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# **Review Article**

# ATIVISA (ACONITUM HETEROPHYLLUM WALL EX. ROYLE): A COMPREHENSIVE REVIEW ON PROPAGATION, TRADITIONAL USES AND PHARMACOLOGY

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**KEYWORDS:** *Aconitum heterophyllum, Ativiṣā,* Diarrhoea, Atisine.

#### **ABSTRACT**

Aconitum heterophyllum Wall ex. Royle is considered an important medicinal plant in traditional system of medicine as the tuberous roots are used for curing different ailments. But over grazing, prolong seed dormancy and many other reasons have led to the exploitation of this plant, so conservation through various modes is the need of the hour. Aims: The present review aims for accounting extensive information on different methods of propagation, traditional uses and pharmacological activities of Aconitum heterophyllum. **Review Methods:** A literature search was done on Aconitum heterophyllum using relevant Ayurvedic and contemporary texts. Different scientific databases such as Pubmed, Scopus, EBSCO, Google Scholar Information were used to collect all information regarding propagation and pharmacology of this plant. **Results:** Available data has reported that this endangered plant can be propagated through various methods such as raising propagules from seeds and daughter tubers, and other plant tissue culture techniques. Plant has reported to have 0.79% of total alkaloids in roots, out of which Atisine (0.4%), Heteratisine (0.3%), histisine, heterophyllisine, heterophylline, heterophyllidine are some major alkaloids. It also possesses important pharmacological activities like antibacterial activity, anti-diarrhoeal activity, enzyme-inhibition activity, antiinflammatory activity, hepato-protective activity and anti-spasmodic activity. **Conclusion:** The results of this review clearly suggests about the valuable traditional use of Aconitum heterophyllum in curing various ailments like diarrhoea, dysentery, bilious complaints, intermittent fever and diseases of children. Further research: Different traditional uses mentioned in Ayurveda texts need further validation through different experimental and clinical studies which is a recommendation of this review.

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#### INTRODUCTION

Aconitum heterophyllum Wall. ex. Royle is described with the synonyms of Aconitum atees Royle and Aconitum cordatum Royle. The plant is known as Ativiṣā in Sanskrit and Atis roots or Indian atis in English. Ativiṣā consists of dried, tuberous roots of Aconitum heterophyllum Wall. ex. Royle (Family: Ranunculaceae). It is a perennial herb, native of western Himalayas and found in Garhwal, Kumaon and Kashmir at altitude between 2,500-4,000m. The plant is common in temperate to alpine zones of

the Himalaya, from Indus to Kumaon, among Shrubs on grass, riverbeds and slopes, occurring in Jammu & Kashmir, Himachal Pradesh and Uttaranchal formerly Uttar Pradesh.<sup>[3]</sup> The plant is in endangered state, so propagation is the need of the hour. The plant thrives well in moist soils and in the light shade of trees, grows well in heavy clay and calcareous soil. Propagation can be done by seeds and vegetative methods.<sup>[1]</sup> This tall herb possess paired white tuberous roots, variable leaves, racemes bearing blue

flowers and follicles enclosing blackish ob-pyramidal seeds.[4] The daughter tubers are usually preferred for the therapeutic purpose. Shriveled mother tubers are often sold as inferior grade drugs. The root contain nontoxic, amorphous alkaloids: Atisine (0.4%), Dehydroatisine, heteratisine and hetisine.<sup>[5]</sup> Atisine exhibits lesser toxicity than aconitine.[4] The root is considered astringent and prescribed in diarrhoea, especially in infants, and for dyspepsia, vomiting and cough.[6] The chief use of *Ativiṣā* is in the treatment of intermittent fever and other periodical fevers, and in these, it often proves most valuable. For combating the debility after fevers and other diseases, it is an excellent tonic, in dose of five to ten grains thrice daily.<sup>[7]</sup> Studies have reported that the plant possesses potent anti-viral, anti-diarrheal and immune stimulant properties.[8] The alkaloids mesaconitine and 3 acetylaconitine are reported to possess anti-inflammatory activity.[9] The aim of this review is to focus on the detailed morphology, propagation, traditional and other ethno-medicinal uses, and pharmacological activities of this wonderful herb.

#### **Review Methods**

Ancient Ayurvedic compendia and other contemporary texts like The Avurvedic Pharmacopoeia of India, reviews on Indian medicinal plants, Indian material medica were reviewed critically to collect all valuable information regarding traditional uses of this endangered medicinal plant. The reason to choose *Aconitum heterophyllum* is the high medicinal value and endangered status of the plant. So, a detailed search was done on different methods of propagation in published research work of peer-reviewed journals. All relevant worldwide accepted databases were searched for the terms "Aconitum heterophyllum", "Ativisa" and "Atees". The literatures available accessible on Aconitum heterophyllum were collected via electronic search using PubMed, Scopus, Science Direct, Google scholar and other traditional books on medicinal plants.

