

Review

Astilbe Rivularis: Bioactive Compounds and Pharmacological Functions

Sunita Timalsena¹ and Prem Prasad Lamichhane²

ABSTRACT *Astilbe rivularis* Buch. Ham., a rhizomatous perennial herb of the Saxifragaceae family, has been listed in rare species. In traditional medicine the plant has been used for the treatment of ulcer, bleeding during child birth, inflammation, body ache, diarrhea, and dysentery. This article reviews and analyses the traditional use, pharmacological activities of the corresponding bioactive compounds, and toxicological data on *A. rivularis* species. *A. rivularis* has been used across Indian subcontinent to treat various human ailments. Its extract consists of alkaloids, flavonoids, coumarins and glycosides. These extracts as well as isolated bioactive compounds demonstrated various biological activities including antimicrobial, anti-peptic ulcer, anti-inflammatory, and antioxidant activity. Toxicological studies of the extract on brine shrimp larvae demonstrated mild toxicity; however no acute toxicity in mice. Although the pharmacological effect of *A. rivularis* has been poorly explored, the available data validated its use in ethnomedicine. To reveal the cryptic therapeutic potential of the species, research should focus on identification and mechanistic studies of the bioactive compounds.

KEYWORDS *Astilbe rivularis*, ethnomedical, pharmacological, bioactive compounds, toxicological

From the pre-historic era natural products are playing a promising role in the prevention and treatment of human ailments.⁽¹⁾ To date, many compounds possessing pharmacological properties have been extracted from these products and successfully used to treat human diseases.⁽²⁻⁴⁾ Among these, the genus '*Astilbe*' Buchanan-Hamilton ex D. Don is popular with a long history of use in traditional medicine. It is rhizomatous perennial herb belonging to the family Saxifragaceae. Variation in the color of flowers like white, pink, yellow, and red make this genus distinct.⁽⁵⁾

The genus comprises of 20 species. Among these, the most common species is *Astilbe rivularis* which has been used extensively as Ayurveda in Nepal and India over a long period of time. The extracts from roots, leaves and rhizome have been successfully used to treat diseases like menstrual disorders,⁽⁶⁾ diarrhea, bleeding disorders as well as peptic ulcers.⁽⁷⁾ Despite of all these ethnomedicinal importance, little is explored about this genus possibly due to inadequate knowledge on morphological characters owing to variation in species level and geographical distribution.⁽⁸⁾ Hence, we tried to review and analyse the pharmacological activities of bioactive compounds, and extracts of *A. rivularis* that validated its traditional use. Moreover, this review will help to focus research on *A. rivularis* that help to uncover the

potential compounds and their mechanism of action.

Taxonomic Classification

The classical name varies with geographical boundaries as well as ethnic group. It is commonly called as false buck's beard, perennial spirea in English, Buro-okhati, Buri-okhati, Gosy, Padah, Padum, Polah, Pothee in India,⁽⁹⁾ Bedngo, Bhudoaushadhi, Ganegurjo, Thuloaushadi and many more in Nepal.⁽¹⁰⁾ It is popular as Uran, Ganchhyung, and Pabale among Tamangs of Nepal.⁽¹¹⁾

Distribution

A. rivularis is native to South-East Asia (SEA) and Northern America along the mountain ravines and woodland.^(5,11) In SEA it is predominantly found in Philippines, Myanmar, Thailand, Laos, Nepal, India and Southern Tibet.⁽¹¹⁾ It is predominant in Darjeeling and Sikkim Himalayas of India.⁽¹²⁾ In Nepal, it is distributed mostly on moist hillsides at an altitude of 2000–3000 m.⁽¹¹⁾

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1. Department of Pharmacology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok (10700), Thailand; 2. Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok (10700), Thailand

Correspondence to: Dr. Sunita Timalsena, E-mail: sunitatimalsena@gmail.com

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Botanical Description

A. rivularis is a perennial herb around 0.6–2.5 m tall (Figure 1). Leaves are stalked and pinnately compound. They have the common petiole with brown long pilose. Leaflets measuring (4–14.5) cm × (1.7–8.4) cm are elliptic to ovate and acuminate. Base is cordate or rounded to cuneate, margin doubly serrate. They have adaxially brown long pilose and are glandular hairy along veins. Panicle is around 42 cm with many flowers. The branches measures 1–18 cm and are brown, crisped, glandular, and hairy.^(11,13)

