical compounds/groups present and pharmacological activities of *A. leptopus* by referring standard flora, journals, and search engines such as Google scholar, ScienceDirect and Pubmed.

Plant Description

A. leptopus (Figure 1) is an extensive, rapidly growing climber reaching up to 40 feet or higher and climbs with the help of slender tendril. Leaves are light to dark green, alternate, up to 12 × 8 cm, ovate or triangular, cordate or hastate at base and acute to acuminate at apex. Petiole is up to 3.5 cm long and stipular sheaths are inconspicuous. Flowers are monoecious, pink or white in color, showy, and occur in terminal or axillary racemes that end in branched tendrils. Perianth segments are 5 in number, petaloid, 2 or 3 outer ones cordate or ovate, inner ones oblong. Stamens are 8 in number. Flowering occurs more or less throughout the year. Fruit is brown, 3-angled at least above and is loosely covered in the enlarged papery perianth-segments [7].

Figure 1: *Antigonon leptopus* Hook. & Arn.

Phytochemistry of *A. Leptopus*

Plants produce several kinds of primary and secondary metabolites. The chemical compounds that are present in plants are known as phytochemicals. Plants produce diverse primary and secondary metabolites. Many of the plant metabolites exert beneficial effects such as avoiding herbivores and controlling pathogenic organisms. Besides, some plant constituents are responsible for contributing color and aroma to plants. Many of these metabolites are responsible for therapeutic potential of plants. The diverse chemical nature of plant metabolites provides leads to develop novel drugs with potential applications. Drugs such as taxol, quinine, vincristine, vinblastine, digoxin, codeine, berberine and nicotine are from plant origin [8-13]. A range of phytochemicals are found in the plant *A. leptopus*. Some studies have detected several groups of phytochemicals in different parts of the plant while few studies have revealed a detailed note on the isolation of purified compounds from the plant. Several bioanalytical techniques have been employed to isolate compounds in pure form from *A. leptopus* and to identify them. Tables 1 and 2 depict the phytochemical groups/chemical compounds identified in different parts of *A. leptopus*. Structures of some of the compounds identified in *A. leptopus* are shown in Figure 2.

Table 1: Phytochemical groups detected in different parts of *A. leptopus*

Part	Phytochemicals detected	References
Flower	Phenol, saponins, tannins, coumarins, steroids	Antonisamy et al. [14]
Leaf	Phenols, hydrocarbons, quinazolines, coumarins, steroids, cadinene, juniper camphor and others	Priya et al. [15]
Root	Steroids, alkaloids, flavonoids, tannins and glycosides	Mamidipalli et al. [16]
Flower	Volatile oils, glycosides, terpenes	Bolla and Bhogavalli [17]
Leaf	Alkaloids, flavonoids, glycosides, tannins, saponins and steroids	Licayan et al. [18]
Flower	Phenol, flavonoids, saponins, steroids, tannins, coumarins	Jeeva et al. [19]
Leaf	Sterol, triterpenes, alkaloids, flavonoids, tannins, saponins, glycosides, coumarins	Elhaj et al. [20]
Leaf	Tannins, cardiac glycosides, steroids, triterpenes, flavonoids	Rashmi and Rajkumar [21]
Leaf	Tannins, alkaloids, flavonoids, phenols, terpenoids	Sravanthi et al. [22]
Whole plant	Alkaloids, glycosides, flavonoids, tannins, saponins, steroids, volatile oils.	Kanthal et al. [23]
Leaf	Alkaloids, flavonoids, tannins, glycosides, terpenoids, saponins	Pradhan and Bhatnagar [24]
Leaf	Saponin, phenolic compounds, tannins, flavonoids, alkaloids, fixed oils and amino acids	Balasubramani et al. [25]
Roots and rhizomes	Triterpenoids, flavonoids and tannins	Battu and Raju [26]