#### **Morphology**

Aconitum heterophyllum Wall ex. Royle. is a Critically Endangered (CR) species. In the Kashmir Himalayas, it constitutes very scattered populations. [10] Aconitum heterophyllum is an erect, leafy herb which is 15cm-2m high having biennial, paired tuberous roots [Figure 1]. Stem is erect, simple or branched, 15-90cm. high, terete, glabrous below, finely crispo-pubescent in the upper part. Leaves are hetero-morphous, glabrous, or the upper ones sparingly pubescent with a few very short crispate hairs; the lowermost leaves with long petioles are usually present at the time of flowering, orbicular-cordate to ovate-cordate in outline, usually deeply 5-

lobed with crenate lobes: the upper leaves are with sessile. short petioles or semi-amplexicaul. intermediate leaves are shortly petioled or sessile, ovate-cordate, often acuminate, 3.5-12cm long, 2.5-7.5cm broad, inciso-crenate or serrate[Figure 2]. Inflorescence is a slender raceme or a lax, leafy panicle or in alpine specimens reduced to few flowers, crispo-pubescent; floral leaves are like the preceding infra floral leaves, but smaller, passing upwards into the rapidly decreasing ovate or lanceolate, crenate or (the uppermost) entire bracts; bracteoles, if present are at or above the middle of the pedicel, elliptic or oblong; pedicels are erect and in the mature state, often adpressed to the rachis. Sepals are more or less blue or violet to greenish blue with purplish veins in panicles, rarely whitish, finely pubescent or glabrous; upper sepals are almost navicular obliquely erect, shortly or obscurely beaked, 18-20mm high; lateral sepals are oblique and broadly obovate with dark tips, 14-20mm long, 12-20mm broad, not clawed; lower sepals are elliptic, obtuse or sub-acute, 8-10 mm long. Nectariesare glabrous, extinguisher-shaped; hood is short upto 4mm and very wide, more or less gibbous above, lip very short and broad, obtusely 2-lobed or entire.[11-12] Filaments are pale green, glabrous or minutely hairy; anthers are brown in colour. Carpels are 5, contiguous, elliptic-oblong, shortly contracted into the slightly shorter style, crispo-pubescent with adpressed hairs [Figure 3]. Follicles are contiguous, linear-oblong, straight, 16-18mm. long, more or less glabrescent, straight, five-chambered [Figure 4]. Seeds [Figure 5] are obpyramidal, 3-4mm long, blackish brown, angles acute or more or less winged, faces smooth.[13] The daughter tuber is thick, cylindrical, fusiform or conical. The external surface is slightly wrinkled or nearly smooth, pale yellow to light brown in colour. Rootlet scars are very few [Figure 6]. The bark is thin and remnants of innovation bud are present at the crown of the root. Internally, the root is pale white and chalky, cambium is discontinuous forming (usually 4 or 5) isolated, slender, cylindrical strands arranged in a ring. The taste of the root is slightly bitter without any tingling sensation.[14]

## **Chemical Composition**

Aconitum heterophyllum Wall. ex Royle is a good source of diterpene alkaloids (0.7%).<sup>[15]</sup> It contains nontoxic, amorphous alkaloids, atisine, dihydroatisine, heteratisine and hetisine; alkaloid Atisine is physiologically a relatively inactive substance.<sup>[16]</sup> The roots also contain Veatchine; Atisenol; 6 Acetylheteratisine, 6 Benzoyl heteratisine, Heterophyllidine, Heterophyllisine. <sup>[17]</sup> The roots in total yield 0.79% of total alkaloids, of

which Atisin is 0.4%. Atisine is much less toxic than aconitine and pseudoaconitine.<sup>[18]</sup> It also contains aconitic acid, tannic acid, a mixture of oleic, palmitic, and stearic acids, glycerides, and vegetable mucilage in addition to starch and sugars. In a preliminary study, roots and leaves of the plant were found to contain alkaloids while saponins and flavonoids were found to be absent. The stem however, contained

flavonoids while saponins and alkaloids were absent.[19]

## **Propagation**

The herb could be cultivated both from the daughter tubers and from seeds. By the end of the growing season, a plant usually produces one or two daughter tubers, which arise from the parent tuber. (Table 1)

Table 1: Conservation parameters of Aconitum heterophyllum Wall ex. Royle

Parameters	Description
Raising Propagules from daughter tubers	The daughter tubers are collected during autumn at the end of the growing season when the aerial shoots had senescenced. Then the daughter tubers are sown in sandy loam soil. Sufficient humus and moisture must be ensured in the sowing plots. With the onset of the next growing season, the daughter tubers grow and produce young leafy shoots which grow further.
Raising propagules from seeds	The seeds exhibit prolonged dormancy. Chilling of the seeds for 30-45 days before sowing gives encouraging results. The seedlings so produced remain in the vegetative phase for atleast 2 years; they reproduce in the third year.
Climate and soil	Plant grows well in moist soils and in the light shade of trees, it also prefers heavy clay and calcareous soil.
Harvest management	The crop will be ready for harvesting after about 3-4 years. Tubers are harvested in the months of November-December, when the aerial shoots had senescenced. These harvested tubers are washed thoroughly, dried in shade and heated at 40°C for an hour. The dried roots so obtained are then grind to fine powder in order to obtain the crude powdered drug. <sup>[20]</sup>
Tissue culture techniques	Tissue culture techniques can also be adopted to enable the mass propagation of this endangered plant. Seeds can be soaked in double distilled water for 2-3 days at 4°C in a refrigerator. Surface sterilization of seeds can be done by using 0.1% mercuric chloride for 3-4 min so as to remove all traces of sterilant. The sterilized seedlings can be kept in dark at 20°C on moist abosorbent cotton in the petri plates. The germinated seedlings can be inoculated on Murashige and Skoog, 1962 basal media fortified with 3% sucrose. This media can be then dispensed into culture tubes and autoclaved for 20 min at 1.5lb pressure and 121°C temperature. This process results in full fledged seedling formation after 4 weeks of their culture. [21]
	Numerous other works have also been done for the improvement of seed germination and dormancy breaking system. Higher concentration of BAP (250 microM) can augment the germination upto 42.5% as compared to control (25%). Nitrogen containing compounds including nitrate, nitrite and cyanide also play vital role in breaking seed dormancy. <sup>[22]</sup> Chilling of the seeds can also improve seed germination at lower altitude. <sup>[23]</sup>

