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BIO-ACTIVE COMPOUND AND PHARMACOLOGY OF *ATEES* (ACONITUM HETEROPHYLLUM WALL.)-A UNANI DRUG

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ABSTRACT

We are living in modern days and everyone is in hurry for everything even for their ailments. They required medicine that is fast acting although cause some harm to the body. That may be managed by time. Unani system of medicine (USM) is one of the oldest systems of medicine in the world providing treatment through its rich formulations based on single drugs. Unani medicinal plants are playing an important role in the drug discovery and development of new molecules. There are a number of unani drugs which are used from ancient time. For this review unani text as well as other ethnobotanical books were searched and presented the studies here. Action and Uses of Atees (*Aconitum heterophyllum* wall) mentioned in Unani literature along with phytochemistry and pharmacology. Total ten pharmacological activities were recognized in different experimental models. The antipyretic action of this drug has been proved in scientific study. The other actions of the drug mentioned in unani literature are to be validated on scientific parameters.

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INTRODUCTION

Humans have used natural products, such as plants, animals, minerals in medicines to alleviate and treat diseases since prehistoric times. As per records on fossils, the human use of plants as medicines may be traced back at least 60,000 years [1-2]. In early time use of natural products as medicines, of course be a challenge to humans. It is highly probable that some time it was happened they often consumed poisonous plants, which led to vomiting, diarrhea, coma, or other toxic reactions perhaps even death. From these accidents they were able to develop knowledge about edible materials and natural medicines [3].

Atees, *Aconitum heterophyllum* wall., Aconitum also known as aconite is a genus consisted of 250 species of angiosperm plants. But here we are only taken *Aconitum heterophyllum* wall because this species is considered similar to the description mentioned in unani literature. It is perennial herbs found in mountainous parts of the Northern Hemisphere [4]. In India it is found in Kedarnath, Himalayan, Kumoan, Shimla and bank of Chambal river region. The favorable soil is moist-retentive and well-drained soils of mountain meadows. Among all the species of genus of aconitum *Aconitum heterophyllum* Wall. showing essential medicinal assets [4-5].

In USM *Atees* has to be considered as class three drug and having action faster than the class first and second drugs. This drug is in used for therapeutic purposes by unani physicians since a long for many ailments. This review is an attempt to showcase the unani literature regarding the action, temperament, uses and formulation related to *Atees* as well the scientific phytochemical and pharmacological activities of the drug.

Habitat:

It is found from Pirpanjal in Kashmir to Kumaon hills at altitudes of 2,500-3,900 m. Flowers are pollinated by bees and timing is from August to September, and the seeds ripen during September to October. It grows in semi shade or no shade light (sandy), medium (loamy) and heavy (clay) soils [4-7].

Botanical description

It is a tall herb and its roots are tuberous and parried. Based on morphology and anatomy, several forms of *A. heterophyllum* are recognized (white, Yellow, Black and Red) amongst which the white variety which iscommonly available is the best. The white tuberous roots are plumpy with a pale-yellow colour.The plant of *Atees* is 0.3 - 1.2 m tall. Root are biennial tuberous, paired, whitish or green. Leaves ovate- cordate to rounded, the upper ones clasp the stem. Lowest leaves deeply lobed and long stalked. Flowers bright blue usually in lax spike like cluster with very variable bracts greenish purple conspicuously dark veined. Follicles 16- 8 mm long, shortly hairy erect. Seeds obpyramidal, blackish brown [4-9].

Taxonomic Scientific classification of *A. heterophyllum*

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

Temperament

Hot and dry in second degree of temperament [10-15]

Part used:

Root

Courtesy: India Mart.

Action:

Dafe humma (antipyretic) [10-14], *Dafe sual* (antitussive) [11,13], *Dafe zaheer* (antidiarrhoal) [10-12,15], *Habis* (Astringent/ Retentive) [13-14], *Habis-e-dam* (heamostatic) [11,13], *Dafe qay'* (antiemetic) [15], *Hazim* (digestive) [11-12,15], *Kasir-e-riyah* (carminative) [12,15], *Mane qai* (Anti emetic) [11], *Moarriq* (diaphoretic) [11], *Mohallil riyah* (carminative) [11], *Muqawwi-e-baah* (aphrodisiac) [11-13,15], *Muqawwi-e-asab* (nervine tonic) [10-12], *Mushil-e-balgham* (phlegmagogue) [11-12], *Mushil-e-safra* (purgative of bile) [12], *Qabiz* (astringent) [12,14], Q*abiz-e-ama* (antiparistaltic) [10], *Qatil kirm shikam* (vermicidal) [11,13].