Table 2: Chemical compounds identified in *A. leptopus*

Part	Phytochemicals detected	References
Flower	Gallic acid, protocatechuic acid, p-hydroxy benzoic acid, chlorogenic acid, vanilic acid, caffeic acid, syringic acid, p-coumaric acid, ferulic acid, sinapic acid	Kaisoon et al. [27]
Aerial parts	2,3,4-trihydroxy benzaldehyde	Mulabagal et al. [28]
Aerial parts	quercetin-3-O-a-rhamnopyranoside, 1,8-dihydroxy-6-(hydroxymethyl)-3-methoxy-2-pyrrolidinium anthraquinone, 1,8-dihydroxy-6-(methyl)-3-methoxy-2-pyrrolidinium anthraquinone, 1,8-dihydroxy-6-(hydroxymethyl)-3-methoxy-2-piperidinium anthraquinone, 1,8-dihydroxy-6-(methyl)-3-methoxy-2-piperidinium anthraquinone.	Olaoluwa et al. [29]
Arial parts	n-hentriacontane, ferulic acid, 4-hydroxycinnamic acid, quercetin-3-rhamnoside, and kaempherol-3-glucoside, b-sitosterol, b-sitosterol-glucoside and d-mannitol	Vanisree et al. [2]

Ethnomedicinal Uses of *A. Leptopus*

Ethnobotany is the relationship between man and plants. Worldwide, plants have been used as medicine. Traditional medicinal practitioners use many plants in certain formulations for treating several diseases or disorders. An estimate by WHO highlights that around 80% of population rely on medicinal plants for primary healthcare needs. Plants are known to be essential component of indigenous systems of medicine *viz*. Ayurveda, Unani and Siddha [12,30-35]. The plant *A. leptopus* is one among several plants that have been used traditionally for treating various ailments. Different parts such as roots, aerial parts, leaves and seeds of the plant are used ethnomedicinally worldwide. A brief description of ethnomedicinal uses of *A. leptopus* is presented in Table 3.

Table 3: Ethnomedicinal uses of *A. leptopus*

Geographical area	Uses	Reference
Iloilo, Philippines	Gastrointestinal disorders	Tantiado [36]
Amarkantak region, M.P., India	Paste made from fresh leaves is applied externally in skin problems.	Srivastava et al. [37]
Pratapgarh tehsil, Rajasthan, India	Seeds are used as famine food; leaves are used to treat blisters.	Meena et al. [38]
Malayali tribals, Eastern Ghats, Tamil Nadu, India	Seeds are used in diabetes.	Vaidyanathan et al. [39]
Fatehpur, UP, India	Decoction of aerial parts used for prevention of cough and flu related pains.	Agarwal [40]
Trinidad and Tabago	Diabetes	Lans [41]
Nigeria	Antimicrobial	El-Ghani [42]
Sonora, Mexico	Leaves and roots used in stomachache.	Salazar et al. [43]
Himalayan region, India	Medicinal	Sekar [44]
Irula tribes, Walayar valley, Southern Western Ghats, India	Decoction made from roots orally to treat dermatological infections/diseases	Venkatachalapathi et al. [45]
Burhanpur district, M.P., India	Leaves are used in skin diseases.	Siddiqui and Sainkhediya [46]
Bhil tribe of Alirajpur district, M.P., India	Flower is used in pain and cold; leaf is used in blood pressure and as heart tonic.	Bhargav and Patel [47]
Eastern Nicaragua	Root is used as food and medicine	Coe and Andersen [48]

Pharmacological Activities of *A. Leptopus*

Plants have been extensively used as therapeutic agents for treatment of various disorders throughout world. Such medicinal uses of plants can be identified by subjecting the plants and their formulations to *in vitro* as well as *in vivo* pharmacological studies. The findings of such pharmacological studies can possibly highlight the potential utilization of plants in the treatment of diseases or disorders by traditional systems of medicine. The plant *A. leptopus* is investigated for various pharmacological properties. Studies have shown a tremendous range of biological activities such as antimicrobial, antioxidant, anti-inflammatory, analgesic, hepatoprotective and antidiabetic activities exhibited by the plant *A. leptopus* and are discussed below.