# **Therapeutic Uses**

Aconitum heterophyllum is used in Medical Systems like Āyurveda, Folk, Tibetian, Unani and Sidha. Roots are extensively used as a febrifuge, stomachic, bitter tonic, aphrodisiac and antiperiodic. It is also used to create an excellent tonic for combating debility after fever. [24] In Āyurveda system of medicine, the root is considered as bitter, tonic, hot, stomachic, digestive; helps in alleviating dysentery and bilious complaints. Drug is quiet useful in diarrhoea and vomiting of children and causes

constipation when taken in large doses. It is also useful in bites from poisonous snakes, scorpions, rats etc.<sup>[11]</sup> The powder of Indian *Atees*, dried *Aegle marmelos*, root of *Pavonia odorata*, *Cyperus rotundus* and the horny excrescence of *Rhus succedanea* should be taken in equal parts after mixing them properly. This compound powder must be given in doses according to age with the addition of honey for curing fever with diarrhoea. The plain powder of the tuberous root mixed with honey can be given in

cough, coryza, fever and vomiting of children where it is applied on tongue.[25] It is also indicated to use 1 part of *Ativisā* (*Aconitum heterophyllum*) and 4 parts of Ankola (Alangium salvifolium) pounded with rice water to relieve abdominal disorders.[26] In Unani system of medicine, the drug is considered useful for strengthening the body. It helps in alleviating dysentery, piles, bilious complaints, plethoric conditions and removes excess gas from the stomach.[11] Root is considered as an Aphrodisiac in various indigenous system of medicines.[27] It is reported that the decoction of the plant serves as antiseptic and is given to cure dyspepsia, especially when appetite is lost after illness.[28] The aqueous extract of the root can be given in a dose of 5-10 ml twice a day, early in the morning empty stomach and at night after meals for 7 to 28 days in chronic fever, and digestive disorders, in diarrhoea and as cold remedy. Roots mixed with Ajuga parviflora leaves and Podophyllum hexandrum roots are dried in shade and powdered. This powder is given half teaspoonful twice a day early in the morning and at night after meals upto three months for the treatment of

Diabetes, Leucorrhoea and as Carminative. [29] One teaspoon dry powder of *Picrorhiza kurroa* and *Aconitum heterophylum* in a ratio of 5:1 respectively is given twice a day for 15-30 days to the women suffering with menstrual problems since long duration. [30] The root powder of *Ativiṣā* with honey is prescribed for cough irritations and bronchitis, it is an ant-helmintic and in action it is potent against guinea-worms. [15]

## **Ethnobotany**

The powdered root is considered as an antidote to poison, also given in gastro enteric fever of the infants and children.<sup>[31]</sup> The plant finds use in diarrhoea, intestinal parasites and fever.<sup>[32]</sup> Leaves are used as analgesic<sup>[33]</sup> and in malarial fever.<sup>[34]</sup> The root is used as an antidote for snake bite and poisoning.<sup>[35]</sup> In case of fever, Gastralgia and Vomiting, especially in infants, 1gm of root powder is given with mother's milk 2-3 times a day, for 5 days.<sup>[36]</sup> *Aconitum heterophyllum* is also used to cure cold, for which a small quantity of root powder mixed with Tobacco is given.<sup>[37]</sup> (Table 2)

Table 2: Different Ayurvedic Formulations of Aconitum heterophyllum Wall ex. Royle

