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Review Article

Phytochemistry, pharmacology, and novel clinical applications of *Aconitum heterophyllum*: A compressive review.

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ABSTRACT

Aconitum heterophyllum is a medicinal plant native to India that belongs to the Ranunculaceae family. *A. Heterophyllum* is reported to have a variety of medicinal properties. Since ancient times, this plant has employed several formulations in India's traditional treatment system, Ayurveda. It has been used to treat urinary infections, diarrhea, and inflammation in patients. It's also been utilized to promote hepatoprotective activity and as an expectorant. Alkaloids, carbohydrates, proteins and amino acids, saponins, glycosides, quinones, flavonoids, terpenoids, and other compounds have been discovered in various plant portions, according to chemical investigations. The therapeutic characteristics of *A. Heterophyllum*, as well as their phytochemistry and pharmacognosy, are discussed in this study. Scientific data on the plant was gathered from various sources, including electronic sources (Google scholar, Pubmed) and some old Ayurvedic and ethnopharmacology textbooks. The research also includes a review of the literature on *A. heterophyllum*, as well as the most relevant pharmacological and other results on this drug. This review article should be helpful to new researchers who are starting a study on the plant *A. heterophyllum* and will serve as a beneficial tool for them.

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INTRODUCTION

Traditional medicine encompasses health practices, approaches, knowledge, and beliefs that include plant, animal, and mineral-based medicines, spiritual therapies, manual techniques, and exercises, which are used singly or in combination to treat, diagnose, and prevent illnesses, as well as to maintain well-being. Traditional medicine has grown in popularity in Cameroon during the last decade, owing in part to the country's long-term unsustainable economic position. The therapeutic approach to alternative traditional medicine as a possibility for a concerted search for new chemical entities has been prompted by the high cost of pharmaceuticals and the rise in drug resistance to prevalent ailments such as malaria, bacterial infections, and other sexually transmitted diseases (NCE). The World Health Organization (WHO) has established a strategic framework for the practice and development of TM in Cameroon in partnership with the Cameroon government (Fokunang, 2011). Aconitum heterophyllum (A. Heterophyllum) is an ayurvedic medicinal plant that is utilized as the major ingredient in several Ayurvedic formulas in India. Aconitum species are also commonly utilized in Chinese and Bhutanese herbal medicine. In Indian English, this plant is known as atees and atis root; in Sanskrit, it is known as ativisha, shuklakanda, aruna, and vishada; in Urdu, it is known as atees; in Hindi, it is known as atis and atvika; in Bengali, it is known as ataish; in Telugu, it is known as ati vasa (Paramanick, 2017). The plant kingdom's 'Magnoliophyta' division includes A. Heterophyllum, which belongs to the

Ranunculaceae family, and the Aconitum genus (Anonymous, 2008). There are around 300 species of Aconitum worldwide, with 24 species identified in India. The dried tuberous roots of A. heterophyllum Wall. ex. Royle, a perennial plant native to the western Himalayas and found in Kashmir, Uttarakhand, Sikkim, and Nepal at altitudes between 2,500 and 4,000 m, are used to make medicinal A. Heterophyllum. The majority of the species are highly toxic, earning them the title of "Queen of all Poisons," with numerous species having been utilized on the ends of hunting spikes and still being used today. As a result, this plant must be handled with caution (Beigh, 2008; Singh, 2015).

Antidiarrheal, expectorant, diuretic, hepatoprotective, antipyretic and analgesic, antioxidant, alexipharmic, anodyne, anti-atrabilious, anti-flatulent, anti-periodic, anti-phlegmatic, and carminative properties have been reported for A. Heterophyllum; it can also be used to treat patients with reproductive disorders (Shyaula, 2012; Verma, 2010; Ukani, 1996). Figs. 1, 2 show pictures of the plant and its root. Table 1 presents its scientific classification.

Table 1. Scientific classification of *Aconitum Heterophyllum* (Anonymous, 2008).

Kingdom:	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Order	Ranunculales
Family	Ranunculaceae
Genus	Aconitum
Species	*A. heterophyllum*

Description

The roots of *A. Heterophyllum* are white-grey in color and range in length from 2.0 to 7.5 cm, with upper extremities 0.4-1.6 cm thick or more, tapering to a tapered end (Fig. 2). Simple and branching stems are 15 to 20 cm tall and green in hue. A. Heterophyllum is a tiny plant with a straight stem and branches on occasion. It's a tree that blooms in August and September with blue or yellow flowers (Fig. 1). This herb's leaves feature a heteromorphous dark green color. The leaves' upper halves are amplexicaul, while the lower portions are lengthy petioles. The plant is arranged in a spiral (alternative) pattern (Rajakrishnan, 2016). Tables 2 and 3 show the macroscopic and microscopical properties of the plant, respectively.

