Ethnopharmacological Investigations of Phytochemical Constituents Isolated from the *Genus Atropa*

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Abstract

Medicinal plants play a vital role in the development of human culture. Medicinal plants are a source of traditional medicine, and many modern medicines come directly from plants. According to WHO the world's people in progressing countries 80 percent rely on traditional medicine for their primary health care more over about 85% of traditional medication involves the make use of plant extracts. Herb and shrubs of the genus *Atropa* (Solonaceae) inhabitate various ecosystems in worldwide. This review present a complete study of the text on, phytochemistry, pharmacognosy and traditional biological meditional uses of *Atropa*. *Atropa* genus contain many chemical constituents like, flavonoids, phenolic compounds like Alkoloids, alcohols, terpenes and flavonoids have been identified in this genus. Some published studies have shown a broad spectrum of biological and pharmacological activities, including anticancer, antioxidant, anti-tumor agent, antibacterial, antimicrobial, antifungal and antiviral effects. Other have indicated anti-malaria agent, hypoglycemic and act as bioactive agent with anti-proliferation activities of this species. In vitro studies and in vivo models have provided a simple explanation for bioscientific and its various pharmacological uses. All information about the *Atropa* genus was collected from

electronic search (using Pubmed, Google Scholar, Science Direct.com and Web of Science) and a library search for articles published in peer-reviewed journals.

Key words Solonaceae, *Artopa*, Alkoloids, alcohols, terpenes and flavonoids, Ethnopharmacological properties

Introduction

Atropa belongs to the family *Solonaceae* and is a high Asian perennial subalpine plant local in Asia. It is a Indian medicinal plant widely distributed in the northwestern part of the Himalayas. [1, 2, 3]. *Atropa bella-donna*, commonly known as *Belladonna* or deadly nightshade, is a perennial herb of the *Solanaceae* family, native to West Asia and North Africa Europe, [4]. *Genus Atropa* is medically important as it has analgesic, carcinoma, anti-cholinergic, encephalitis, mydriatic, anti-spasmodic, and anti-dote, Parkinsonism, anodyne, sedative, hallucinogenic, narcotic and dysmenorrhoea, and spastic. *Atropa* genus belonging to the family *Solonaceae*, Hyoscyameae, consist of 4 species.

A large number of biologically active compounds are isolated from Atropa. This emphasizes the need to review the literature to report additional information on the medicinal importance of this genus.

Sr no	Species of *Atropa*	Region of existence in the world	Region of existence in the Pakistan	Ref#
1	*Atropa acuminata* Royle	it is distributed in Chakrata and Muzzafarabad North West Himalaya in Kashmir, and Western Himalayan,	Kashmir	5. 6
2	*Atropa belladonna* L	The plant species are native to Europe (Austria, Ukraine and Albania), North Africa (Algeria, Morocco) and West Asia (Iran, Turkey). It is grown in Europe, North and South America, and a few regions in India and Pakistan.	Present in Pak	7, 11
3	*Atropa baetica* Willk	Native to the central and southern parts of the Iberian Peninsula and North Africa, it has recently been classified as a	Absent in Pak	7

		rare endangered species commonly known as belladonna Andalusia.		
4	*Atropa pallidiflora* Schönb.-Tem	Western and north America	Absent in Pak	5,6

Traditional/Medicinal Uses:

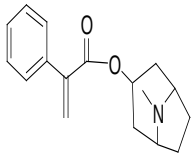
Plant Name	**Part of Plant used**	**Traditional uses**	**Reference**
Atropa Acuminata	Roots	Widely used in traditional medicine against arthritis and inflammatory disorders	1
Atropa Acuminata	Plant extract	Homeopathic skin treatment during breast cancer radiotherapy	8,9,10
Atropa Acuminata	Extract	Ayurvedic medicine to treat fever, chickenpox, colds, colitis, conjunctivitis (inflamed eyes) and diarrhea	8
Atropa Acuminata	Aerial parts of the plant	Muscle and joint pain, inflammation, pancreatitis, peritonitis, scarring, Parkinson's disease and neurological diseases.	1
Atropa Acuminata	Roots	Used against sore throat, ulcerative colitis, whooping cough	46
Atropa Acuminata	Root Paste	For Boiling	46
Atropa Acuminata	Leaves	Sedative	8
Atropa Acuminata	Young Leaves and Flowers	Decrease in emission of sweats and gastric glands	1,8