Formulation	Therapeutic uses
Gangadhar Churna <sup>[38]</sup>	This herbal medicine is well known for its astringent and alternative property. This is specially indicated in Sprue Syndrome, diarrhoea and dysentery. It can cure diarrhea, sprue and colic associated with all the three types of <i>Doshas</i> . It is also beneficial in purpueral disorders.
Yograja Guggul <sup>[39]</sup>	Pacifies <i>Tridosha</i> and is a good rejuvenator, helps in curing disorders like Rheumatoid arthritis, skin disorders, hemorrhoids, irritable bowel syndrome. This formulation possesses good anti inflammatory, anti arthritic, carminative and anti spasmodic activity.
Pushyanuga Churna <sup>[40]</sup>	It is used for the management of Menorrhagia, Metrorrhagia, Leucorrhoea, menstrual disorder, excessive menstrual bleeding of various etiology. It is also used in treating other uterine infections and Hemorrhoids.
Sudarshan Churna <sup>[41]</sup>	Traditionally <i>Sudarshana Churna</i> is used in the treatment of fever originating from all the three <i>Doshas</i> , chronic fever and fever associated with vitiation in <i>Dhatus</i> . It is one of the widely used Ayurvedic medicines for fever. This formulation is also used for curing anaemia, jaundice and other joint disorders.
Chandraprabha Vati <sup>[42]</sup>	Prameha, Mutrakrichha, Mutragata, Ashmari, Vibandha, Aanaha, Granthi, Arbuda, Andavridhi, Aantrvridhi, Vicharchika, Kushtha, Arsha, Dantaroga, Vrishya, Rasayana This formulation is useful for the management of diabetes, dysuria, renal calculi and other urinary tract disorders. It is also used as a herbal remedy for erectile dysfunction, premature ejaculation and other emotion related stressful conditions.
Kutajavleha <sup>[43]</sup>	It is used for curing bleeding piles associated with all the three <i>Doshas</i> . This remedy is also helpful in curing hyperacidity, anorexia, anaemia, jaundice, emaciation and other disorders.
Mahatiktaka Ghrita <sup>[44]</sup>	It helps in curing skin diseases, boil, rash, pus discharge, malarial fever, epistaxis, thyroid disorders, filariasis and erysipelas.
Grahanikapata Rasa <sup>[45]</sup>	This formulation is used for curing diarrhea and sprue disorder associated with

	vitiation of all <i>Doshas</i> . It also helps in stimulating digestive fire.
Triphala Guugul <sup>[46]</sup>	It is used in management of severe gouty arthritis, skin diseases and different types of wounds.
Panchtikta Guggulu Ghrita <sup>[47]</sup>	Diseases of vitiated <i>Vata</i> located in joints, bones and marrow; skin disorders, fistula in ano, respiratory disorders and oedema.

# **Pharmacology**

## **Anti-bacterial Activity**

In a study, it was observed that the crude alkaloid extract displayed moderate to strong level of against S. antibacterial activity aureus. bronchiseptica, B. subtilis, P. putida and X. campestris at higher concentration of 100 µg/ disc. This activity was almost absent against S. typhimurium, E. coli and P. fluorescence at the same concentration.[48] In an another study, the methanolic extract of aerial parts of the plant showed significant inhibition of the growth of Gram positive bacteria, Staphylococcus aureus and Bacillus subtilis.[49] In another study, tubers of Aconitum heterophyllum showed antibacterial activity against gram negative (diarrhea causing) bacteria Escherichia coli, Shigella flexineri, Pseudomonas aeruginosa and Salmonella typhi. This activity is because of some new aconitine type non-diterpenoid alkaloids 6-dehydroacetyl sepaconitine and 13-hydroxylappaconitine, isolated from the tubers along with the known alkaloids lycoctonine, delphatine and lappaconitine.[50]

## **Anti-pyretic Activity**

The antipyretic effects of roots of *Aconitum heterophyllum* was examined in the form of aqueous, chloroform and hexane extracts using the method of yeast induced pyrexia. In this study, aspirin was used as a standard antipyretic agent for comparison. The results showed that the extracts were nontoxic (up to 1.6g/kg) and had no significant antipyretic activity.<sup>[51]</sup>

#### **Anti-diarrhoeal Activity**

Anti-diarrhoeal of activity Aconitum *heterophyllum* was evaluated in a study as it possess astringent and tonic properties.[52] In another study, the drug is used as a key ingredient of Diarex Vet. whose activity was investigated against lactose induced diarrhea in wistar rats and found to be a potent anti-diarrhoeal agent at the dose of 750mg kg-1 of b.wt.[53] In one study, ethanolic extract of Aconitum heterophyllum caused either a decrease in mucosal secretion or increase in mucosal absorption, which allows the feces to become desiccated thus retarding its movement through the colon. This activity was well supported with a potential antibacterial activity. The study clearly revealed a significant reduction in excretion rate of feces in rats treated with ethanolic extract, which suggests an

anti-motility and anti-secretory property of extract.<sup>[54]</sup>

# **Enzyme Inhibition Activity**

Enzyme inhibition activity of *Aconitum heterophyllum* was evaluated in a study. The alkaloids Heterophylline A and Heterophylline B isolated from *Aconitum heterophyllum* Wall and were found to possess activity of inhibiting muscle contracting enzyme Acetyl-cholinestrace and butyryl-cholinestrace responsible for Alzheimer disease. [55]

# **Anti-inflammatory Activity**

In one study, *Aconitum heterophyllum* extract was evaluated for anti-inflammatory activity. The extract has been found to inhibit the weight of wet cotton pellet in a dose dependent manner. The reduction in the weight of cotton pellet granuloma with different doses of extract 225, 450 and 900mg/kg was found to be 17, 26 and 51% respectively. The higher dose of *A.heterophyllum* exhibited inhibition of inflammation very close to the inhibitory effect of Diclofenac sodium. The decrease in inflammation by *Aconitum heterophyllum* 900mg/kg was comparable to diclofenac sodium, which reduced the weight of cotton pellet granuloma by 64%.<sup>[56]</sup>

