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PHYTOCHEMICAL CONSTITUENT OF *ACONITUM S*PECIES-A REVIEW

Gajalakshmi S, Jeyanthi P, Vijayalakshmi S, Devi Rajeswari V*

School of Biosciences and Technology, VIT University
*** sdevirajeswari@gmail.com**

ABSTRACT: Aconitum species were used as the major component in the Chinese and Bhutanese herbal medicines. The species posses many phytochemical compounds which possess many of the pharmacological activities. Diterpene alkaloids were the main compound with the pharmacological activities such as analgesic and against inflammation. This alkaloid possesses certain toxic hydrolyzed bases which could be detoxified by the intervention of recent technologies. Apart from this, the plant possess many alkaloids, amide alkaloids, flavonoids, flavonol glycosides, diterpenoid and norditerpenoid compounds which possess medicinal values. The above mentioned compounds of potent importance were isolated and characterized by the chromatographic separation techniques and their structures were usually elucidated by the spectroscopic studies especially with Nuclear Magnetic Resonance techniques. These compounds were the central target of the medicinal chemist as they possess both medicinal and toxic nature. The measures to be taken in such a way that the medicinal compounds of the plant should be isolated and formulated without the toxic nature. This review encompasses the total phytochemical compounds that have been isolated from various species of the plant genus *Aconitum*.
Keywords: Aconitine,Ematemesis, Flavonol glycosides, Diterpenoid alkaloids, Hypaconitine.

INTRODUCTION

Aconitum is proved to be an essential component in the formulations of Chinese and Japanese traditional medicine. They possess various pharmacological properties such as cardio tonic effect, blood pressure elevation, analgesic, anesthetics, and anti-inflammatory effect [1]. There are about 100 species of the plant genus, *Aconitum* that belongs to the family Ranunculaceae. Even though, some of the species are highly toxic they possess variety of medicinal importance. In Bhutan, there were around 19 *Aconitum* species and three species of this genus are included in more than 25 varied multi-ingredient products of Bhutanese traditional medicines which were known as 'g.so-ba-rig-pa' [2].

In Chinese herbal medicine, the plants tubers and roots are generally preferred for the treatment of various diseases, such as collapse, syncope, rheumatic fever, painful joints, gastroenteritis, diarrhea, edema, bronchial asthma, various tumors, and some endocrinal disorders like irregular menstruation. But, still the cardio- and neurotoxicity of the drug is found to be potentially lethal and it is said that the improper use of *Aconitum* in China, India, Japan and some other countries have resulted in a severe risk as they cause severe intoxications.

The State Food and Drug Administration of China (SFDA) has put up a regulation, which says that, only the processed, detoxified tubers and roots of *Aconitum* are permitted to administer orally. They are used in clinical decoctions and considered as raw materials for pharmaceutical manufacturing as there were around 70 techniques which are useful for the processing of *Aconitum* roots for their medicinal use [5].

Aconitum species are characterized chemically by means of the diterpene alkaloids which are being highly toxic and hence used in China as a complete source of arrow poison. But, the hydrolyzed bases are found to be non-toxic and hence employed in the Chinese and Japanese traditional medicine for its analgesic and anti-inflammatory properties. The genus *Aconitum* is found to be complex and needs certain criteria in order to distinguish the species and subspecies [6]. Overdoses of the constituent include certain disease such as arrhythmias, as they constitute the potent arrhythmogenic called as aconitine [20].

Medicinal uses

Table1: List of various species of Aconitum and their medicinal uses.