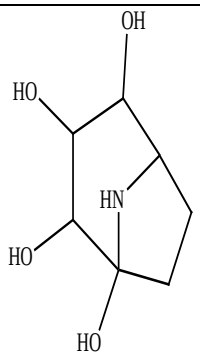
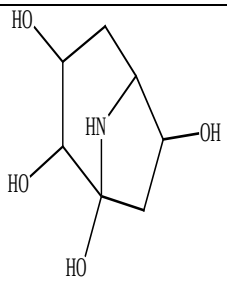
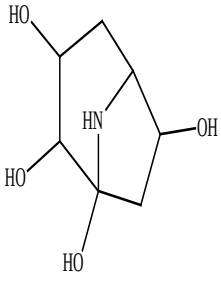
Plant Name	Part of Plant used	Traditional uses	Reference
Atropa Belladona	Whole Plant	Medicinal tropane alkaloids	12
Atropa Belladona	Stem and leaves	Muscarinic and scopolamine which are widely used as Anticholinergics, and the role of the parasympathetic nervous system	13
Atropa Belladona	Roots	Anticancer molecules	14,15
Atropa Belladona	Leaves	It has been used in herbal medicine for centuries as an analgesic, muscle relaxant and anti-inflammatory drug, and is used to treat menstrual problems, peptic ulcer disease, histamine response and motion sickness	16,17
Atropa Belladona	Leaves and Flowers	Anti-cholinergics	18
Atropa Belladona	Whole toxic plant	Symptoms of belladonna poisoning include pupil dilation, sensitivity to light, blurred vision, tachycardia, loss of balance, paralysis, headache, rash flushing, dry mouth and throat, unclear speech, urinary retention, constipation, confusion, hallucinations, paralysis and convulsions	16,19
Atropa Belladona	Transgenic hairy roots of belladonna	bioreactors to produce medicinal tropane alkaloids .	20

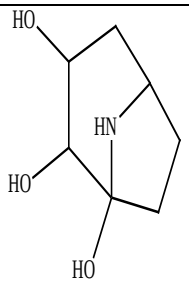
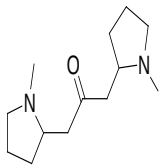
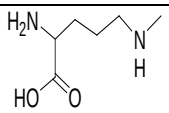
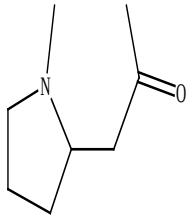
Plant Name	Part of Plant used	Traditional uses	Ref
Atropa baetica Willk	Whole Plant	Anticholinergic and antispasmodic effects	21,22
Atropa baetica Willk	Leaf and hairy roots	Anticholinergic drugs scopolamine and purine are used to treat motion sickness, ophthalmology, anesthesia, and heart disease and gastrointestinal diseases.	23,24

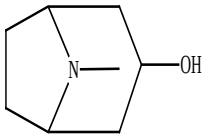
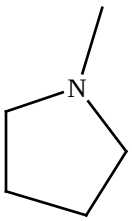
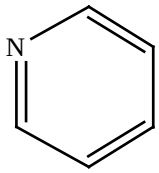
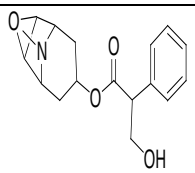
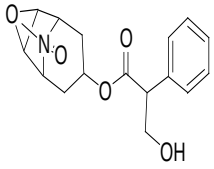
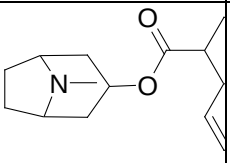
Plant Name	Part of Plant used	Traditional uses	Ref
Atropa pallidiflora Schönb.-Tem.	The leaves of Atropa pallidiflora contain a relatively large proportion of scopolamine, with alkaloid content	No literature is available on its medicinal importance	25