Antimicrobial Activity

Battu and Raju [26] evaluated antimicrobial activity of methanol, hexane and ethyl acetate extracts of root and rhizomes of *A. leptopus*. Among extracts, methanol extract was shown to display stronger antimicrobial property. Bolla and Bhogavalli [17] determined antibacterial activity of flower extract of *A. leptopus* by disc diffusion method. It was observed that ethanol extract displayed marked inhibition of test bacteria when compared to chloroform extract. In a study, Udayaprakash et al. [49] evaluated antibacterial activity of various solvent extracts of leaves of *A. leptopus* by disc diffusion method. Among extracts, acetone and methanol extracts exhibited dose dependent inhibitory activity while chloroform and hexane extracts were ineffective. In the study carried out by Gupta et al. [50], ethanolic extract of *A. leptopus* flower exhibited higher inhibitory activity against Gram positive

and Gram negative bacteria when compared to chloroform extract. Jeeva et al. [19] determined antibacterial activity of methanolic extract of flowers of *A. leptopus* against a panel of bacteria. The extract was found to exhibit inhibitory activity against 9 out of 12 test bacteria with maximum antibacterial activity against *Bacillus cereus*. The study of Rashmi and Rajkumar [21] showed marked antifungal activity of leaf extract against *Macrophomina phaseolina* isolated from diseased maize. Sravanthi et al. [22] found antimicrobial activity in hexane, ethyl acetate and aqueous extracts of leaves of *A. leptopus*. Ethyl acetate extract exhibited stronger antimicrobial activity. The study carried out by Balasubramani et al. [25] revealed the marked potential of methanolic leaf extract of *A. leptopus* to inhibit fish pathogens *viz. Providencia* and *Aeromonas* when compared to clinical pathogens. Pushpavathi et al. [51] showed potent antifungal activity of methanolic leaf extract of *A. leptopus* against seed-borne fungi isolated from sorghum seeds. *Curvularia* sp. and *Aspergillus* flavus were inhibited to highest and least extent respectively by the extract.

Anthelmintic Activity

Chloroform fraction of methanol extract of leaves of *A. leptopus* was shown to exhibit anthelmintic activity against earthworm model in a dose dependent manner [15]. Raju and Rao [52] evaluated anthelmintic activity of ethyl acetate and methanolic extract of roots and rhizomes of *A. leptopus* in earthworm model. Both extracts exhibited significant anthelmintic activity and the methanolic extract was more active. The study of Kanthal et al. [23] revealed dose dependent anthelmintic activity of chloroform extract of *A. leptopus* whole plant.

Analgesic Activity

Mamidipalli et al. [16] evaluated analgesic activity of methanol extract of leaves of *A. leptopus* (200 and 400mg/kg body weight) by hot plate and acetic acid writhing response in mice. The extract was shown to exhibit dose dependent analgesic potential which was related to peripheral and central mechanisms. In another study, Ranjan et al. [53] determined analgesic activity of methanol and chloroform extracts of leaves in albino rats by tail immersion method. A significant dose dependent analgesic activity was observed.

Anti-inflammatory Activity

Anti-inflammatory activity of two concentrations, *viz.* 200 and 400 mg/kg body weight, of methanol extract of leaves of *A. leptopus* was determined by Carrageenan induced paw edema in rats [16]. The extract was shown to display inhibition of paw edema in a dose dependent manner. In a similar study carried out by Carey et al. [54], the methanolic extract of roots of *A. leptopus* was shown to produce a significant inhibition of peritoneal and cutaneous vascular permeability induced by acetic acid, granuloma induced by cotton-pellet and migration of leucocytes and neutrophils induced by carrageenan in animals at the doses of 100, 200 and 400 mg/kg. The tea as a dried extract prepared from aerial parts of *A. leptopus* was shown to inhibit cyclooxygenases COX-1 and COX-2 by 38% and 89%, respectively at 100 μg/ml [28].

Hepatoprotective Activity

Raju and Rao [55] screened hepatoprotective activity of ethyl acetate and methanol extracts of roots of *A. leptopus* against carbon tetrachloride induced liver damage in Wistar albino rats. The extracts showed significant hepatoprotective activity as evidenced by significant reduction in serum enzymes and total bilirubin. Methanol extract was more effective than ethyl acetate extract. The study carried out by Babu et al. [56] revealed a significant hepatoprotective activity of aqueous extract obtained from root of *A. leptopus* against hepatotoxicity induced by paracetamol in albino rats.