PLANT SPECIES	MEDICINAL USES
Aconitum heterophyllum Wall	Diarrhea, dysentery, cough, dyspepsia, chronic enteritis, and as a febrifuge and bitter tonic in combating debility after malaria [2]
Aconitum bulleyanum	Influenza, rashes and snake bite [2]
Aconitum orochryseum Stapf.	Common cough and cold, bilious fever, dysentery, as an antidote for snake bite and also as a febrifuge for fevers associated with malaria infection, kidney dysfunction and stomach ulceration [2]
Aconitum carmichaeli Debx.	Analgesic and cardio tonic [3], analgesic, diuretics, anti-inflammatory and cardio tonic actions [27]
Fuzi	Oriental medicine [33]
Aconitum brachypodum Diels	Anti-rheumatic and analgesic properties[5]
Aconitum napellus L	Homeopathic preparations [5]
Aconitum kusnezoffii Rchb	Analgesic and anti-rheumatic herbal medicine [23], treat heart failure congestion, neuralgia, rheumatism, gout, etc. homeopaths [50]
Aconitum coreanum (L`evl.) Rapaics	Cardialgia, facial distortion,epilepsia, migraine headache, vertigo, tetanus, infantile convulsion and rheumatic arthralgia, anti-arhythmia , analgesic and anti-inflammatory effects [31]
Aconitum taipeicumHand-Mzt	Anti-inflammatory and analgesic [32]
Aconitum finetianum Hand-Mazz	Enteritis, poisonous snake-bites and fractures [35]
Aconitum delavayi Franch	Rheumatism, traumatic injuries, blood stasis, swelling,pain, matemesis, hemoptysis, hematochezia, piles hemorrhage [36]
Aconitum sungpanense hand. Mazz	Rheumatism arthritis, neurological disorder and as an analgesic medicine [38]
Aconitum vulparia Rchb	Rheumatism, neuralgia and chronic skin disorders [42]
Aconitum naviculare (Bru¨ hl) Stapf	Colds, fevers and headaches, sedative, analgesic and febrifuge [43]
Aconitum kirinense Nakai	Rheumatic arthritis, rheumatoid disease [44]

The extracts obtained from *Aconitum* species are usually employed in the traditional Chinese and Japanese medicine as analgesics, antirheumatics and also for the treatment of neurological disorders. The pharmacological effects are proved mainly due to the presence of the diterpenoid alkaloids [21]. *Aconitum* genus is found to be a rich source of diterpenoid-alkaloids and also some species under this genus possessing the diester alkaloids are found to be highly toxic and also e possess anti-rheumatic and pain-relieving efficacy in it [23]. *Aconitum* alkaloids are broadly used as an antirheumatic, analgesics, anesthetics, and also in the treatment of various neurological disorders [25]. In order to reduce their toxicity the tubers and roots of aconites are applied only after cautious processing .The processed drugs are in turn used as the potent painkillers and also as the antirheumatic agents [26].

Phytochemical constituents

Flavonol glycosides such as quercetin 3-O-β-D-glucopyranoside-7-O-(6-E-p-coumaroyl)-β-D-glucopyranosyl(1→ 3) - α-L-rhamnopyranoside , quercetin 3-O-β-D-glucopyranoside-7-O-β-Dglucopyranosyl -(1→3)-α-L-rhamnopyranoside , quercetin 3-O-β-D-glucopyranoside-7-O-(6-E-caffeoyl)-β-D-glucopyranosyl-(1→3)-α-L-rhamnopyranoside were isolated from the aerial parts of *A.burnatii Gayer*[4].

Flavonol glycosides such as 3-O-((b-D-gluco pyranosyl -(1→3)-(4-O-(E-p-coumaroyl))-a-L-rhamnopyranosyl-(1→6)-b-D-galacto pyranoside))-7-O-a-L-rhamno pyranoside , kaempferol 3-O-((b-Dglucopyranosyl(1→3) -(4-O-(E-p-coumaroyl))-a-L-rhamno pyranosyl-(1→6)-b-D-galactopyranoside))-7-O-a-L-rhamnopyranoside and flavonoids such as quercetin 3-O-a-L-rhamno pyranosyl -(1→6)-b-D-galactopyranoside-7-O-a-L-rhamnopyranoside or clovin and kaempferol 3-O-a-Lrhamnopyranosyl-(1→6)-b-D-galactopyranoside-7-O-a-Lrhamno pyra -noside or robinin were isolated from *Aconitum anthora* [7]. *Aconitum variegatum* possess norditerpene alkaloids such as 16b-hydroxycardiopetaline,8-ethoxysach aconitine, 14-acetylgenicunine B, N-deethyl-N-19-didehydrosachaconitine and diterpene alkaloids such as 15-veratroyldictizine,15-veratroyl-17-acetyldictizine,15-veratroyl-17-acetyl-19-oxodictizine,N-ethyl-1a-hydroxy-17-veratroyldictizine, variegatine and also the alkaloids such as sachaconitine,14-O-acetylsachaconitine,karakoline,talatizamine,hydroxytalatizamine,14 acetyltalatizamine, 14-acetyl-10-hydroxytalatizamine,N-methyl armepavine, pengsheninB, delsoline, dihydro delsoline, delcosine and genicunin B[9].