## **Hepato-protective Activity**

The hepato-protective activity of ethanolic extract of *Aconitum heterophyllum* root was evaluated by the assessment of biochemical parameters such as serum glutamic oxaloacetic transaminases (SGOT), serum glutamic pyruvic transaminases (SGPT), alkaline phosphatise (ALP), totalbilirubin, serum protein, and histopathological studies of the liver. Ethanolic extract of *Aconitum heterophyllum* root significantly reduced the liver damage and all biochemical parameters. The 450mg/kg extract showed greater response than 225mg/kg. The ethanolic extract of *Aconitum heterophyllum* root possess hepato-protective activity and this activity may be due to the presence of antioxidants and other components.<sup>[57]</sup>

#### **Analgesic Activity**

In one study, 48 Adult albino mice (Swiss strain) weighing 25-30 grams were selected and 24 animals were allocated to each experimental model, with 4 groups in each. The control group was given

vehicle (normal saline10ml/kg, p.o), standard group received aspirin (300 mg/kg) and dried ethanolic extract of *Aconitum heterophyllum* (225 mg/kg, 450 mg/kg p.o. respectively) were given to test groups. The drugs were administered orally one hour before placing the animal over the hot plate and one hour before putting tail clip. All the tested doses of *Aconitum heterophyllum* on acute administration significantly delayed the reaction time in hot-plate method and tail clip method, indicating that extract is having analgesic activity and acting on both central and peripheral pain mechanism.<sup>[58]</sup>

## **Anti-oxidant Activity**

Anti-oxidant activity of ethanol extract of *Aconitum heterophyllum* roots was assessed using 2,2-diphenyl-picrylhydrazyl, nitric oxide radical scavenging, hydrogen peroxide and ferric reducing antioxidant power scavenging activity assays. It was observed that anti-oxidant activity of root extract was almost equal to Vitamin C.<sup>[57]</sup> In another study, higher antioxidant activity was recorded in methanolic extract of *Aconitum heterophyllum* as compared to its ethanolic extract. The ethanolic extract of *Aconitum* depicted a low IC<sub>50</sub> value compared to the ascorbic acid IC<sub>50</sub> value.<sup>[59]</sup>

# **Immunomodulatory Activity**

In one study, the immunomodulatory activity of ethanolic extract of *Aconitum heterophyllum* tubers along with other medicines of the Āyurveda and Unani systems of medicine were observed on delayed type hypersensitivity (DTH), humoral responses to sheep red blood cells, skin allograft rejection and phagocytic activity of the reticulo-endothelial system in mice. It was found that the extract enhanced the phagocytic activity and inhibited the humoral component of the immune system. The results showed that *Aconitum heterophyllum* has good immunomodulatory activity.<sup>[60]</sup>

#### **Hypo-lipidemic Activity**

Hypo-lipidemic activity of Aconitum *heterophyllum* was evaluated in which the methanolic extract was orally administered in diet-induced obese rats. Blood samples were collected after four weeks for the estimation of serum lipids and lecithincholesterol acyltransferase (LCAT). Liver was also collected for the assay of HMG-CoA reductase (HMGR). The fecal samples were also collected to estimate the fecal fat content. It was found that Aconitum heterophyllum extract markedly lowered total cholesterol, triglycerides and apolipoprotein B concentrations in blood serum. The extract also lowered HMGR activity, which helps to reduce endogenous cholesterol synthesis and also activated LCAT which helps to increase HDL-c. An increase in

fecal fat content is also an indication of the hypolipidemic effect of *Aconitum heterophyllum*.<sup>[61]</sup>

## **Anti-spasmodic Activity**

Aconitum heterophyllum Wall. inhibited acetylcholine induced contractions in frog's rectus abdominis i.e., it showed anti-spasmodic activity. [62]

# **Nephro-protective Activity**

In one study, nephro-protective activity of ethanolic extract of *Aconitum heterophyllum* was observed in which different groups of rats were given normal saline, 50% glycerol (10ml/kg) alone, glycerol and 250mg/kg of ethanolic extract of *Aconitum heterophyllum*; and glycerol and 500mg/kg of ethanolic extract of *Aconitum heterophyllum* roots. The root extract treated animals showed significant attenuation of biochemical parameters and histopathological changes of the kidney compared to glycerol treated group and it was found to be more significant with the extract at 500mg/kg than 250mg/kg.<sup>[57]</sup>

#### **Substitutes and Adulterants**

In Āyurveda Compendia, it is mentioned to use *Mustaka (Cyperus rotundus)* or *Haritaki (Terminalia chebula)* in non-availability of *Aconitum heterophyllum*.<sup>[63]</sup> These are still a big issue of research and need further work. Roots of *Cherophyllum villosum* from *Apiaceae* family are commonly sold in North Indian markets in place of genuine drug. These roots are long, cylindrical, gradually tapering, aromatic and sweet in taste.<sup>[64]</sup>

