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ИЗВЕСТИЯ

НАЦИОНАЛЬНОЙ АКАДЕМИИ НАУК
РЕСПУБЛИКИ КАЗАХСТАН

АО «ИНСТИТУТ ТОПЛИВА, КАТАЛИЗА И
ЭЛЕКТРОХИМИИ ИМ. Д.В. СОКОЛЬСКОГО»

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ХИМИЯ ЖӘНЕ ТЕХНОЛОГИЯ СЕРИЯСЫ

♦

СЕРИЯ ХИМИИ И ТЕХНОЛОГИИ

♦

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НАН РК сообщает, что научный журнал «Известия НАН РК. Серия химии и технологий» был принят для индексирования в Emerging Sources Citation Index, обновленной версии Web of Science. Содержание в этом индексировании находится в стадии рассмотрения компанией Clarivate Analytics для дальнейшего принятия журнала в the Science Citation Index Expanded, the Social Sciences Citation Index и the Arts & Humanities Citation Index. Web of Science предлагает качество и глубину контента для исследователей, авторов, издателей и учреждений. Включение Известия НАН РК в Emerging Sources Citation Index демонстрирует нашу приверженность к наиболее актуальному и влиятельному контенту по химическим наукам для нашего сообщества.

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ALKALOID-BEARING SPECIES OF THE GENUS *ACONITUM* L.

Abstract. Analytical review of alkaloid-bearing plants of the genus *Aconitum* L. has been carried out. The obtained data will serve as a basis for scientific research of some plantspecies in the genus *Aconitum* L., isolation of alkaloids including high purity aconitine tocreate a new drug substance.

By identifying specific habitats of species of this genus in the flora of Kazakhstan, it is established that most herbarium materials have been collected in mountainous floristic regions of the flora of Kazakhstan, which justifies the need to study samples of the genus *Aconitum* L. from the indicated floristic areas. The herbarium fund of the InternationalResearch and Production Holding "Phytochemistry" JSC (KG) includes herbarium materials of 9 species of the genus *Aconitum* L., of which the most common species are*Aconitum leucostomum* Worosch. and *Aconitum monticola* Steinb.forming large thickets inthe nature.

Keywords: *Aconitum* L., alkaloids, chemical study, herbarium materials, cameral treatment.

Representatives of the genus *Aconitum* L.belong to one of the most valuable alkaloid-bearing plants of the family *Ranunculaceae*,and area rich source of polyfunctional heterocyclic compounds - diterpene alkaloids. Plants of the genus *Aconitum* L. are accessible and widely spread in Kazakhstan, CIS countries, China and Central Asia;howeverthey differ in qualitative composition and contentdepending on the area of their growth. The increased attention of researchers to diterpene alkaloids is due to the known complexity of their structure resulting in a broad spectrum of pharmacological activity. Diterpene alkaloids have a wide range of biological activities: anti-inflammatory, local anesthetic, antiarrhythmic, antispasmodic, antitumor, and muscle relaxant, which allows them to be considered as a source of promising pharmacological compounds.

The pharmacological study of plants of the genus *Aconitum* L. revealed that during the flowering stage all the aerial parts - stalks, leaves, and flowers are very poisonous. Moreover, the most deadly are rhizomes and tubers of the plant when the accumulation of alkaloidsoccurs. It has been determined that in pips of thisplant speciesthe amount of alkaloids gradually increases during the whole vegetative period and reaches its maximum in the autumn.

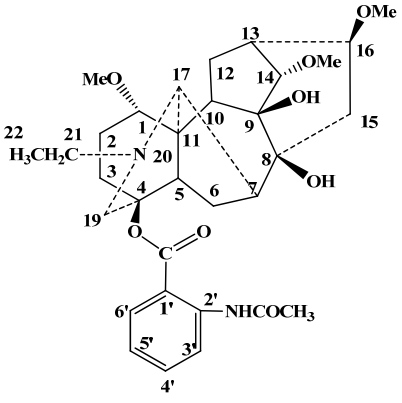
Aconitum species are of interest as medicinal plants because they have numerous isoprenoid compounds as major secondary metabolites, i.e. tetracyclic diterpenoid alkaloids. The structure of isoprenoids of the genus *Aconitum*is unusual since the lowest terpenoids (mono-C-10 and C-15sesquiterpenes) are present only in small amountsin these plants, mainly in flowers, whereas all other parts accumulate diterpenoid compounds of peculiar structural types.

Over 70% of modern homeopathic remedies are produced from medicinal plant materials. Plants of the genus *Aconitum* L. are one of the most popular in homeopathy. Homeopathic Pharmacopoeias of the leading countries of the world (Germany, France, the USA, and others) include aconite preparations obtained from the following plant species*: Aconitum napellus* L., *Aconitum ferox* Wall., *Aconitum lycoctonum* L.

According to the Flora of the USSR, there are over 300 *Aconitum* species all over the world, 70 of which are in the territory of the former USSR. In turn, 14 species are found in the flora of Kazakhstan.

They grow in the mountains on forest and subalpine meadows, among bushes [1-2]. N.G. Gemedzhiyeva in her research [3-4] noted that all 14 species belong to alkaloid-bearing plants.