Diterpenoid alkaloids showed the pharmacological properties such as arrhythmogenic (neurocardiotoxic), local anesthetic, antiarrhythmic, curariform, analgesic, hypotensive, anti-inflammatory, spasmolytic, neurotropic and psychotropic in nature [8]. Fourteen toxic *Aconitum* alkaloids such as aconitine, mesaconitine, jesaconitine,hypaconitine and deoxy aconitine and their hydrolysis products such as benzoylaconines and aconines was established by using the capillary liquid chromatography (LC) fast atom bombardment mass spectrometry (FAB-MS) [11].
Diesterditerpene-type *Aconitum* alkaloids such as aconitine, mesaconitine and hypaconitine are found to be both intoxicant and active [12]. *Aconitum napellus subsp. Neomontanum* possess flavonol *glycosides* quercetin7-O-(6-trans-caffeoyl)-b-glucopyranosyl-a-rhamnopyranoside-3-O-b-glucopyranoside, kaempferol 7-O-(6-trans-caffeoyl)-b-glucopyranosyl-a-rhamno pyranoside-3-O-b-glucopyranoside and kaempferol 7-O-(6-trans-p-coumaroyl)-b-glucopyranosyl-a-rhamnopyranoside-3-O-b-glucopyranoside in their flowers[14]. *Aconitum leave* contains lycoctonine-type norditerpenoid alkaloid such as swatinine, delphatine , lappaconitine , puberanine and N-acetylsepaconitine in their aerial parts [15].
Aconitum which is termed as Fuzei contains three highly toxic C19 diterpenoid alkaloids such as aconitine, mesaconitine, and hypaconitine in its root [13, 19 and 28]. Bioassay-guided fractionation by means of the 1,1-diphenyl-2-dipicrylhydrazyl (DPPH) radical scavenging test of the polar extracts of some Italian *Aconitum* species such as *A. napellus* subsp. *tauricum*, *A. napellus* subsp. *neomontanum*, *A. paniculatum*, *A. vulparia* has led to the isolation of thirteen flavonol glycosides [16]. Alkaloids such as 6-benzoylheteratisine,heteratisine,14-benzoyl talatisamine,talatisamine,1-benzoylnapellien and songorine are utilized as an analgesics in traditional Chinese medicine [17].
6-Benzoylheteratisine which is the main alkaloid of *Aconitum tanguticum* is found to be a monoester diterpene alkaloid that is structurally related to aconitine. This alkaloid is found to be less toxic than the aconitine and also possess certain anti nociceptive properties [18].Another four toxic *Aconitum* alkaloids such as aconitine, mesaconitine, hypaconitine and jesaconitine was also established using high-performance liquid chromatography (HPLC) combined with ultraviolet absorbance detection, solid-phase extraction and mass spectrometry (MS) in the blood and urine sample [22].
Aconitum roots possess aconitine, mesaconitine, hypaconitine, benzoylaconine, benzoylmesaconine, benzoylhypaconine and several other compounds were also reported [24]. *Aconitum* episcopale possess diterpenoid alkaloids such as liaconitine A (N-ethyl-1a,6a,16b,18-tetramethoxy-13b-ol-2,3-dehydroaconitane-8-acetate-14-anisoylate),B(N-ethyl-1a,6a,16b,18-tetramethoxy-13b-ol-2,3-dehydroaconitane-8,14-dianisoylate and C (N-ethyl-1a,6a,16b,18-tetramethoxy-8-ethoxy-13b-ol-2,3-dehydroaconitane-14-anisoylate) in their roots [29]. *Aconitum transsectum* contains various norditerpenoid alkaloids such as transconitine A, B and C yunaconitine, crassicauline A, foresaconitine, talatisamine, S-deacetylyunaconitine, geniconitine, indaconitine,forestine, 14-acetyltalatisamine and chasmanine [30].