# **Purification, Dosage and Toxicity**

Tubers of *Aconitum heterophyllum* are purified by warming them in the fresh extract of Cow dung juice and then drying in sunlight.<sup>[65]</sup> The ED<sub>50</sub> for the Cardiac toxicity in a study was found to be 19.5mg for crude drug and for purified aconite with cows urine and milk, it was 32.5mg and 75mg respectively.<sup>[66]</sup> Root powder is given in a dose of 1-3gm (Therapeutic dose). 4-6gm of root powder causes symptoms like dryness of mouth, tremors etc.<sup>[2]</sup> Tannic acid and Astringent can be given to overcome these symptoms.<sup>[64]</sup>

#### CONCLUSION

Aconitum heterophyllum or Ativiṣā is an important medicinal plant which possesses different therapeutic properties like anti-periodic, aphrodisiac, and astringent, tonic and is considered highly beneficial in diarrhoea, dyspepsia and cough. It possesses an alkaloid – Atisine which is of intense bitter taste but is non-poisonous. It also possesses some other important chemical constituents which are responsible for its different pharmacological activities like antibacterial, anti-oxidant, anti-diarrheal, hypo-lipidemic and hepatic-protective

activities. But there are many important traditional uses which are mentioned in Avurveda treatise and are used as ethno medicine which further need evaluation. Moreover, the concept of substitutes and method of purification of Aconitum heterophyllum mentioned in Avurveda texts are still the area of research and need further validation. This important medicinal plant is in endangered state, so propagation should be promoted so as to prevent use of different market adulterants and get a genuine drug for therapeutic purpose.

#### REFERENCES

- 1. Sancheti I.C., Basu Shyamal K., Mitra Anupama, Pal Dulal Ch., Datta Javashree. Encyclopedia of Himalayan Medicinal Flora. Vol. 1. Kolkata: Horticulture Development Foundation; August 2007. p. 22.
- 2. Anonymous. The Ayurvedic Pharmacopoeia of India, Part-I. Vol-I. 1st ed. New Delhi: Controller of Publication Civil Lines, Ministry of Health and Family Welfare, Government of India; 2001. p.28.
- 3. Sharma B.D., Balakrishnan N.P., Rao R.R. and Hajra P.K. Flora of India. Vol. 1. Calcutta: Botanical Survey of India; 1993. p. 16.
- 4. Daniel M. Medicinal plants: Chemistry and properties. New Delhi: Oxford & IBH Publishing Co. Pvt. Ltd.; 2008. p. 15.
- 5. Chauhan Narain Singh. Medicinal and aromatic plants of Himachal Pradesh. New Delhi: Indus Publishing Company; 1999. p. 70.
- 6. Gupta A.K., Tandon Neeraj, Sharma Madhu, 21. Jabeen Neelofar, Shawl A.S., Dar G.H. Callus editors. Reviews on Indian medicinal plants. Vol. 1. New Delhi: Indian Council of Medical Research; 2004. p. 170.
- 7. Swami Brahmananda. Common medicinal plants of India. New Delhi: Wisdom Press; 2013. p. 28.
- 8. Venkatasubramaniam P., Subrahmanya Kumar K., Nair VSN. Cyperus rotundus a substitute for Aconitum heterophyllum: Studies on Aurvedic concept of Abhava Pratindhi Dravya (drug substitution). J Āyurveda Integr Med; 1: 33-39 (2010).
- 9. Ameri A. The effects of Aconitum alkaloids in central nervous system. Prog Neurobiol; 56: 211-235 (1998).
- 10. Singh Kamraj, Saloni Surabhi, Phytochemical screening and TLC profiling of different extracts of leaves, roots and stem of Aconitum Heterophyllum: A rare medicinal plant of Himalayan region. Int J Pharm Bio Sci 2015 April; 6(2): (P) 194 – 200.
- 11. Kirtikar K.R., Basu B.D. Indian Medicinal Plants. Vol. I. Dehradun: International Book Distributors; 2005. p. 34, 35.

- 12. Bhutva Ramesh Kumar. Ayurvedic Medicinal Plants of India. Vol. 1, Jodhpur: Scientific Publishers; 2011. p. 14.
- 13. Sharma B.D., Balakrishnan N.P., Rao R.R., Hajra P.K. Flora of India. Vol. 1. Calcutta: Botanical Survey of India; 1993. p. 15.
- 14. Gupta A.K., Tandon Neeraj, Sharma Madhu, editors. Reviews on Indian medicinal plants. Vol. 1. New Delhi: Indian Council of Medical Research: 2004. p. 176.
- 15. Ukani M.D., Mehta N.K., Nanavati D.D. Aconitum heterophyllum (Ativisā) in Āyurveda. Ancient science of life. Vol. no XVI. 2 Oct 1996; p. 166 -171.
- 16. Chopra R.N., Nayar S.L., Chopra I.C. Glossary of Indian Medicinal Plants. 6th ed. National Institute of Science Communication and Information Resources (CSIR); 2002. p. 4,5.
- 17. Govil J.N., Singh V.K. Recent Progress in Medicinal Plants. Vol. 14, USA: Stadium Press LLC; 2006. p.196, 203, 204.
- 18. Khare C.P. Indian medicinal plants-An illustrated dictionary. New Delhi: Springer (India) Private Limitated; 2007. p. 14,15.
- 19. Gupta A.K., Tandon Neeraj, Sharma Madhu, editors. Reviews on Indian medicinal plants. Vol. 1. New Delhi: Indian Council of Medical Research; 2004. p. 183.
- 20. T. Pulliah. Encyclopaedia of World Medicinal Plants. Vol. I. New Delhi: Regency Publications: 2006. p. 45-47.
- induction and Organogenesis from explants of Aconitum heterophyllum- Medicinal Plant. Biotechnology 5 (3): 287-291, 2006.
- 22. Pandey H., Nandi S.K., Nadeem M., Palni L.M.S. Chemical stimulation of seed germination in Aconitum heterophyllum Wall and A. balfourii Stapf. Important Himalayan species of medicinal value. Seed Sci. Technol. 2000; 28: 39-48.
- 23. BeighS.Y., Nawchoo I.A. and Igbal M. Cultivation and conservation of Aconitum heterophyllum. A critically endangered medicinal herb of the North west Himalayas. J. Herbs. Spices Med. Plants, 2005; 1:47-56.
- 24. Deorani S.C., Sharma G.D. Medicinal plants of Nagaland. Dehradun: Bishen Singh Mahendra Pal Singh; 2007. p. 3.
- 25. Nadkarni K.M. Indian Materia Medica. Vol. I. Mumbai: Bombay Popular Prakashan; 2007. p. 26-27.
- 26. Srivastava Nivedita. Medico Botany of Garhwal Himalayas. New Delhi: Deep Publications; 2014. p. 24.