Antidiabetic Activity

Angothu et al. [57] determined antidiabetic activity of methanolic extract of aerial parts of *A. leptopus* (200 and 400 mg/kg body weight) in alloxan induced diabetic rats. The extract displayed a dose-dependent fall in fasting blood glucose levels. The results of biochemical parameters and histopathological studies also suggested that the extract possesses significant antidiabetic property. In a similar study, Rani et al. [58] showed antidiabetic effect of toluene, ethyl acetate and butanone fractions of methanol extract of leaves of *A. leptopus* on streptozotocin - induced diabetic rats. Oral administration of toluene, ethyl acetate, and butanone fractions at 50 and 100 mg/kg body weight significantly reduced the fasting blood glucose level in diabetic rats. Among the fractions tested, ethyl acetate fraction was shown to be more effective. In another study by Sujatha et al. [59], the methanolic extract of flower of *A. leptopus* was shown to exhibit antihyperglycemic activity in alloxan induced diabetic rats.

Cytotoxic Activity

Elhaj et al. [20] determined cytotoxicity of ethanol extract of leaves of *A. leptopus* against Vero cell line by MTT assay. The extract was shown to exhibit dose dependent cytotoxicity with an IC_{50} value of 289.60 µg/ml. The study by Kanthal et al. [23] showed a dose dependent cytotoxic effect of chloroform extract of whole plant (by MTT assay) against two cell lines *viz.*, A-549 and CHOK 1. The study of Pradhan and Bhatnagar [24] revealed dose dependent cytotoxicity of various solvent extracts viz. hexane, ethyl acetate, methanol and chloroform extract of leaves of *A. leptopus* against brine shrimp larvae.

Antithrombin Activity

The antithrombin activity of methylene chloride and methanol extracts prepared from *A. leptopus* was investigated by a chromogenic bioassay. The extract was found to demonstrate a significant activity [60].

Juvenoid Activity

The study of Neraliya and Gaur [61] revealed potent juvenoid activity of extract of *A. leptopus* against filarial mosquito *Culex quinquefasciatus*.

Antioxidant Activity

The tea as a dried extract prepared from aerial parts of *A. leptopus* was shown to inhibit lipid peroxidation [28]. In a study, Udayaprakash et al. [62] screened free radical scavenging potential of methanolic leaf extract of *A. leptopus* by DPPH assay. The extract was shown to scavenge radicals dose dependently with an EC_{50} value of 38.33 µg/ml. The study of Elhaj et al. [20] revealed scavenging of DPPH radicals by ethanolic extract of leaves of *A. leptopus*. Licayan et al. [18] observed antioxidant potential of methanolic extract from leaves of *A. leptopus* by DPPH, ABTS and FRAP assays. The content of total phenolics and total flavonoids was found to be mg 37.29 mg Gallic acid equivalents/g and 111.47 mg Quercetin equivalents/g of extract respectively. Tea prepared by brewing dried flowers at 90, 95 and 100°C for 3, 5 and 10 minutes were evaluated for antioxidant activity FRAPS method [63]. Total phenolic content was higher in tea that was brewed for 10 minutes. The tea samples exhibited ferric reducing potential. The study carried out by Pradhan and Bhatnagar [24] revealed dose dependent antioxidant activity of various solvent extracts of *A. leptopus* leaf (evaluated by DPPH and nitric oxide radical scavenging activity and FRAP assay). Ethyl acetate and methanol extracts showed marked antioxidant potential while chloroform and hexane extracts displayed lower activity.

Biological Activities of Purified Compounds from *A. Leptopus*

A wide range of compounds have been purified from different parts of *A. leptopus* and investigated for some bioactivities. 4-hydroxycinnamic acid, quercetin-3-rhamnoside, and kaempherol-3-glucoside (Figure 2) isolated from aerial parts of *A. leptopus* were shown to inhibit lipid peroxidation by 19.5%, 41.0% and 60.5%, respectively, at 5 µg/ml concentration. These compounds were also effective in inhibiting COX-1 and COX-2 enzymes indicating their potential antioxidant and anti-inflammatory potential [2]. A compound 2,3,4-trihydroxyl benzaldehyde (Figure 2), isolated from the tea (as a dried extract) prepared from aerial parts of *A. leptopus*, was shown to exhibit inhibitory activity against COX-2 while COX-1 enzyme was not inhibited [28]. Novel anthraquinones isolated from aerial parts of *A. leptopus* were shown to exhibit antibacterial activity [29]. A new steroidal saponin (Figure 2), isolated from crude methanolic extract of leaves of *A. leptopus* was shown to be a noncompetitive inhibitor of xanthine oxidase [64].

