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Evaluation of the Toxicity of Aconitum Heterophyllum

Mr. Amanpreet Singh

Assistant Professor, School of Bio Sciences, RIMT University, Mandi Gobindgarh, Punjab, India

Correspondence should be addressed to Mr. Amanpreet Singh; amanpreetsingh@rimt.ac.in

ABSTRACT- Aconitum heterophyllum, commonly known as aruna, belongs to the Ranunculaceae family and is used in Ayurvedic formulations to treat diarrhoea, liver difficulties, and other ailments. Alkaloids, proteins, carbohydrates, saponins, amino acids, quinones, flavonoids, glycosides, terpenoids, and other phytochemicals are found in this plant. Not only are the different medicinal characteristics of this plant mentioned in this study, but the profile of its toxicological experiments conducted on rats is also examined. Unlike other Aconitum species, Aconitum heterophyllum was proved to be helpful in a rat poisoning study. To begin, the plant's ethanolic extract was tested for oral toxicity, but it was found to be harmless. Castor oil's action was reversed by an ethanolic extract of the plant. Furthermore, this plant possesses antibacterial properties. After summarizing all of this plant's medicinal characteristics, it might prove to be a great source of information for academics, traditional medicine practitioners, and the pharmaceutical business.

KEYWORDS- Aconitum Heterophyllum, Anti-Bacterial Role, Castor Oil, Phytomolecules, Rats, Toxicity.

I. INTRODUCTION

Ayurveda is one of the ancient traditional medical systems of India & Aconitum heterophyllum is being used in many ayurvedic formulations till date. Moreover, many species of Aconitum are being used in various traditional medicines of the nations of East Asia and the Himalayan nations. This plant is known as aruna in Sanskrit, atees in Urdu, and atis in Hindi. Aconitum heterophyllum is from the kingdom plantae, division 'Magnoliophyta', family Ranunculaceae, genus Aconitum & species is Heterophyllum (Table 1). The tuberous roots of this plant are used for its various roles such as antidiarrheal, hepatoprotective etc. In figure 1, an image of this plant has been illustrated. This plant is found in the high Himalayas. As many species of the plant has poisonous characteristics therefore one needs to be cautious while utilizing this plant. The primary aim of this review is to expand upon the therapeutic function of this plant [1,2].

Figure 1: Image of the plant Aconitum heterophyllum. It is used in many Asian traditional medicine preparation. It belongs to the family Ranunculaceae Figure courtesy [3]

Table 1: Botanical taxonomy regarding Aconitum heterophyllum. It's a widely used medicinal plant in Ayurvedic & the traditional Chinese medicines [4]

Botanical name	Aconitum heterophyllum
Family	Ranunculaceae
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Ranunculales
Genus	Aconitum

A. Description

Aconitum heterophyllum's tapering roots have grey hue, 7 cm in length & breadth at 1.5 cm. It's a tiny plant with a straight, basic, branching and green coloured stem reaching a height of 20 cm. It produces blooms of yellow/blue hues beginning from the months of August until September. The leaves have dark green colour with top regions having aamplexicaul structure & the bottom portions are petioler. This plant is organized spirally with the macroscopic & the microscopic characteristics are listed in Tables 2 & 3[5,6].

Table 2: Morphological features of Aconitum heterophyllum. It's a short plant with dark green leaves and tapering roots[1]

Stems	Simply branched
	Height is 30 cm
	Colour is green
	Short heighted plant having straight stem
	Branches may occur
Leaves	Dark green heteromorphous
	Amplexicaulated upper parts
	Petiolated lowest parts
Roots	5 cm in length
	Paired
	Tapering at end

Table 3: Microscopic features regarding Aconitum heterophyllum. Root section shows cells with thin walls[3]

Roots	Mature roots' transverse section
	Tabular brown cells
	Tangentially elongated cells with thin walls
	Cork cambium
	Parenchymatous cells having thin walls

B. Cultivation

Aconitum heterophyllum is cultivated in the higher Himalayan areas with wet soil & moderate rainfall. This plant is either sprouted from the seeds or from the tuberous roots from March until April. In the fall, 2 daughter tuberous roots are harvested after the shoots have reached senescence, only to be replanted in the spring season. The freshly germinated plant displays green development in the 1st year with the blossoming of flowers happening in the 2nd year of growth[4].