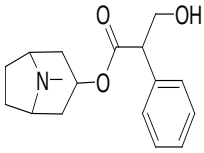
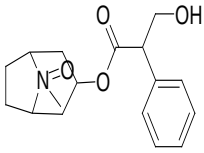
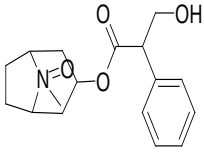
Chemical constituents of *genus Atropa*

Sr No.	Name	Biological Source	Biological Use	Structure	Ref
1	Apoatropine	Atropa belladonna, Datura pruinosa, Datura stramonium, Duboisia leichhardtii, alkaloids of Anisodus Tanguticus root, Hyoscyamus	Anti-spasmodic agent		*26*

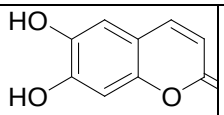
		orientalis, Mandragora spp. , Physochlaina alaica and other spp. (Solanaceae). Also obt. by Atropine is dehydrated with acid, acetic anhydride, and the like			
2	8-Azabicyclo[3.2.1] octane-1,2,3,4-tetrol; (1R,2S,3R,4S)-form	Alkaloids from Atropa belladonna, Solanum tuberosum, Solanum dulcamara, Solanum melongena, Solanum dimidiatum, Solanum kwebense and Datura wrightii (Solanaceae), leaves of Calystegia Arvensis and Calystegia sepium (Convolvulaceae)			*27*
3	8-Azabicyclo[3.2.1] octane-1,2,3,6-tetrol; (1S*,2R*,3S*,6S*)-form	Alkaloids from Atropa belladonna and Nicandra physalodes (Solanaceae), Calystegia Arvensis and Calystegia sepium (Convolvulaceae)			*27*
	8-Azabicyclo[3.2.1]octane-1,2,3,6-tetrol; (1S*,2R*,3S*,6S*)-form $C_7H_{13}NO_4$	Alkaloid from *Atropa belladonna* and *Nicandra physalodes* (Solanaceae), *Calystegia arvensis* and *Calystegia sepium* (Convolvulaceae			*27*

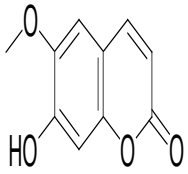
4	8-Azabicyclo[3.2.1]octane-1,2,3-triol; (1R,2S,3R)-form	Alkaloids from Atropa belladonna (Solanaceae), Calystegia arvensis and Calystegia sepium (Convolvulaceae) and Solanum tuberosum (potato) (Solanaceae			*27*
	Cuscohygrine	Atropine from belladonna (Atropa belladonna), Hyoscyamus niger, Datura spp., Erythroxylum coca and other Erythroxylum spp. , Solanum, Cyphomandra, Margaranthus, Acnistus, Salpichroa, Scopolia, Solandra, Convolvulus, Mandragora, Anthocercis and Lycianthes spp. (Solanaceae)			*28, 29*
	2,5-Diaminopentanoic acid; (S)-form,N^5-Me	Present in Atropa belladonna			*30*
	Hygrine	Alkaloids from Erythroxylum truxillense, Erythroxylum coca, Nicandra physaloides, Convolvulus Hamadana, Datura, Atropa, Hyoscyamus, Physalis, Dendrobium and Cochlearia spp. (Red carp, Solanaceae, Convolvulaceae, Orchidaceae, Cruciferae)	Intermed. in biosynth. of tropane alkaloids		*31*