- 27. Sharma Ravindra. Medicinal Plants of India An Encyclopaedia. Delhi: Daya Publishing House; 2003. p. 8, 9.
- 28. Rawat G.S. Alpine Meadows of Uttaranchal. Gopeshwar: Herbal Research and Development Institute; 2004. p. 60.
- 29. Kumar Mukesh, Khare Anjali, Shukla C.P. Medicinal Plants Aspects and Prospects. New Delhi: Biotech Books; 2014. p. 152.
- 30. Trivedi Pravin Chandra. Medicinal Plants: Ethnobotanical Approach. India: Agrobios; 2012. p. 256.
- 31. Nishteshwar K., Hemadri Koppula. Dravyaguna Vijnana. Delhi: Chaukhamba Sanskrit Pratishthan; 2010. p. 4.
- 32. Srivastava T.N., Rajshekhran S., Badola D.P., Shah D.C. An index of the available medicinal plants used in Indian System of Medicine from Jammu And Kashmir State. Ancient Sci Life1986; 6, 49-63.
- 33. Balodi B., Singh D.K. Medico-ethnobotany of Ladakh. Ann for 1997; 5, 189-197.
- 34. Chauhan V., Chauhan N.S. Ethno-botany of Trans-Giri area of Sirmour district of Himachal Pradesh. Bull Med Ethnobot Res 1988; 9, 106-122.
- 35. Malhotra C.L., Balodi B. Medicinal plants of Alpine region of Gori Valley, Kumaon. J Sci Res Plant Med 1984; 5 (1&2), 1-8.
- 36. Singh V.K., Anwar Ali Zaheer. Herbal Drugs of Himalaya. Vol. 15, New Delhi: Today and Tomorrow's Printers and Publishers; 1998. p. 17.
- 37. Bhattacharjee Supriya Kumar. Handbook of Medicinal Plants. 4<sup>th</sup> ed. Jaipur: Pointer Publishers; 2009. p.13.
- 38. Mishra S.N., editor. Bhaisajya Ratnawali, (Grahani Chikitsa 8/44). Varanasi: Chaukhambha Surbharati Prakashan; 2007. p. 260.
- 39. Srivastava Shailaja, editor. Sharangadhar Samhita, (Madhyam khanda 7/58). 4<sup>th</sup> ed. Varanasi: Chaukhambha Orientalia; 2005. p. 202.
- 40. Pandey Gangasahaya, editor. Charak Samhita (Chikitsasthana 30/91), Part-II Varanasi: Chaukhambha Sanskrit Sansthan, Varanasi, Reprint: 2006. p. 763.
- 41. Srivastava Shailaja, editor. Sharangadhar Samhita, (Madhyam khanda 6/29). 4<sup>th</sup> ed. Varanasi: Chaukhambha Orientalia; 2005. p. 177.
- 42. Srivastava Shailaja, editor. Sharangadhar Samhita, (Madhyam khanda 7/40). 4<sup>th</sup> ed. Varanasi: Chaukhambha Orientalia; 2005. p. 200.
- 43. Dwivedy Ramanath, editor. Chakradatta, (Arsha Chikitsa 5/118) Varanasi: Chaukhamba Sanskrit Sansthana; 2005. p. 64.