II. LITERATURE REVIEW

Conitum Heterophyllum (A. Heterophyllum) may aid people with bladder infections, diarrhea, and irritation, according to Debashish Paramanick's study. It's also been utilized to boost hepatoprotective qualities and as an expectorant. Chemical investigation has found alkaloids, carbohydrates, proteins and amino acids, saponins, glycosides, quinones, flavonoids, terpenoids, and other plant components. A analysis of relevant literature on A. Heterophyllum is also included, as well as the most significant pharmacological and other achievements in this subject. This review research should be valuable to new academics who are concerned in the plant A. Heterophyllum [7].

Ravindra Kumar Pandey in his study discloses P. harmala Linn (P. harmala) as an endemic plant of India . It is found to be a branching and bushy perennialherb. Parts of the plant are recognized to offer medicinal properties. The herb is used locally in Indian medicine to treat different ailments. It is utilized in stomach complaints, urinary and sexual diseases, epilepsy, menstrual difficulties, mental and neurological ailments etc. the chemical analysis of the plant shows that the plant includes significant alkaloids(harmine, harmaline, harmalol and peganine), steroid(lanosterol and kryptogenin)and Fatty acids/volatile acids/fixed oil(palmitic, stearic, arachidic, behenic, oleic, linoleic acids, β-sitosterol) etc[8,9].

Balasubramani SP demonstrates how system . this system of top germplasm based on biochemical markers might aid in the conservation of endangered species in his paper. Under the all-India cooperative campaign on vulnerable species, six species were selected for research: Podophyllum hexandrum Royle (syn = Sinopodophyllum hexandrum (Royle) T. S. Ying), Picrorhiza kurroa Royle ex Berth., Aconitum heterophyllum Wall. ex Royle, Aconitum heterophyllum Wall. ex Royle, Aconitum heterophyllum Wall. ex Royle, Aconitum heterophyllum Wall. ex The method worked, and the species was rescued from the brink of extinction. [10,11].

III. DISCUSSION

A. Pharmaceutical Roles of A. Heterophyllum

Aconitum heterophyllum when taken up with ginger powder, nutmeg &/bel has been found to have antidiarrheal function. This plant works as an expectorant when combining its root's juice with milk with its seeds serving as a diuretic. Moreover, this herb has pro-fertility functions and possesses hepatoprotective, analgesic roles among others. The phytochemicals of Using a high-performance liquid chromatography test using an ultraviolet photodiode array detector, Aconitum heterophyllum was discovered (HPLC-UV-DAD). Peak heights were calculated as a function of aconite concentration. This test is not only fast but also repeatable leading to the concentration based detection of aconitine, hypaconitine, mesaconitine, benzoylmesaconine, benzoylaconine & benzoylaconine. The therapeutic applications of different Aconitum species have been listed in Table 4. These phyto-molecules with their chemical names have been listed in Table 5 & 6. In Figure 2 & Figure 3 different phytomolecules of this plant has been shown [12-13].

It may be utilized for determining which species of these genus is helpful for which illness & the chemical structures of the phytomolecules might be used for creating different lead agents [14-16].

Table 4: Medicinal uses of different Aconitum species. Most of species of this genera are poisonous[17,18]

Species of Plant	**Uses in traditional pharmaceutical formulations**
Aconitum heterophyllum	Dyspepsia, cough
Aconitum kirinense	Rheumatoid disease
Aconitum bulleyanum	Rashes, Snake bite
Aconitum orochryseum	Snake bite, dysentry
Aconitum carmichaeli	Diuretics, analgesic
Fuzi	Traditional east Asian medicines
Aconitum brachypodium	Analgesic

Table 5: Various phytomolecules isolated from Aconitum heterophyllum. These phytomolecules are responsible for its therapeutic activities [19]

Class	Leaf	Stem	Root
Alkaloids	+	+	+
Carbohydrates	+	+	+
Amino acids & Proteins	+	+	+
Saponins	+	+	+
Glycosides	+	+	+
Quinones	-	+	+
Flavonoids	+	+	+
Terpenoids	-	+	+