Phytochemistry

Aconitum heterophyllum includes diterpene alkaloids such as heterophylline, heterophyllidine, heterophyllisine, and hetidine, as well as atidine, atisine, hetisine, and heteratisine. Aconitic acid, tannic acid, pectin, abundant starch, flat, oleic, palmitic, and stearic glycerin combination, vegetable mucilaginous materials, sucrose, and ash 2 percent are all present in the tuber. 0.79 percent of total alkoloids are found in the roots. Atisenol, Atsine, Heteratisine, Histisine, heterophyllisine, heterophylline, heterophyllidine, – atidine, Hetidine, Banzolheteratisine, F-dihydroatisine, and Hetisinone are reported to have been isolated (Paramanick, 2017).

Figure 1. Aerial parts of *Aconitum heterophyllum.*

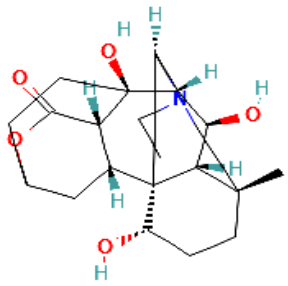
Figure 2. Roots of *Aconitum heterophyllum.*

Pharmacological activity

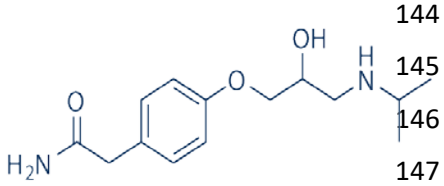
Heterophyllum is used for a variety of therapeutic purposes. When combined with fine powdered dry ginger, Beel (Bellpetra in India), or Nutmeg, it is said to have antidiarrheal properties (jaiphal in India). When consumed with milk, the root's juice functions as an expectorant. As a diuretic, the seeds are employed. The herb also has hepatoprotective, antipyretic and analgesic, antioxidant, alexipharmic, anodyne, anti-atrabilious, anti-flatulent, anti-periodic, anti-phlegmatic, and carminative qualities, and is used to treat individuals with reproductive issues.

Antiplasmodial activity

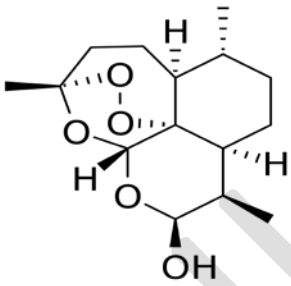
This study aimed to conduct a phytochemical investigation of A. heterophyllum roots for the preparation of extract, fractions, and isolation of pure molecules to identify active fractions/molecules responsible for the anti-plasmodial activity, and



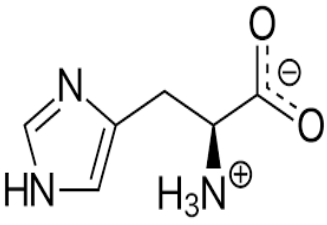
Heterophyllidine



Atisenol



F-dihydroartemisinin



Hetidine

Figure 3. Major phytochemicals of *Aconitum heterophyllum.*

Ant-inflammatory activity

Using chromatographic separation techniques, the phytochemical components of Aconitum heterophyllum were extracted and described, and their structures were explained using nuclear magnetic resonance techniques. The plant possesses ant-inflammatory activity which was evaluated by using cotton pellet granuloma method (Buddhadev, 2017).

Another study found that clinical and therapeutic potential of *Aconitum heterophyllum*. The constituents of *Aconitum heterophyllum* such as alkaloids, flavonoids, diterpenoid and nonditerpenoid compounds were isolated and characterized by using chromatographic separation techniques. The study of the structure of these compounds were done by the technique of nuclear magnetic resonance. The anti-inflammatory activity of ethanolic root extract of *Aconitum heterophyllum* was determined by cotton pellet induced granuloma in rats. The results revealed the activity (Sadia, 2015).

Hepatoprotective activity

The phytochemistry and pharmacognosy as well as the medicinal properties of *Aconitum heterophyllum*. *Aconitum heterophyllum* has been used in some formulations in the traditional healing system of India (Ayurveda). It was reported to have use in treating patients with urinary infection, diarrhea and inflammation. The plant has been also used as an expectorant and for the promotion of hepatoprotective activity. The chemical studies of plant have revealed that it contains alkaloids, saponins, glycosides, flavonoids etc (Debashish, 2017).