Scientists of a number of countries are conducting rigorous studies of plants of the genus*Aconitum* L. A great contribution to the study of plant species of the genus *Aconitum*has been made by Uzbek researchers S.Yu. Yunusov, M.S. Yunusov, V.A. Telnov, E.F. Akhmetova, I.A. Bessonova, as well as foreign scientists H.Takayama, W.S.Pelletier, and otherswho determined the main composition of alkaloids. They developed cost-effective and environmentally-friendly production technologies of the *Allapinin* on the basis of lappaconitine **1** from the roots and rhizomes of *Aconitum leucostomum* Worosch. and*Aconitum septentrionale* Koelle.; *Antiaritmin*drug **2** from the by-products of allapinin production, cumulativeantiarrhythmic drugs *Aklezin* from the aerial parts of *Aconitum leucostomum* Worosch., and *Aksaritmin* from the rhizomes of*Aconitum septentrionale* Koelle.. The production technology of the *Aconitine* bioreactant substance **3**has been developed from the tubers of *Aconitum soongaricum* Stapf.[5-12].



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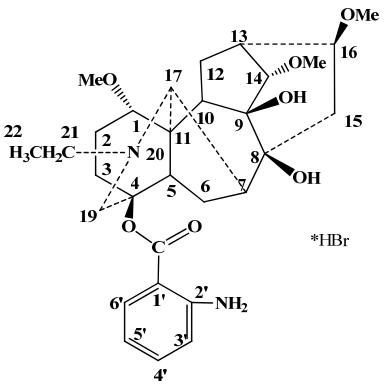

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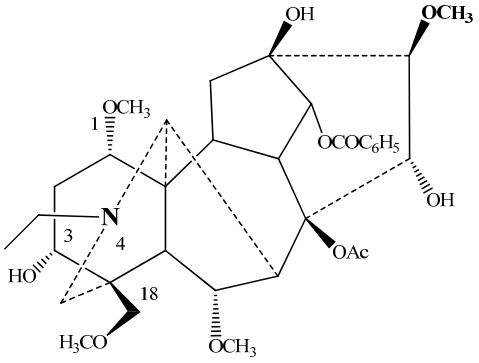


3

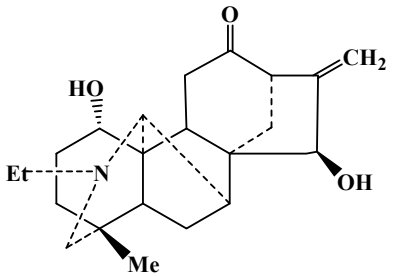
Thanks to the research of academicians-chemists S.Yu.Yunusov and M.S. Yunusov and academician-cardiologist E.I. Chazov alkaloid lappaconitine has firmlytakenits place in a series of antiarrhythmic agents in the form of *Allapinin*drug. It is indicated for supraventricular and ventricular extrasystoles, paroxysmal forms of flickerand atrial flutter, tachycardia. Lappaconitineis worth mentioningbecauseit happened to be susceptible to the synthetic transformations resultingin substances with the preserved pharmacological activity butwithout major harmful side effects. It should be noted that the introduction of a bromine atom into alappaconitine molecule leadto a compound witha 5 times lower toxicity and 10 times higher activityas an antiarrhythmic drug. Lappaconitineis producedby two species *Aconitum lycoctonum* L. and *Aconitum septentrionale* Koelle. According to the research of aprominent botanist N.I. Fedorov, only in the territory of Bashkiria the available stock of the roots of *Aconitum lycoctonum* L. is sufficient to meet the demands of the health care system of Russia.

Several *Aconitum* species, ofwhich the most promising producer is *Aconitum soongaricum* Stapf,contain aconitine. Due to the highest toxicity this alkaloid has not been applied in medicine. However, experimental pharmacology could not have been conceived without it. Unlike other antiarrhythmics whichinfluence only the calcium channels and cover both the calcium and sodium channels of arrhythmia, aconitine is a selective sodium channel blocker. The studies of antiarrhythmic drugs without aconitine are unreliable.

In 1820, Peschierwas the first who pointed out thataconitineis present in the leaves of *Aconitum*. Geiger and Hesse isolated aconitine from the parts of *Aconitum* in 1838, and Morzon in 1839;while Plaita in 1850 proposed a chemical formula for amorphous aconitine [13]. Aconitine is one of the major alkaloids related to some of the extremely toxic ones, which are contained in some*Aconitum* species [14].

Alkaloid songorine**4**has a more balanced structure interms of functionalization;it exhibits an effect on the central nervous system. It is produced by *Aconitum barbatum* Pers.spread in Altai, which can be cultivated.

Alkaloidsaconitine, mesaconitine, napelline, aconifine, 8-acetylexcelsinehave been isolatedduring the chemical studies of *Aconitum karakolicum* Rapaics., *Aconitum altaicum* Steinb., and *Aconitum kirinense* Nakai..Altaconitine and anovelalkaloid acofine**5** have been isolated for the first time from *Aconitum karakolicum* Rapaics. and *Aconitum altaicum* Steinb.. *Aconitum soongaricum* Stapf. and *Aconitum karakolicum* Rapaics. species are closely relatedto each other morphologically [15-20].