	8-Methyl-8-azabicyclo[3.2.1]octan-3-ol; (1RS,3RS	From Atropa belladonna, Hyoscyamus niger, Datura spp. Alkaloids. And several other genera, almost all Solanaceae; hydrolysis from ester alkaloids such as Tropine tropate			*32*
	1-Methylpyrrolidine	Minor alkaloid from tobacco (*Nicotiana tabacum*), also found in *Atropa belladonna* (Solanaceae)			*33*
	Pyridine	Extracted in quantity from coal tar. Found in traces in some plants, e.g. *Nicotiana paniculata*, *Atropa belladonna* (Solanaceae			*34*
	Scopolamine; (-)-form	Alkaloid from *Atropa*, *Datura*, *Hyoscyamus* and *Scopolia* spp. and several other genera in the Solanaceae. Coml. sources are *Datura metel*, *Datura meteloides* and *Datura fastuosa* var *alba*			*35*
	Scopolamine; N-Oxide	Alkaloid from Atropa, Datura, Hyoscyamus and Scopolia spp. (Solanaceae)			*36*
	Tropine tropate; (±)-form	Alkaloid from Atropa belladonna, Datura stramonium, Anthocercis and other Solanaceae	Smooth muscle relaxant. Used in preanaesthetic medication to prevent reflex brachycardia and bronchospasm and to decrease gland secretions. Reduces rigidity in parkinsonism.		*35*

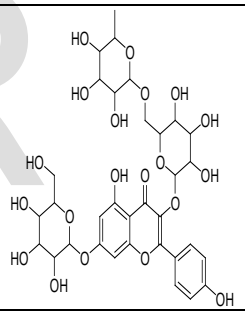
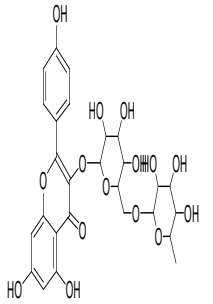
			. Nontoxic to some spp., e.g. rabbits. Reference material used in elemental microanalysis		
	Tropine tropate; (S)-form	Alkaloid from Atropa, Datura, Duboisia, Hyoscyamus, Anthocercis and Scopolia spp. , Mandragora officinarum and several other genera in the Solanaceae, esp. some strains of Duboisia myoporoides	Antimuscarinic agent with approx. twice potency of atropine. Spasmolytic agent. Bronchodilator, sedative, analgesic		*35*
	Tropine tropate; (S)-form, N-Oxide (equatorial O)	Alkaloid from Atropa, Datura, Hyoscyamus, Scopolia and Mandragora spp. (Solanaceae)			*35*
	Tropine tropate; (S)-form, N-Oxide (axial O)	Alkaloid from Atropa, Datura, Hyoscyamus, Scopolia and Mandragora spp.			*35*

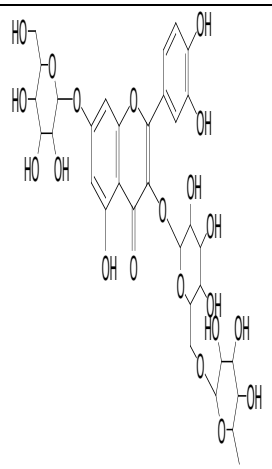
Benzopyranoids

17.	6,7-Dihydroxy-2*H*-1-benzopyran-2-one	Metab. of infected sweet potato also found in *Aesculus*, *Atropa*, *Datura*, *Digitalis* and other plants; found in some ferns	Shows antifungal, anti inflammatory and antifungal props		37, 38