Bioactivities of Nanoparticles Synthesized using *A. Leptopus*

Studies have shown the green synthesis of nanoparticles using *A. leptopus*. Nanoparticles produced from *A. leptopus* were shown to exhibit some bioactivities. The study of Gunaie et al. [65] revealed a simple, single pot approach for synthesizing bimetallic Ag/Au nanoparticles using aqueous extract prepared from different parts of *A. leptopus*. Balasubramani et al. [66] screened antioxidant and cytotoxic potential of gold nanoparticles synthesized using decoction of leaves of *A. leptopus*. The nanoparticles exhibited stronger antioxidant effect when compared to leaf extract. The nanoparticles also exhibited marked cytotoxicity against human adenocarcinoma breast cancer (MCF-7) cells with a growth inhibitory concentration (GI_{50}) of 257.8 µg/ml. Sravanthi et al. [67] described the synthesis of copper oxide nanoparticles from copper sulfate solution using leaf extract of *A. leptopus*. The synthesized copper oxide nanoparticles were shown to exhibit potent and moderate antibacterial activity against gram positive gram negative bacterial strains respectively. The gold nanoparticles produced from aqueous extract of *A. leptopus* were found to catalyze the degradation of organic pollutants *viz.* Congo red and Ramazol brilliant blue [68].

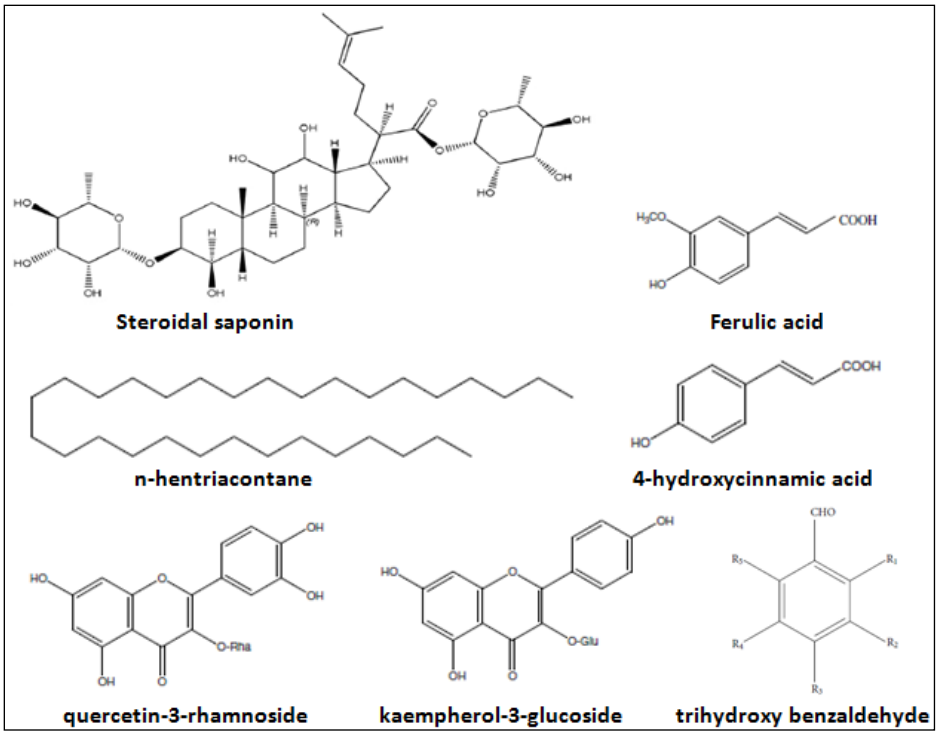

Figure 2: Structures of some compounds identified in *A. leptopus*

CONCLUSION

An extensive literature survey indicated that the plant *A. leptopus* is widely used in ethnomedicine for treatment of several ailments such as skin problems, cough, pain and diabetes. Several pharmacological studies have been carried out using *A. leptopus* and indicated potent bioactivities such as antimicrobial, antioxidant, hepatoprotective, antidiabetic, analgesic, anti-inflammatory and cytotoxic activity. Besides, isolated chemicals from *A. leptopus* have been shown to exhibit antibacterial, enzyme inhibitory and lipid peroxidation inhibition activity. The presence of various phytochemicals in different parts of the plants can be attributed to potential medicinal properties of the plant *A. leptopus*. The plant can be utilized as a remedy for various ailments and to develop drugs with potent pharmacological activities that can benefit human beings.

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