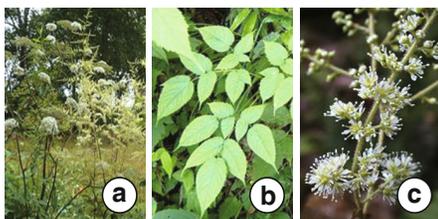


Figure 1. Plant (a), Leaves (b) and Flowers (c) of *A. rivularis*

Flowering season is July to October. Flowers are yellowish white with 5–10 stamens and 2 carpels. Base is connate having sub superior ovary. Sepals are 4 or 5, green, ovate or elliptic to oblong. Petioles have long brown hairs, especially at the point of attachment of the leaflets.^(11,13) Stems are long brown glandular and hairy.^(11,13) Fruiting season is October to November. Fruit is an ovoid capsule and bears ellipsoidal seeds that taper at either end.^(11,13) Although, germination is by vegetative method, it also germinates via seeds in presence of moist and light within 1 to 4 weeks at 15 °C.⁽¹⁴⁾ Roots are thick wiry or rhizomatous.^(11,13)

Ethnomedicinal Uses

The importance of *A. rivularis* is reflected by the fact that all of its parts have ethnomedicinal value. Juice of the plant is applied to sprains and muscular swellings. Root is valued during diarrhea, dysentery, prolapse of the uterus and hemorrhage.⁽¹¹⁾ Rhizome paste along with honey is taken to control postpartum bleeding, diarrhea and dysentery. This paste is also applied over bone fracture and dislocation of joints for quick cure.⁽⁷⁾ The juice of root is beneficial for patients with peptic ulcer, diarrhea and dysentery. Also the root bark is used in body ache and menstrual disorder. Leaves are used as blood purifier.⁽¹⁵⁾

Phytochemistry

A. rivularis contains alkaloids, tannins,

flavonoids, coumarins and glycosides.⁽¹⁶⁾ The principal chemical compounds present include aesculetin, astilbic acid, astilbin, aticoside, dimethylaesculetin, daucosterol, eucryphin, palmitine, peltoboykinoleic acid, scopoletin, sitosterol and stilbene.⁽¹⁰⁾ Bergenin and bergenin derivatives were isolated from the rhizome⁽²⁾ as well as aerial parts. Moreover, β -amyrin and β -sitosterol were also isolated from aerial parts.⁽¹⁷⁾

Pharmacological Activities

Antimicrobial Activity

The incidence of drug resistance against microbes is the major and leading cause for the failure of the antimicrobial agents. The natural products have been able to solve this challenge and further replace those expensive drugs and minimize the side effects.⁽¹⁸⁾ *A. rivularis* and its constituents show significant effect in the prevention and treatment of bacterial as well as viral diseases.

Compounds like arbutin and bergenin in the methanol extract of rhizome of *A. rivularis* have been attributed to act synergistically to show the bactericidal effect against gram-negative bacteria (*Escherichia coli*) in a dose dependent manner. When the *in vitro* anti-microbial activity of the extract was carried out using agar well diffusion assay, minimum inhibitory concentration shown was between 0.0007%–0.00152% with maximum zone of inhibition being around 22 mm.⁽¹⁶⁾ Moreover, the compound bergenin extracted from the rhizome demonstrated antiviral activity against *Herpes simplex virus type I* in Vero cells with half inhibitory concentration (IC_{50}) < 6.25 μ g/mL.⁽¹⁹⁾ Besides this, bergenin was shown to possess anti-influenza A virus activity with IC_{50} value < 6.25 μ g/mL.⁽¹⁴⁾

This implies that potentiality of *A. rivularis* as antimicrobial needs to be explored with diverse range of bacteria and viruses.

Anti-peptic Ulcer Activity

Peptic ulcer is the gastro-intestinal disorder which occurs due to the imbalance between the offensive (acid, pepsin and *Helicobacter pylori*) and defensive factors (mucin, prostaglandin, bicarbonate, nitric oxide and growth factors).⁽²⁰⁾ This leading cause of gastrointestinal disease has annual incidence rate of 0.1%–0.19% and prevalence rate of 0.12%–1.5% in countries like the United States, and European nations (the United Kingdom, the Netherlands, Spain, Finland, Denmark,

Belgium).⁽²¹⁾ Though there are modern medicines to treat peptic ulcer but the incidences of relapse, adverse effects and threat of drug-drug interaction has led to search for alternatives like medicinal plants.