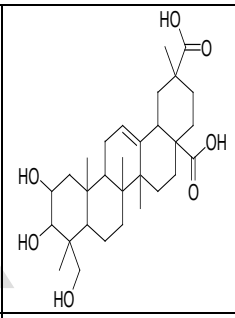
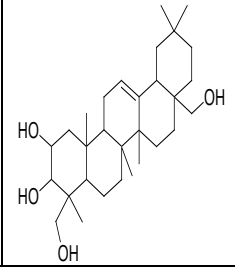
18.	7-Hydroxy-6-methoxy-2*H*-1-benzopyran-2-one	Occurs widely in the plant world, for example, the root of *Gelsemium sempervirens*, *Atropa belladonna*, *Convolvulus scammonia*, *Ipomoea orizabensis*, *Prunus serotina*, *Fabiana imbricata* and also *Diospyros* spp., *Peucedanum* spp., *Heracleum* spp., *Skimmia* spp. Also occurs in the Chinese crude drug Toki (from *Angelica acutiloba*)	Antispasmodic agent, anti inflammatory, eicosanoid release inhibitor		[38]

2.3.Flavnoids

19.	Kaempferol 3,7-diglycosides; 3-*O*-[α-L-Rhamnopyranosyl-(1→6)-β-D-galactopyranoside], 7-*O*-β-D -glucopyranoside	Isol. from Atropa belladonna, Strychnos variabilis and Vinca sp.			[39]
20.	Kaempferol 3-glycosides; 3-*O*-[α-L-Rhamnopyranosyl-(1→6)-β-D-galactopyranoside]	Isol. from Atropa belladonna, Medicago spp., Rumex chalepensis, Trigonella spp. and other plant spp.			40 41

21.	Quercetin 3,7-diglycosides; 3-*O*-[α-L-Rhamnopyranosyl-(1→6)-β-D-galactopyranoside], 7-*O*-β-D -glucopyranoside	Isol. from Atropa belladonna and Strychnos variabilis			42

Terpenes and terpenoids

22.	2,3,24-Trihydroxy-12-oleanene-28,30-dioic acid; (2α,3α)-form	Constit. of Atropa acuminate			[43]
23.	12-Oleanene-2,3,24,28-tetrol; (2α,3α)-form	Constit. of Atropa acuminate			[43]

Others

24.	Kaempferol 3-glycosides; 3-O-[Rhamnosyl-(1→?)-galactoside]	Isol. from leaves of Atropa belladonna and Gliricidia maculata			42

25.	Quercetin 3,7-diglycoside; 3-O-[Rhamnosyl-(1→?)-β-D-glucopyranoside], 7-O-glucoside	Constit. of Atropa belladonna, Baptisia lecontii and Euonymus sp.			44
26.	Tropinesterase	Isol. from mammalian tissues, e.g. rabbit; from plants, e.g. Atropa belladona, Datura tatula; and from Pseudomonas spp.	Catalyses hydrol. of atropine (BCM99) to prod. tropine (CCB72) and tropate		45

Ethnopharmacological activities:

Atropa acuminata (local name: Galakafal) is used to treat chronic leucorrhoea,, diarrhea, dysentery and general weakness [46]. Roots and leaves are commercial sources of drugs and are considered anti-asthma, anti-spasmodic, analgesics, diuretics, febrifuge, anesthetics and neuroleptics [47]. Atropa acuminata has been used in folk medicine to treat several inflammatory diseases such as arthritis, asthma, conjunctivitis, encephalitis, pancreatitis, peritonitis, acute infections and neuroinflammation. [5]. This study aimed to investigate the anti-arthritic effects of *Atropa acuminata* and to characterize the possible mechanism of action [1]. The plant extract also reports various biological activities such as spasm, anxiety, arthritis, asthma, bedwetting and intestinal diseases. However, there is no data on the hepatoprotective and antioxidant properties of the plant. Therefore, this study aimed to investigate the protective effect of Atropa ethanol extract on acetaminophen (APAP)-induced hepatotoxicity in rats [48]. Therefore, this study confirmed the cytotoxicity of native Indian herbs. Further research is necessary for the chemical characterization of the active ingredients and for a broader biological evaluation to demonstrate the role of Atropa acuminata in traditional medicine. Plants contain flavonoids such as quercetin, kaemferol, robinin and clitorin. It also contains starch, tannins, resins and anthocyanins.