- 44. Sharma Anant Ram, editor. Sushruta Samhita, (Chikitsa sthana 9/8). Vol. II, Varanasi: Chaukhamba Surbharati Prakashan; 2001. p. 251.
- 45. Laksmipati Sastri, Sastri Brahma sankar, editors. Yogaratnakara, (Grahani chikitsa1-5). Varanasi: Chaukhambha Prakashan; 2010. p. 172.
- 46. Misra B.S., editor. Bhava prakasa Samhita, (Vatarakta Chikitsa 29/213). Part II, 9<sup>th</sup> ed. Varanasi: Chaukhambha Sanskrit Sansthan; 2005. p. 318.
- 47. Upadhyaya Yadunandana, editor. Astanga Hridaya (Chikitsa sthana 21/60). Varanasi: Chaukambha Prakashan; 2007. p. 421.
- 48. Sinam Yoirentomba Meetei, Kumar Sanjeev, Hajare Sachin, Gautam Satyendra, Devi G.A., Sharma Arun. Antibacterial property of Aconitum heterophyllum root alkaloid. International Journal of Advanced Research 2014; Vol. 2, Issue 7, 839-844.
- 49. Srivastava Nidhi, Sharma Vikas, Saraf Kirti, Dobriyal Anoop Kumar, Kamal Barkha and Singh Jadon Vikas. In vitro antimicrobial activity of aerial parts extracts of Aconitum heterophyllum Wall. ex Royle. Indian Journal of Natural Products and Resources Vol. 2(4) December 2011; pp. 504-507.
- 50. Ahmad M, Ahmad W, Ahmad M, Zeeshan M, Obaidullah, Shaheen F. Norditerpenoid alkaloids from the roots of Aconitum heterophyllum Wall with antibacterial activity. J Enzyme Inhib Med Chem 2008; 23: 1018-22.
- 51. Ikram M, Khattak SG, Gilani SN. Antipyretic studies on some indigenous Pakistani medicinal plants: II. J Ethnopharmacol1987; 19: 185-92.
- 52. Singh K.P. and Chaturvedi G.N. Some traditional anti-diarrhoeal drugs. Nagarjun, 1982; 26: 130-135.
- 53. Mitra S.K., A. Sachan and V. Udupa. Experimental evaluation of Diarex Vet. In Lactose induced diarrhea in rats. Indian Vet. J., 2001; 78:212-216.
- 54. Prasad S.K., Jain D., Patel D.K., Sahu A.N., Hemalatha S. Antisecretory and antimotility activity of Aconitum heterophyllum and its significance in treatment of diarrhea. Indian J Pharmacol 2014; 46:82-7.
- 55. Nisar M., Ahmad M., Wadood N., Lodhi M.A., Shaheen F. and Choudhary M.I. New diterpenoid alkaloids from Aconitum heterophyllum Wall.: Selective butyrylcholinestrace inhibitors. J. Enzyme inhibition Med. Chem., 2009; 24: 47-51.
- 56. Verma Santosh, Ojha Shreesh and Raish Mohammad. Anti-inflammatory activity of Aconitum heterophyllum on cotton pellet-induced granuloma in rats. Journal of Medicinal

- Plants Research 4 August, 2010; Vol. 4(15), pp. 1566-1569.
- 57. Konda Venu Gopala Rao, Eerike Madhavi and Lakshmipathy Prabhu. Evaluation of hepato protective activity of ethanolic extract of Aconitum heterophyllum root in paracetamol induced liver toxicity. Int J Pharm Bio Sci 2013 Oct; 4(4): (P) 714-721.
- 58. Madhavi E., Konda V.R., Rajeshwaramma G, Ruckmani A., Prabhu L.R., Kumar M.R., Saradha S. Evaluation of analgesic activity of ethanolic extracts of Aconitum heterophyllum root in Swiss albino mice. International Journal of Pharmacy. 2013; Photon 104, 266-270.
- 59. Munir Neelma, Ijaz Wasqa, Altaf Imran, Naz Shagufta. Evaluation of antifungal and antioxidant potential of two medicinal plants: Aconitum heterophyllum and Polygonum bistorta. Asian Pac J Trop Biomed 2014; 4 (Suppl 2): S639-S643.
- 60. Atal CK, Sharma ML, Kaul A, Khajuria A. Immunomodulating agents of plant origin. I: Preliminary screening. J Ethnopharmacol 1986; 18: 133-41.

- 61. Subash A.K., Augustine A. Hypolipidemic effect of methanol fraction of Aconitum heterophyllum wall ex Royle and the mechanism of action in diet-induced obese rats. J Adv Pharm Technol Res 2012; 3: 224-8.
- 62. Nisteswar K., Dhyani S.C. and Baxi A.J. Action of ushna and sheetavirya drugs on skeletal muscle (Frog rectus abdominis). Sachitra Ayurved 1980; 33, 212-214.
- 63. Laksmipati Sastri, Sastri Brahmasankar. Yogaratnakara. Varanasi: Chaukhambha Prakashan; 2010. p. 172.
- 64. Lucas Shanth Kumar. Dravyaguna Vijnana. Vol. II. Varanasi: Chaukhambha Visvabharati; 2013. p. 11.
- 65. Pandit Narhari, Tripathi Indradeva. Raj nighantu. 3<sup>rd</sup> ed. Varanasi: Chaukhambha Krishnadas Academy; 2003. p. 162.
- 66. Singh L.B., Singh R.S., Bose R., Sen S.P. The use of poisonous plant aconite in Indian system of medicine. J Sci Res Plant Med 1980; 1 (3-4), 48-49.

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Figure 1: Habit of A. heterophylum



Figure 2: Heteromorphous Leaves



Figure 3: Close view of flowers



Figure 4: Follicle



Figure 5: Seeds of A. heterophyllum



Figure 6: Tubers of A. heterophyllum