Root powder of *A. rivularis* was shown to possess anti-peptic activity in both gastric and duodenal ulcers. Rats pretreated with root powder were induced of gastric ulcer. It was shown that protective efficiency was around 50%, 55%, 54.79%, 61.01%, and 56%, respectively, for ulcer induced by either ethanol or hydrochloride or indomethacin or swimming stress or pyloric ligation. However, the anti-peptic activity was less than that of the standard treatment: omeprazole⁽²²⁾ and the active constituents underlying this activity need to be elucidated. Moreover, pretreatment of rats with the root powder showed around 54.83% protection from duodenal ulcer induced by cysteamine.⁽²³⁾

Apart from the root, leaves of *A. rivularis* were also shown to possess the anti-ulcerogenic activity. But this activity varies with the seasonal collection. Albino rats were orally fed with powder of the leaves 0.5 h prior to the induction of gastric ulcer by ethanol and duodenal ulcer by cysteamine hydrochloride and measured for anti-ulcerogenic activity. The anti-ulcerogenic activity of collected leaves showed seasonal variations with maximum activity (anti-gastric ulcer activity -51.98%, anti-duodenal ulcer activity -47.84%) in May-June and minimum in January-February (anti-gastric ulcer activity -4.96%, anti-duodenal ulcer activity -3.01%).⁽²³⁾ These seasonal variations in the anti-ulcerogenic activity of leaves; as well as the involved active compounds need to be explored.

Anti-inflammatory Activity

Inflammation is the physiological defense

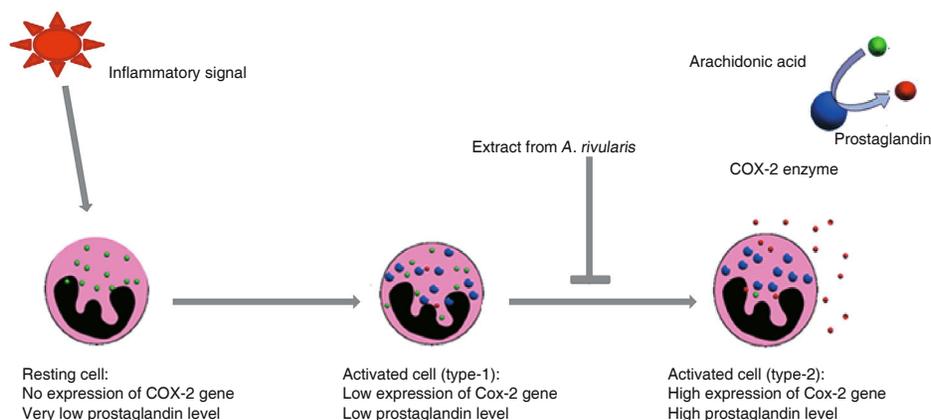


Figure 2. Inhibition of COX-2 by *A. rivularis*

mechanism that helps body to protect against infection, burn toxic chemicals, allergen and other stimuli. The unbalanced inflammatory process plays a vital role in the development and progression of severe diseases.⁽²⁴⁾ *A. rivularis* has been long known for its anti-inflammatory activity. Oral administration of dried rhizome at a dose of 200 mg/kg body weight was shown to inhibit carrageenan induced Albino rat paw inflammation by 56.20% at 24 h. This anti-inflammatory activity was comparable with standard dose (20 mg/kg body weight) of non-steroidal anti-inflammatory drug, the Ibuprofen.⁽²⁵⁾ The observed anti-inflammatory activity could be attributed for the presence of flavonoids;⁽³⁾ bergenin and astilbic in context of *A. rivularis*.⁽¹⁰⁾ These compounds inhibited cyclooxygenase-2 (COX-2) activity halting the release of prostaglandins⁽²⁾ as shown in Figure 2. These observations are promising for the use of natural products.

Antioxidant Activity

Antioxidants are the substances that protect the cells from the damage caused by unstable molecules known as free radicals. Many plants have been identified with the property free radical scavenging activity which can protect against chronic oxidative stress. The flavonoids present in the plant are the most potent compounds to act as antioxidant.⁽²⁶⁾

The extract of *A. rivularis* has been shown to possess potent antioxidant activity. A dose of 100 μ g/mL of plant (bark) extract exhibited antioxidant activity of 95.23% as measured by 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical assays, 80.40% as measured by superoxide scavenging activity, and 45.83% as measured by lipid peroxidation. This was comparable with reference standard.⁽²⁵⁾ Moreover, we evaluated the antioxidant activity of *A. rivularis*.