Table 6: Phytochemical composition of Aconitum heterophyllum. Knowing the chemical structures of these compounds would help in designing of effective lead agents [14-19]

Chemical composition
12-secohetisan-2-ol
N-succinoylanthranilate
Atesinol 6-benzoylheterastine
N-diethyl-N-formyllaconitine
Methyl aconitine
Aconitine
Anthorine

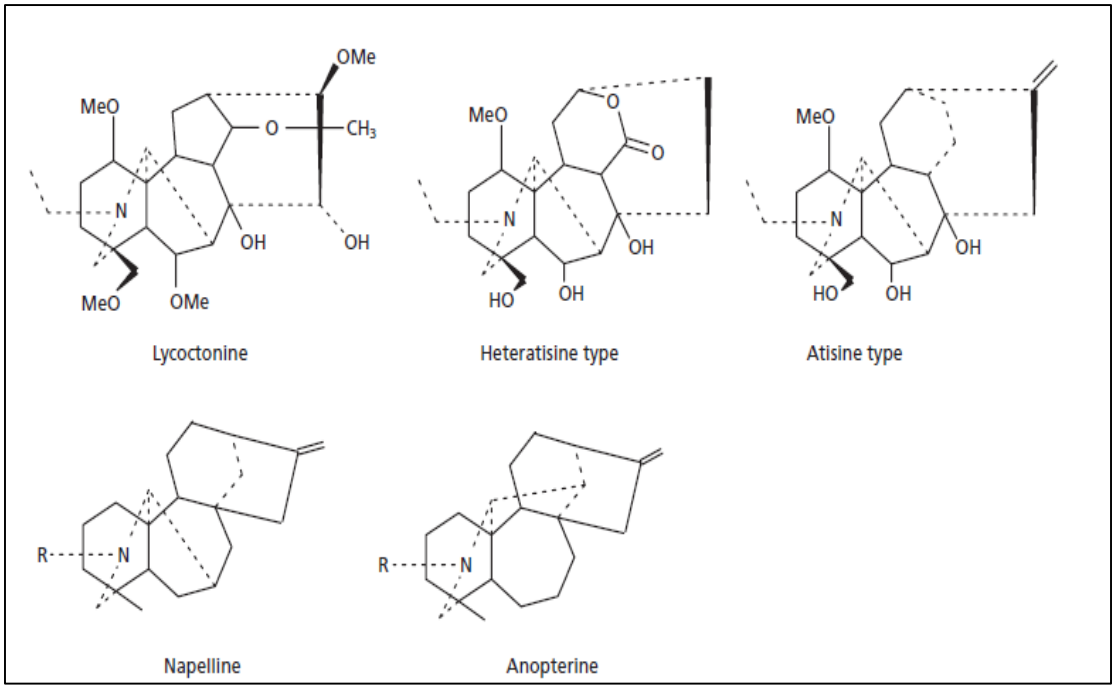

Figure 2: Chemical structures of some of the phytomolecules isolated from Aconitum heterophyllum. They are Lycoctonine, Heteratisine type, Atisine type, Napelline & Anopterine [10-22]

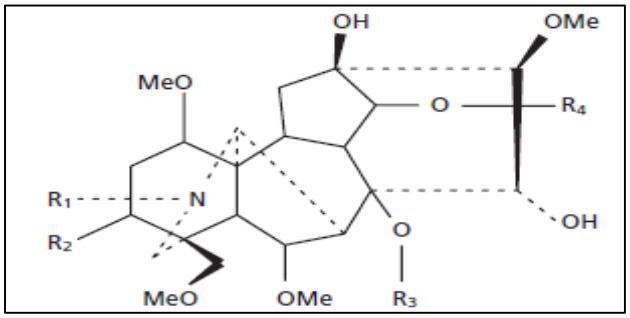

Figure 3: Chemical structure of Aconitum. The genera Aconitum is derived from this alkaloid, Aconitum. The alkaloid Aconitum has been blamed for inducing cardiac tachycardia Figure courtesy [14]

Aconitum heterophyllum's ethanolic extract (EAH) was examined for its acute oral toxicity for 48 h and monitored for any neurological & behavioural abnormalities. However no toxicity for the quantity of 2g/Kg was found.