Aconitum coreanum contains Alkaloids and diterpene alkaloid isomers in their roots [31, 49]. *Aconitum taipeicum* possess amide alkaloids 3-isopropyl-tetrahydropyrrolo [1, 2-a] pyrimidine-2, 4 (1H, 3H)-dione and 1-acetyl-2, 3,6-triisopropyl-tetrahydropyrimidin-4(1H)-one in its root[32]. Franchetine is the norditerpenoid compound isolated from the roots of *Aconitum franchetti* Fin[34] .*Aconitum finetianum* was found to possess certain diterpenoid alkaloids such as anthranoylly coctonine (inuline) and lycoctonine in its roots[35]. *Aconitum delavayi* contains C18-norditerpenoid alkaloids such as delavaconitine F 1 and delavaconitine G 2 in its roots [36]. *Aconitum orientale* possess diterpenoid alkaloids such as demethyll appaconitine; 7, 11, 14-trihydroxy-2, 13-dioxohetisane, 6, 13, 15-trihydroxyhetisane and N-deethyldelphatine lappaconitine, lycoctonine and browniine [37]. The diterpenoid alkaloids such as Aconitine, mesaconitine, and hypaconitine were isolated from the roots of *Aconitum carmichaelii Debx* [10,47].
Diterpenoid alkaloids such as demethyllappaconitine, 7,11,14-trihydroxy-2,13-dioxohetisane,6,13,15-trihydroxy hetisane and N-deethyldelphatine was isolated from *Aconitum orientale* [37].Trans-2,2V,4,4V-tetramethyl-6,6V-dinitroazobenzene were the compounds derived from the leaves of *Aconitum sungpanense* [38].Franchetine-type C19-diterpenoid alkaloid known as 3-hydroxyfranchetine and aconitine-type C19-diterpenoid alkaloid called asatropurpursine was isolated from the roots of *Aconitum hemsleyanium var. atropurpureum* [39].

Quercetin3-O-(6-transcaffeoyl)-β-glucopyranosyl-(1→2)-β-glucopyranosyl-7-O-α-rhamnopyranoside and quercetin-3-sophoroside-7-rhamnopyranoside were isolated from *Aconitum napellus sp. Lusitanicum* [40]. The above-ground parts of *Aconitum nasutum* contain a new norditerpenoid alkaloid 3-hydroxy talatisamine [41]. Flavonol glycosides were also isolated from the flowers of *Aconitum vulparia* [42]. 3-O-[b-D-glucopyranosyl-(4-O-trans-p-coumaroyl)-a-L-rhamno pyranosyl-b-D-glucopyranosyl]-7-O-[b-D-glucopyranosyl-a-L-rhamno pyranosyl] kaempferol, 3-O-[b-D-glucopyranosyl-(4-Otrans-p-coumaroyl)-a-L-rhamnopyranosyl-b-D-glucopyranosyl]-7-O-[b-D-gluco pyranosyl-a-L-rhamnopyranosyl] quercetin and 7-O-[b-D-glucopyranosyl-a-L-rhamno pyranosyl] quercetin were the compounds isolated from the aerial parts of *Aconitum naviculare* [43].

Two new C20±diterpenoid alkaloids such as kirinines B and C was isolated from the roots of *Aconitum kirinense* [44]. *Aconitum karacolicum Rapcs* possess certain alkaloid compound that consists of a 14-benzoylaconine moiety substituted on C-8 by an azeloyl chain [45]. Norditerpenoid alkaloids such as 1-*epi*-chasmanine, talatisamine,isotalatizidine, vilmorrianine D, nevadenine, pseudaconine, viresenine, lycoctonine, hordenine and the diterpenoid alkaloid were isolated from the *Aconitum racemulosum* Franch var.*pengzhouense* [46]. *Aconitum sinomontanum* Nakai posses the alkaloids which includes lappaconitine, 3 ranaconitine, *N*-deacetyllappaconitine and *N*-deacetylranaconitine[48].A water -insoluble glucan (AKP) compound was isolated from the roots of *A. kusnezoffii Reichb* [50].

CONCLUSION

Medicinal plants were the potent source of phytochemical constituents that are responsible for its pharmacological activities. Many phytochemical compounds were isolated from various species of the above genus and yet in the progress of further exploitation. These compounds possess medicinal value that was proved from the history of ancient formulations. The new compounds isolated in the past few years were also investigated for their medicinal as well as their toxic nature. The technologies available were not enough and yet to be discovered further to reduce the toxicity of certain compounds.

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