Another study revealed that the hepatoprotective activity of ethanolic extract of *Aconitum heterophyllum* root in Parecetamol induced hepatic damage in wistar albino rats. The hepatoprotective activity of ethanolic extract of *Aconitum heterophyllum* root was evaluated by the assessment of biochemi parameters such as SGOT, SGPT, ALP, total bilirubin, serum protein and histopathological studies of the liver. Ethanolic extract of the *Aconitum heterophyllum* root significantly reduced the liver damage and all biochemical parameters (Venu, 2013).

Anti-diarrheal activity

Current study evaluated anti diarrheal activity of ethanol extract of *Aconitum heterophyllum* at 50, 100 and 200 mg/kg using fecal excretion and castor oil induced diarrheal models. The results depicted a significant reduction in normal fecal output. The study concluded antisecretory and antimotility effect of *Aconitum heterophyllum*, which mediates through nitric oxide pathway (Satyendra, 2014).

Antifungal Activity

The antifungal and antioxidant activity of *Aconitum heterophyllum.* The invivo antifungal activity of *Aconitum heterophyllum* were determined by measuring diameters of inhibitory zones of the extract against *Aspergillusniger* and *Alternaliasolani.* Against

both species examined, the methanolic extract of Aconitum heterophyllum demonstrated substantial antifungal activity. The extract also showed antioxidant activity, measured using a radical scavenging method (Neelma, 2014).

Antibacterial activity

The antibacterial activity of Aconitum heterophyllum root alkaloid extract. S. aureus, B. bronchiseptica, B. subtilis, P. putida, and X. campestris were all resistant to this alkaloid extract. The present study revealed the antibacterial activity of all alkalids from root was due to synergistic effect of different alkaloids (Yoirentomba, 2014).

Hypolipidemic effect

The hypolipidemic effect of methanol fraction of *Aconitum heterophyllum* wall. The use of Aconitum heterophyllum was found to lower serum TG and LDL-C levels. Aconitum heterophyllum also aids in the improvement of lipid HDL-C levels. The results suggest that Aconitum heterophyllum's alteration in lipid profile is attributable to the inhibition of HMGR and the activation of LCAT enzymes. The extract also able to block intestinal fat absorption which helps to reduce cholesterol level. Hence, *Aconitum heterophyllum* methanol fraction exhibits potential hypolipidemic activity (Arun, 2012).

Antioxidant activity

Standardization of physicochemical parameters and evaluation of Aconitum heterophyllum antioxidant activity in vitro. The quantitative estimations shows that the root to be highly rich in alkaloids while phenols, tannins, flavonoids and saponins were found in less quantity. The in- vitro antioxidant study showed a moderate to low activity in all models which may be due to low phenolic and flavonoid content (Satyendra, 2012).

Anticancer activity

We recently synthesized from aconitine a series of drugs with in vitro and in vivo antitumor properties, among which bis[O-(14-benzoylaconine-8-yl)]suberate (BBAS) was the most active (Eur J Med Chem 2012; 54: 343). In the present work, we used the NCI panel of 60 human tumor cell lines to identify the most sensitive cell lines and drugs with comparable cytotoxicity profiles. GI50 values of BBAS ranged between 0.12 and 6.5 μM. Activity was higher than average for leukemia and melanoma cell lines, especially SK-MEL-5 and SK-MEL-28, for the COLO-205 and HT-29 (colorectal) and MDA-MB-468 (breast) cancer cell lines. Together, our results allowed the identification of a potentially new class of anticancer agent displaying a mechanism of action related to that of nitrosoureas (Chodoeva, 2014).

CONCLUSION

Global interest in the investigation of natural herbs and traditional medicines is increasing day by day due to the presence of novel medicinal agents having promising pharmacological values and their ability to treat various diseases. A wide range of plant-derived phytomedicine has entered the global market due to its medicinal importance and explores globally for the utilization and treatment of several types of diseases. Similarly, *Aconitum heterophyllum* is a versatile plant cultivated all over the world with a plethora of medicinal value. Almonds are a rich source of minerals and a wide range of phytochemicals such as Atisenol, Atsine, Heteratisine, Histisine, heterophyllisine, heterophylline, heterophyllidine, – atidine, Hetidine, Banzolheteratisine, F-dihydroatisine and Hetisinone and lignans with diverse medicinal importance. Thus, it is concluded that there is a wide scope for scientific investigations to explore its nutritional and medicinal value to claim the traditional use as well as exploring novel and promising lead compounds from almonds. In the current review, the authors are trying to present and compile all major information related to its phytochemical and pharmacological behavior published till now.

CONFLICT OF INTEREST

None declared.

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REFERENCES

Anmol, Kumari S, Kumar R, Singh R, Aggarwal G, Agrawal P, Sahal D, Sharma U. Antiplasmodial diterpenoid alkaloid from *Aconitum heterophyllum* Wall. ex Royle: Isolation, characterization, and UHPLC-DAD based quantification. Journal of Ethnopharmacology. 2022; 287:114931.