Our study revealed that the extract with effective concentration 50 (EC₅₀) of 4.05 µg/mL possessed potent potential to reduce free radicals as measured by DPPH assay. Also, we evaluated the ability of extract to reduce hexaferricyanide to hexaferrocyanide by Fe³⁺-Fe²⁺ transformation assay and found a dose dependent reduction with 90% reduction by 100 µg/mL of extract. Further, we determined total phenol and flavonoid contents in the extract of *A. rivularis*. The total phenolic and flavonoid contents were found to be more than 183 mg gallic acid equivalent per gram dry weight of extract and 857 mg quercetin equivalent per gram dry weight of extract, respectively.⁽²⁷⁾ However, the active compounds in the extract that showed the antioxidant activity needs further elucidation. The identification, isolation and characterization of active antioxidant compounds in the extract are the interest of future research.

Other Activities

Apart from the above mentioned pharmacological activities, a little has been reported for other activities of *A. rivularis*. It was also found that *A. rivularis* possessed activity against urolithiasis induced by 3% glycolic acid in albino rats.⁽²⁾ Although these results are promising, additional research is needed to support the anti-urolithiasis activity of *A. rivularis* extract and identification of active compound(s). The potent compound bergenin present in the root has been reported to possess antitussive property,⁽¹⁴⁾ analgesic, antifeedant, antiarrhythmic, hepatoprotective, hypolipidemic and antipyretic activities.⁽²⁸⁾ The pharmacological potential of the plant and its extract needs to be studied in depth to reveal its potential use in the cure of human ailments.

Dosage

The dried rhizome of *A. rivularis* is the main part which is used during the treatment of different diseases. The juice of root about 6 teaspoons 3 times a day is given to the patient with peptic ulcer, diarrhea and dysentery. For the treatment of toothache, a few pieces of rhizomes are used as infusion or poultice or as a powder. Similarly, decoction prepared from the rhizome is given 1–2 times daily at a dose of one cup to treat body ache during childbirth. The mixture of ghee with 100 mg of rhizomes thrice per day for 3 days induce uterine contraction during parturition.⁽¹⁵⁾

Toxicological Studies

Cytotoxicity study of *A. rivularis* and its extract has been reported in some studies. The methanolic

extract of dried rhizome of *A. rivularis* was screened for cytotoxicity against brine shrimp larvae at different concentrations: 1000, 750, 500, 100, 80 and 10 parts per million (ppm) to determine the lethal concentration 50 (LC₅₀). The LC₅₀ was found to be 92.01 ppm which was considered as mildly toxic. However, it was shown that the acute exposure of plant extract possesses no any danger of toxicity.⁽¹⁶⁾ Acute toxicity study in mice administered with oral doses 100, 200, 500, 1000 and 3000 mg/kg did not show any toxic symptoms.⁽¹⁹⁾ In other study, oral administration of root powder in doses ranging from 100 to 3000 mg per kg body weight in albino mice showed normal physical behavior and absence of organ toxicity with 100% survival.⁽²²⁾ As the herbal extract consists of many chemical constituents, using high amount of crude extract may lead to toxicological effects. Hence, enough toxicological assessment of the plant and its extract is warranted.

Conclusion

Ayurveda has described the beneficial effects of *A. rivularis* during childbirth and viral infection. However, enough research on its potential effects is still lacking restricting it to ethnomedicine. Hence, further studies on isolation and assessment of medicinal values of the potential compounds in needed. On the other hand, the attack of pathogen named *Pucciniostele clarkiana* especially in the leaves of this plant leads to the occurrence of chlorosis on leaf lamina.⁽²⁹⁾ Due to this, *A. rivularis* is declining and listed as a rare specy. Therefore, intense effort must be carried out for its preservation.

Future Prospects

There are several medicinal plants like *A. rivularis* that possess immense potential for new drug development. But, they are in the state of continuous extinction due to deforestation and urbanization. Moreover, the emerging diseases and the serious side effects of commercial medications, the herbal formulations are gaining their importance. As plants are valuable source of bioactive compounds, they can serve as the source of molecular target for drug development and pharmacological applications. Even they can provide relief from the costly modern medicines. Another major problem for the use of herbal medicines is that there are only few formulations that have been experimentally validated and scientifically approved. Therefore, it is being necessary to screen plants with pharmacological significance and prove them scientifically for the development of new and effective therapeutics.

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Conflict of Interest

The authors declare that they have no competing interests.

Author Contributions

Timalsena S and Lamichhane PP conducted this review. Both authors wrote the manuscript. Both read and approved the final version of the manuscript.

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