Potent Action:

Dafe Humma (antipyretic); *Qatil kirm shikam* (vermicidal) [13].

Uses:

Balghami sual (productive cough) [11], *bawasir* (piles) [11-12,14-15], *Faalij* (hemiplegia) [10], *Humma* (fever) [10], *Humma Ajamiya* (malarial fever) [10,14], *Ishal* (diarrhoea) [11,14], *Ishal-e-balghami* (phlegmatic diarrhoea) [12], *Istirkha'* (atony/flaccidity) [10], *Istisqa Ziqqi* (Ascitis) [11-13,15], *Kathrat-i-Hayd* (polymenorrhoea) [12,14], *Laqwa* (facial palsy) [10], *Nafth al-Dam* (haemoptysis) [14], *Peecish* (dysentary) [12,14], *Qay'* (vomiting) [12], *Ra'sha* (tremor) [10], *Su'al al-Atfal* (infantile cough) [11], *Zahir* (dysentery) [10], *Zahir al-Atfal* (infantile diarrhoea) [12], *Zof-e-Asab* (Atony) [10].

Dose:

Unani scholars has mentioned different therapeutic doses in their treatise, that are 3.75 gm to 9.75 gm [11,15], 648 mg – 1296 mg [12], 1-3 gm [10,13,14].

Substitute:

In case of non availability of the main drug a substitute drug may be used for therapeutic purposes. In this situation unani scholar has recommended *Afsanteen roomi* (*Artemisia absinthium* Linn.) as substitute of *Atees* [13].

Corrective:

The drug may cause adverse effect in the body so to counter the adverse reaction of the body, Honey and Nabaat safaid (Sugar) has to be added in therapeutic dose for the same [13].

Chemical Constituents:

Following phytoconstituents were isolated form plant *Aconitum heterophyllum*. alkaloids, carbohydrates, protein & amino acid, saponins, phenolic compounds and tannins, cardiac glycosides, quinones, flavonoids, steroids, terpenoids. Acotinine [17], atidine, hetisine, heteratisine, Diterpene alkaloids [18-20], heterophylline, heterophylline, heterophyllidine heterophyllisine, hetidine, atidine & Atisenol, a new entatisene diterpenoid lactone from roots. F-dishydrçatisine, hetidine, hetisinone, heteratisine, hetisine, benzylleteratisine, beta-sitosterol, carotene and 3-isoatisine [21-27].

Pharmacological studies:

Anthelmintic activity

Aqueous and alcoholic extract showed encouraging results of anthelmintic activity against *Pheritemapostuma* (earthworm), using piperazine citrate as standard [28].

Anti-diarrheal activity

Ethanolic extract in different strength successfully reduced the normal fecal output time in castrol induced diarrhoea in experimental models. The data clearly indicates that the drug is having antisecretory and antimotility effect [29].

Anti bacterial activity

The new aconitine type nor-diterpenoid alkaloids 6-dehydroacetylsepaconitine and 13-hydroxylappaconitine, lycoctonine, delphatine and lappaconitine showed antibacterial activity against different bacterial strains e.g., gram negative (diarrhea causing) bacteria *Escherichia coli, Shigella flexineri, Pseudomonas aeruginosa* and *Salmonella typhi* [30].

Antihyperlipidemic activity

Methanol fraction of *A. heterophyllum* markedly lowered total cholesterol, triglycerides and apolipoprotein B concentrations in blood serum. It also showed positive effects (increase) on serum high-density lipoprotein cholesterol (HDL-c) and apolipoprotein A concentrations. It also lowered HMGR activity, which helps to reduce endogenous cholesterol synthesis and also activated LCAT (lecithin-cholesterol acyltransferase), helping increase in HDL-c. An increase in fecal fat content [31].

Anti-inflammatory activity

Ethanolic extract showed anti-inflammatory activity in cotton pellet induced granuloma method [26].

Antioxidant activity

Ethanolic extract of *A. heterophyllum* root in graded concentrations showed antioxidant activity in four different in vitro methods DPPH Assay, NO Assay, H2O2 Assay and FRAP Assay in compared with the standard antioxidant, vitamin C [32].