Anonymous. The ayurvedic Pharmacopoeia, 2008; 2:15 6-67.

Arun K, Anu Augustine. Hypolipidemic effect of methanol fraction of *Aconitum heterophyllum* wall ex Royle. Journal of Advanced Pharmaceutical Technology and Research. 2012; 3(4): 224-228.

Beigh SY, Nowchoo IA, Iqbal M. Cultivation and conservation of *aconitum heterophyllum*: a critically endangered medicinal herb of the Northwest himalayas. J Herbs Spices Med Plants. 2008;11(4):47-56.

Buddhadev, SG, Buddhadev. SS. A complete review on *ativisha –Aconitum heterophyllum.* An International Journal of Pharmaceutical Sciences. January- March 2017; 8(1): 111-114.

Chodoeva A, Bosc JJ, Lartigue L, Guillon J, Auzanneau C, Costet P, Zurdinov A, Jarry C, Robert J. Antitumor activity of semisynthetic derivatives of Aconitum alkaloids. Invest New Drugs. 2014;32(1):60-67.

Debashish P, Ravindra P, Shiv, SS, Vikash S. Primary Pharmacological and Other Important Findings on the Medicinal Plant "*Aconitum heterophyllum*" (Aruna). Jounal of Pharmacopuncture. 2017; 4(2):47-46.

Fokunang CN, Ndikum V, Tabi OY, Jiofack RB, Ngameni B. Traditional medicine: past, present and future research and development prospects and integration in the National Health System of Cameroon. African journal of traditional, complementary, and alternative medicines. 2011, 8: 284–295.

Neelma M, Wasqa I, Imran A. Evaluation of antifungal and antioxidant potential of two medicinal plants: *Aconitum heterophyllum* and *Polygonum bistorta* . Asian Pacific Journal of Tropical Biomedicine. 2014; 4(2): S639-S643.

Paramanick D, Panday R, Shukla SS, Sharma V. Primary Pharmacological and Other Important Findings on the Medicinal Plant "*Aconitum Heterophyllum*" (Aruna). Journal of Pharmacopuncture. 2017, 20(2):89-92.

Paramanick D, Sharma N, Parveen N, Patel N, Keshri M. A review article on ayurvedic/ herbal plant? aruna?. International Journal of Advanced Research. 2017;5(2):319-325.

Rajakrishnan R, Lekshmi R, Samuel D. Analytical standards for the root tubers of ativisha - *aconitum heterophyllum* Wall. ex royle. International Journal of Scientific and Research Publications. 2016;6(5):531-4.

Sadia, K, Muhammad, SA, Kainat, FM. Clinical and therapeutic potential of *Aconitum heterophyllum.* Journal of Coastal Life Medicine. 2015, 3(12): 1003-1005.

Satyendra KP, Divya J, Dinesh KP. Antisecretory and antimotility activity of Aconitum heterophyllum and its significance in treatment of diarrhoea. Indian Journal of Pharmacology. 2014; 46(1): 82-87.

Satyendra KP, Kumar, R., Patel, DK., Sahu, AN., Hemalatha S. Physicochemical standardization and evaluation of *in-vitro* antioxidant activity of *Aconitum heterophyllum* Wall. Asian Pacific Journal of Tropical Biomedicine. 2012; S526-S531.

Shyaula SL. Phytochemicals, traditional uses and processing of aconitum species in Nepal. Nepal Journal of Science and Technology. 2012;12:171-178.

Singh K, Saloni S, Shalini. Phytochemical screening and TLC profiling of different extracts of leaves, roots and stem of *aconitum heterophyllum* a rare medicinal plant of himalayan region. International Journal of Pharmaceutical and Biological Sciences. 2015;6(2):194- 200.

Ukani MD, Mehta NK, Nanavati DD. *Aconitum heterophyllum* (ativisha) in ayurveda. Anc Science of Life. 1996;16(2):166-171.

Venu GRK, Madhavi E, Lakshmipathy P. Evaluation of hepatoprotective activity of ethanolic extract of *Aconitum heterophyllum* root in paracetamol induced liver toxicity. International Journal of Pharma and Biosciences. 2013; 4(4): 714-721

Verma S, Ojha S, Raish M. Anti-inflammatory activity of *aconitum heterophyllum* on cotton pellet-induced granuloma in rats. Journal of Medicinal Plants Research. 2010;4(15):1566-9.

Yoirentomba M, Sanjeev K, Sachin H, Arun S. Antibacterial property of *Aconitum heterophyllum* root alkaloid. International Journal of Advanced Research. 2014; 2(7): 839-844.