Anti-inflammatory activity

The aim of this study was to investigate the regulation of *Atropa acuminata* (AAEE) ethanol extract on acute and in-vivo models of acute inflammation, to explore its potential as an anti-inflammatory agent, and to explore the underlying mechanisms of its action. Inhibition of

various inflammations, eicosanoid metabolites (prostaglandins and leukotrienes), NO and cytokines. This is the first report on the pharmacological properties of Atropa acuminata [49]. The anti-inflammatory activity of the extract was determined by carrageenan [50]. Carrageenan has been widely used to understand the pathophysiological basis of inflammation and to study the effects of traditional anti-arthritic medicinal plants [51]. Our results for *Atropa acuminata* show a highly potent anti-inflammatory effect by inhibiting the release of inflammatory mediators, Nitric oxide, prostaglandins, leukotrienes and pro-inflammatory cytokines [52].

Anti-arthritis activity

The aim of this study was to probe the anti-arthritic activity of *Atropa acuminata* (AAEE) ethanol extract and investigate its possible mechanism of action. In male wistar rats, the anti-arthritic activity of AAEE was assesed in the dose range of 125-500 mg / kg Bwin adjuvant-induced arthritis. Therefore, this study shows that AAEE is an effective anti-arthritis drug. Multiple attacks on inflammatory mediators and T helper cytokines and strong potency of AAEE may be associated with inhibition of chronic inflammatory responses in arthritis. The pattern of diversity of anti-arthritic activity of *Atropa acuminata* can be attributed to the additive effect of bioactive components that may be present therein, and also due to the high polyphenol and flavonoid content present in the extract. AAEE has been shown to have significant high phenolic, total flavonoid and flavanol content. It has been reported that many naturally occurring compounds such as polyphenols, diterpenoids, and triterpenoids can improve chronic inflammatory response. Experimental data reveals a significant correlation between the high content of phenolic compounds and the pharmacological activity of natural products. [53].

Anti-spasmodic activity

It has been found that chemically *Atropa acuminata* consist of tropane alkaloids and highly oxidized tri-terpenes [43]. All parts of the plant contain purine atropine, and alkaloids, bellodonnine, which are used as sedatives, anti-caries agents, for septic diseases and as antidote to poisoning [54]. They are commonly used as anesthetics and antispasmodics as well as for ophthalmic surgery.

Anti-dote activity

All parts of *Atropa acuminata* contain alkaloids, purine, atropine and bellodonnine, which are used as sedatives, anti-caries agents, for septic diseases and as antidote to poisoning [54].

Anti-hepatotoxic activity

In view of this, the aim of this study was to evaluate the effects of two doses of 250 mg / kg and 500 mg / Kg on the anti-hepatotoxicity and anti-oxidant activity of Atropa acuminata ethanol extract on acetaminophen-induced hepatotoxicity in rats. It was observed that the ethanol extract of AC confers significant liver protection. Biochemical and histopathological observations confirmed the beneficial effects of AC ethanol extract on acetaminophen-induced liver injury in rats. The activity of AC ethanol extract (750 mg / kg B / W) is comparable to the standard drug silymarin (25 mg / kg B / W). However, there is no data on the hepatoprotective and antioxidant properties of the plant. This study was designed to investigate the protective effect of Atropa ethanol extract on acetaminophen (APAP)-induced hepatotoxicity in rats. Acetaminophen (N-acetyl-p-aminophenol, acetaminophen), a widely used analgesic, antipyretic known to cause hepatotoxicity in experimental animals and humans at high doses [55, 56, 57, 58].

Anti-oxidant activity

The ethanol extract of *Atropa acuminata* significantly prevents liver damage and oxidative stress. Free radicals play an important role in the pathogenesis of several diseases, including cancer, rheumatoid disease, and degenerative processes associated with aging and neurodegenerative diseases [59]. Diseases associated with the destruction of free radicals can be controlled by enhancing the antioxidant defense system.