Gastroprotective activity

Hydroalcoholic extract of *Aconitum heterophyllum* showed gastroprotective activity by decreasing in the free and total acidity, volume of gastric content, total proteins and increase in pH of gastric content, total carbohydrates and total carbohydrates to total proteins ratio in against pylorus ligation induced ulcer in wistar albino rats. Histopathological studies further confirmed that pretreatment prevented pylorus ligation induced structural alterations in the gastric mucosa of rats [33].

Hepatoprotective activity

Ethanolic extract of *Aconitum heterophyllum* significantly significantly reduced the liver damage and all biochemical parameters i.e., serum glutamic oxaloacetic transaminases (SGOT), serum glutamic pyruvic transaminases (SGPT), alkaline phosphatise (ALP), total bilirubin, serum protein, and histopathological study against Paracetamol induce hepatotoxicity in the animals [34].

Immunomodulatory activity

Ethanolic extract showed delayed type hypersensitivity (DTH), humoral responses to sheep red blood cells, skin allograft rejection and phagocytic activity of the reticuloendothelial system in mice. It was found that the extract enhanced the phagocytic function and inhibited the humoral component of the immune system. It indicated that *A. heterophyllum* has immunomodulatory activity, which could possibly lead to new immunomodulating agents of herbal origin [35].

Nephroprotective activity

Ethanolic extract treated animals showed significant attenuation of biochemical parameters and histopathological changes of the kidney compared to glycerol treated group in dose dependent manner [32].

Contraindicated and adverse effect:

Unani scholars said *Atess* is contraindicated for kidney ailment [13]

Unani Formulations:

Atees has used an an ingredient in many Unani compound formulations, such as *M. Jograj Gugal* [10,14,36], *Majoon Bawaseer* [37], *Majoon Marruhul Arwah* [37], *Habb Ikseer Bukhar* [38], *Naujivan Gutti* [38].

CONCLUSION

Unani material medica is very rich having single drug from plants, animals and minerals for various therapeutic interventions, and regimens for prevention and treatment of diseases and health promotion is based on the concepts of holistic healing considering the individual's psycho-physical wellbeing [40]. Many single and compound drugs of unani system having cardiprotective, nephroprotective, antiasthamatic, antihyperlipidemic, antipsoriatic, etc. activities [41-71]. *Atees* (*Aconitum heterophyllum*) is one of the important drugs of Unani medicine used for its *daf-e-Humma* (antipyretic) especially for *humma Ijamai* (malarial fever) and *qatil kirm-e-shikam* (vermicidal activity). The antipyretic action of this drug has been proved by in yeast induced pyrexia in aqueous, choloroform and heaxane extract in compared to aspirin [39]. The other action of the drug remains to be validated on scientific parameters. So the human kind to be benefited with the action of this drug in future. *Atees* has multifaceted action at a time it has one has action on respiratory system e.g. *dafe sual* (antitussive) [11,13], simultaneously on digestive system e.g., *dafe zaheer* (antidiarrhoal) [10,11,12,15], *Dafe qay'* (antiemetic) [15], *hazim* (digestive) [11,12,15], *kasir-e-riyah* (carminative) [12,15], *mane qai* (Anti emetic) [11], *mohallil riyah* (carminative) [11], *mushily-e-balgham* (phlegmagogue) [11,12], *mushil-e-safra* (purgative of bile) [12], *qabiz-e-ama* (antiparistaltic) [10], *qatil kirm shikam* (vermicidal) [11,13] etc. It is also active for nervous system. Analgesic and anti-inflammatory action of this drug is proved in other study that shows the positive claims of unani scholars. The recent pharmacological studies i.e. anthelminthic activity, anti-diarrheal activity, anti-inflammatory activity and gastroprotective activity justify the claim of Unani Physicians. It is suggested that *Atees* may be taken for further pharmacological and clinical studies.

Conflict of interest:-

The authors declare that there is no conflict of interest.

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Abbreviations

ALP	-Alkaline phosphatise.
DPPH Assay	- 2,2-diphenyl-1-picryl-hydrazyl-hydrate.
DTH	-Delayed type hypersensitivity.
FRAP Assay	- Ferric reducing ability of plasma.
H2O2 Assay	- Hydrogen Peroxide assay.
HDL-c	- High-density lipoprotein cholesterol.
HMGR	- 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase.
LCAT	- lecithin-cholesterol acyltransferase.
NO Assay	- Nitric Oxide Assay.
SGOT	- Serum glutamic oxaloacetic transaminase.
SGPT	- Serum glutamic pyruvic transaminase.
USM	- Unani system of medicine.

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