Group 1 rats were fed carboxy methyl cellulose (CMC), group 2 rats were fed a 50 mg/kg methanolic of Aconitum heterophyllum (EAH) with CMC, group 3 rats were fed a 100 mg/kg ethanolic extract of Aconitum heterophyllum (EAH) with CMC, group 4 rats were fed a 200 mg/kg ethanolic extract of Aconitum heterophyllum (EAH) with CMC, and group The rats' excrement pellets were collected, weighed, and then dried for 24 hours at 40°C to get the wet: percentage of dry. The rats treated with EAH exhibited increasing suppression of faecal extraction with loperamide totally halting it. The findings of this experiment have been summarized in Table 7 [13-25].
This characteristic of this plant thus promotes a notion that diarrhoeal illnesses may be reversed after therapy by this plant [4].

Table 7: Efficacy of the ethanolic extract of Aconitum on the faecal excretion rate in rats. The rats were divided into 5 groups with Group 1 being fed with Carboxy methyl cellulose (CMC), ethanolic extracts (EAH) 50,100 & 200 and the final group was fed with loperamide, a known drug for preventing bowel movement. The rats fed with EAH showed progressive inhibition of faecal extraction with loperamide completely stopping it [17]

Treatment	1 hour & wet weight of faeces	3 hours & wet weight of faeces	5 hours & wet weight of faeces	7 hours & wet weight of faeces	Faeces weight
Control	0.070	0.450	0.800	1.630	1.630
EAH 50	0.062	0.180	0.360	0.657	1.800
EAH 100	0.060	0.175	0.33	0.551	1.155
EAH 200	0.055	0.155	0.30	0.530	1.111
Loperamide	0.041	0.051	0.55	0.051	0.790

C. Castor Oil-Induced Diarrhoea

Fasting rats were divided into six groups: group 1 was given CMC, group 2 was given CMC and castor oil, group 2 was given EAH 50 and castor oil, group 2 was given EAH 100 and castor oil, group 3 was given EAH 200 and castor oil, and group 6 was given loperamide. As indicated in Table 8, the presence of EAH decreased castor oil-induced diarrhoea in a concentration-dependent manner. This characteristic of this plant thus promotes a notion that diarrhoea may be reversed after therapy by this plant [19].

Table 8: The effectiveness of an ethanolic extract of Aconitum in a castor oil-induced diarrhoea model in rats. Rats were put into six groups: group 1 was given CMC, group 2 was given CMC and castor oil, group 2 was given EAH 50 and castor oil, group 2 was given EAH 100 and castor oil, group 3 was given EAH 200 and castor oil, and group 6 was given loperamide. The addition of EAH reduced castor oil-induced diarrhoea in a concentration-dependent manner[7]

Group	Onset time (min)	Total no. of faeces	Total no. of wet faeces	Loss in body weight	Total weight of faeces	Mean defecation in 4 hours	Diarrhoea score	% protection
Normal		4		0.118	0.475	1		100
Castor oil	52	12	9	0.969	1.9	3	19	-
EAH 50	77.159	11	6.12	0.64	1.300	2.7	12.335	27.459
EAH 100	110	6.7	3.5	0.367	1.081	1.67	6.84	61
EAH 200	114	6.49	3.331	0.34	0.999	1.622	6.67	63
Loperamide	132	6.17	2.67	0.200	0.670	1.540	5.17	72

D. Castor-oil Induced Intestinal Fluid Accumulation

Rats were starved for 18 hours and were split into group 1 fed with CMC, group 2 fed with just castor oil, group 3 fed with EAH 100 mg/Kg with castor oil and group was fed with loperamide with castor oil. After sacrifice, the intestinal fluid was collected & ions were measured. Castor oil caused a loss of sodium & potassium ions which was significantly reduced by the effect of EAH 100. Upon single feeding with castor oil there was an increase in nitric oxide (NO) generation & loss of carbs which were substantially reduced & reversed by EAH 100. The quantities of DNA and total protein increased after feeding with EAH 100, as did the levels of liver functioning enzymes including catalase (CAT), superoxide dismutase (SOD), and lipid peroxidation, as measured by thiobarbituric acid reactive substances (TBARS) [[Tables 9a and 9b] [19].