Anti-cancer activity

In the development of multicellular organisms and homeostasis, cell death is as important as cell proliferation. Although physiological cell death proliferates and inhibits apoptosis is a main feature of cancer cells. Apoptosis is a genetic regulation phenomenon that is encompassed by many chemotherapeutic agents in the treatment of cancer. The induction of apoptosis in tumor cells is supposed to be beneficial not only for the treatment and treatment of cancer, but also for the prevention of cancer [60, 61, 62]. This medicinal plant also demonstrates effective response to homeopathic skin treatment during breast cancer radiotherapy [54].

Anti-microbial activity

It has been reported in the literature that the tropane alkaloid synthesis site in many Atropa species is located at the root. *Atropa* and *Atropa acuminate* are also components of the main storage sites and have the peak point amounts of these alkaloids. These alkaloids can be moved to other plant organs to provide potential deterrent and antibacterial activity [15].

Cytotoxic activity

The above ground extract resists the singularity of the cell line Hep2. Cytotoxicity and anticancer properties are attributed to the presence of flavonoids. Phenolic compounds, including flavonoids, are particularly promising for the prevention of cancer. Phytochemicals in plant ethanol extracts may be responsible for these notable activities. Our laboratory is further studying the synthesis of new derivatives [63]. The ethanol extract of Atropa acuminata plants showed potent cytotoxic activity against Hep2 cells. And study the molecular mechanism responsible for the cytotoxicity of plants. This research may help to improve the scientific understanding of the chemical composition and function of the traditional medicinal plants tested, in order to provide insights into the cytotoxicity of plants to obtain useful chemotherapeutic agents [8].

Analgesic and Antipyretic activity

Collier & Shorley (1960) have demonstrated that analgesic-antipyretic drugs can antagonize bronchoconstriction of bradykinin in narcotic guineapig, and Lecomte (1960) has demonstrated that phenylbutazone prevents blood pressure drop and local increase in capillary permeability. It is widely believed that analgesic-antipyretic drugs have anti-inflammatory properties in human rheumatic diseases and experimentally induce inflammatory responses in other species, but the mechanism of action is unclear. Bradykinin has the potential for certain inflammatory responses proposed by Hilton and Lewis (1955), and their hypothesis is further confirmed by the fact that a group of chemically heterogeneous substances have the ability to inhibit bradykinin and inflammatory responses.It has been reported that polypeptides that are closely related or identical to bradykinin are produced in mammals [64].

Anti-neuroinflammatory disorders

The aerial part of Atropa acuminata has been used in traditional medicine to treat countless diseases such as muscle and joint pain, inflammation, pancreatitis, peritonitis, scarring, Parkinson's disease and neonatal diseases [65].

Anti-lipid per oxidation activity/ Anti lipidemic activity

The antioxidant and adaptive properties of the system caused by the destruction of the free radicals produced by APAP by the ethanol extract of Atropa acuminata [66,67].

Hallucinogenic activity

This plant (Atropa acuminata) is very toxic, causing hallucinations and paralysis, and can even lead to mental illness [68]. Children use “Sikran” as a hallucinogenic and sedative drug used alone or in combination with cannabis and mandala [69].

Anti-organophosphate poisoning activity

Organophosphorus (OP) toxicants inhibit the enzymatic hydrolysis of acetylcholine (ACh), which accumulates at the nerve endings, leading to the prolongation and enhancement of ACh at the effect site [70]. Most deaths from OP poisoning can be avoided by the timely use of atropine sulfate. Due to the practical problem, it is difficult to rapidly (intramuscular or intravenous) atropine sulfate at the incident site of the disease without the trained personnel.

Conclusion

This article briefly reviews the botanical distribution in the world, phytochemistry, biochemistry, traditional knowledge, ethnopharmacological and therapeutic application of the plant *Atropa acuminata*. This is an attempt to compile and document information on different aspects of *Atropa acuminata* and highlight the need for research and development

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