This characteristic of this plant thus promotes a notion that loss of nutrients after a start of diarrhoea may be restored following therapy by this plant.

Table 9a: Efficacy of the ethanolic extract of Aconitum on an intestinal fluid accumulation model induced by castor oil. Rats fasted for 18 hours and were divided into group 1 fed with CMC, group 2 fed with only castor oil, group 3 fed with EAH 100 mg/Kg with castor oil and group was fed with loperamide with castor oil. Castor oil induced a loss of sodium & potassium ions which was greatly inhibited by the action of EAH 100 [4]

Group	Weight of intestinal content (g)	Volume of intestinal content (ml)	% of inhibition	Na+ (mmol/L)	K+ (mmol/L)
Normal	1.460	1.310	100	97.800	6.67
Control	3.48	3.47	-	137.170	9.233
EAH 100	2.22	2.12	39	114	7.51
Loperamide	1.570	1.61	54	109	7.130

Table 9b: Efficacy of the ethanolic extract of Aconitum on an intestinal fluid accumulation model induced by castor oil: Effect on biochemical parameters. Upon feeding with EAH 100, the levels of DNA & total protein showed increase along with recovery in the levels of liver functional enzymes like catalase (CAT), super-oxide dismutase (SOD) & lipid peroxidation, determined by measurement of the thiobarbituric acid reactive substances (TBARS) [10]

Group	**NO (Units in moles/ mg of protein)**	**Total carbohydrates (mg/g) of tissues**	**Total proteins (mg/100 mg of tissue)**	**Total DNA units (mg/100 mg of tissue)**	**TBARS (units in mole/mg of protein)**	**CAT (µmol H_2O_2 consumed/minute/ mg of protein**	**SOD (units/mg of protein)**
Normal	0.900	1.16	1.800	0.151	2.89	112	0.800
Castor oil	3.28	0.500	0.811	0.1	12.80	77.71	1.11
EAH 100	3	0.75	1.20	0.12	6.8	93	1.5
Loperamide	2.5	0.78	1.4	0.14	5.5	105	1.56

E. Antibacterial function of the EAH

A variety of bacteria were grown on standard bacterial culture medium and EAH was treated which exhibited higher inhibition against gram + ve bacteria compared to the gram –ve bacteria. This suggests that Aconitum heterophyllum may be used for producing anti-bacterial medicines [14].

Table 10: Anti-bacterial properties of Aconitum heterophyllum. The bacterial species tested here are B. cereus, S. aureus, E. faecalis, S. flexneri, S. typhi, S. dysentriae, P. vulgaris, E.coli, K.pneumoniae, P.aruginosa & S.boydii [17]

Bacterial strains	**50 mg/ ml**	**100 mg/ ml**	**Ciprofloxacin**	**MIC (mg/mL)**
B. cereus	9.2	13	26	0.2
S. aureus	9.9	14.9	28	0.4
E. faecalis	-	-	30	-
S.flexneri	7.3	9.9	21	1.6
S.typhi	7	8.8	26	3
S.dysenteriae	7.9	10	24	0.8
P.vulgaris	7.67	9.7	24	6.3
E.coli	9	12	27	0.4
K.pneumoniae	-	-	29	-
P.aeruginosa	9.3	14	27	0.79
S.boydii	10	14	26	0.4

IV. CONCLUSION

Aconitum heterophyllum is being utilized in ayurveda formulations & other traditional systems of medicines for the treatment of diarrhoea, liver problems etc. This plant is mostly grown in the Himalayas and is well-known for its toxicity. This toxicity is caused by alkaloids, proteins, carbohydrates, saponins, amino acids, quinones, flavonoids, glycosides, terpenoids, and other phytochemicals. This page discusses not only the various medicinal properties of this plant, but also the characteristics of its toxicological tests done on rats. Aconitum heterophyllum, unlike other Aconitum species, was shown to be beneficial in a rat poisoning model.

To begin, the oral toxicity of this plant's ethanolic extract was investigated, but no damage was foundThe diarrhoea caused by castor oil was restored by giving an ethanolic extract of the plant. In addition, this plant has shown to have good antibacterial properties. After summarizing all of this plant's pharmacological features, it may prove to be a valuable source of knowledge for academics, traditional healers, and the pharmaceutical industry.

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