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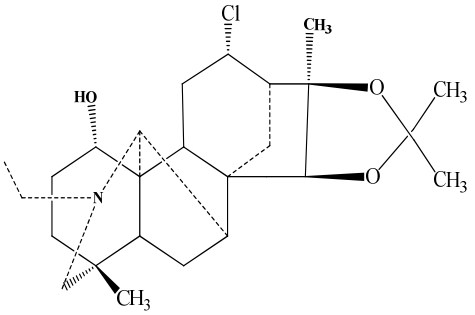
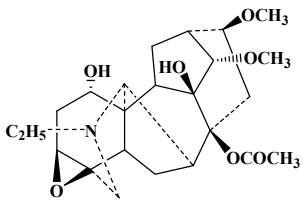


5

Researchers isolated alkaloids talassamine, talatizamine, 14-*O*-acetyltalatizamine, isotalatizidine, isoboldine, talatizidine, crystalline hydrochloride from *Aconitum talassicum* M. Pop. Extraction of *Aconitum talassicum* M. Pop. was carried out with chloroform, with the raw material preliminarily alkalinized withbicarbonatum natrium, then the extract wasacidified with sulfuric acid and the alkaloids separated with chloroform. The sum of alkaloids was eluted with a chloroform-methanol (100:1) mixture on a silica gel column followed by recrystallization with methanol [21-23].

Researchers of the Institute of Organic Chemistry of the UrB RAS (Ufa) isolated 6 previously known alkaloids hypaconitine, mesaconitine, neoline and three aporphine alkaloids glaucine, N-methyllaurotetanine, and isoboldine from *Aconitum neosachalinense* H.Lev.. The extraction was performed with water in the presence of acetone followed byseparation on a column [24].

The Russian scientists [25] developed an isolation method for the diterpene alkaloids from *Aconitum kirinense* Nakai. growing on the territory of Primorsky Krai. The alkaloids were separated by gas and high performance liquid chromatography (GC and HPLC) methods with mass spectrometric detection of separated peaks and fragmentation in atmospheric-pressure chemical ionization (APCI), atmospheric-pressure ionization - electrospray(API-ES), and electron impact modes. Using liquid chromatography – mass spectroscopy(LC-MS) with fragmentation in APCI and API-ES modes,the following 6 diterpene alkaloids were identified in *Aconitum kirinense* Nakai.: 8-acetylexcelsine**6**, tugiaconitine**7**, akiramine**8**, kirinine **9**, lepenine**10**.



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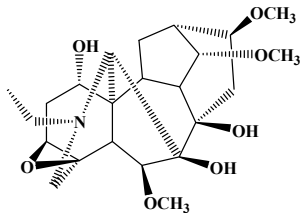

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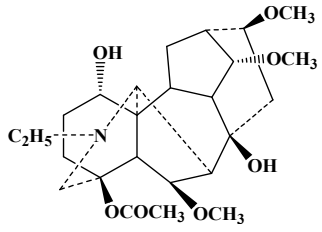

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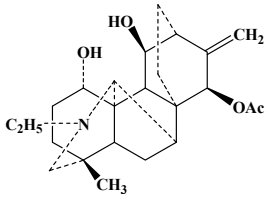

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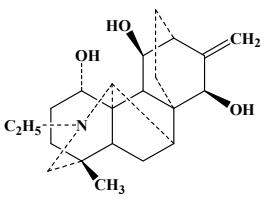


10

During the study of callus formation of*Aconitum barbatum* Pers., theoptimal conditions for the cell

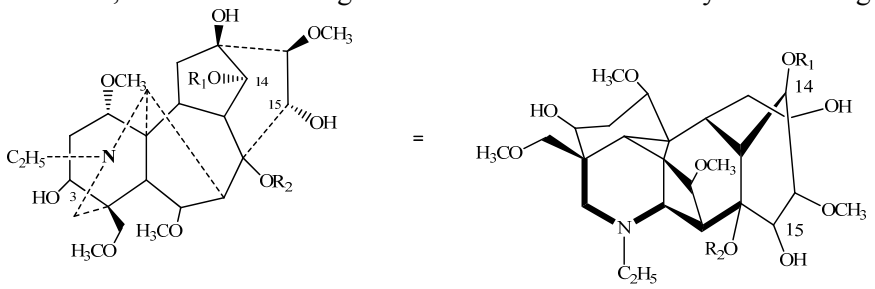
culture of this plant were selected, callus culture viability was determined, the sum of alkaloids wasobtained from the callus mass of intact plant raw materials, individual diterpene alkaloidswereisolated and purified using a liquid column chromatography. It has been found that the tissue culture contains the following alkaloids: songorine, songoramine, napelline, 12-epi-napelline N-oxide,and mesaconitine [26].

The Chinese scientists were the first to isolate C19-diterpene alkaloids habaenine C, vilmorrianine C, classicauline C from *Aconitum habaense* W.T.Wang. [27].

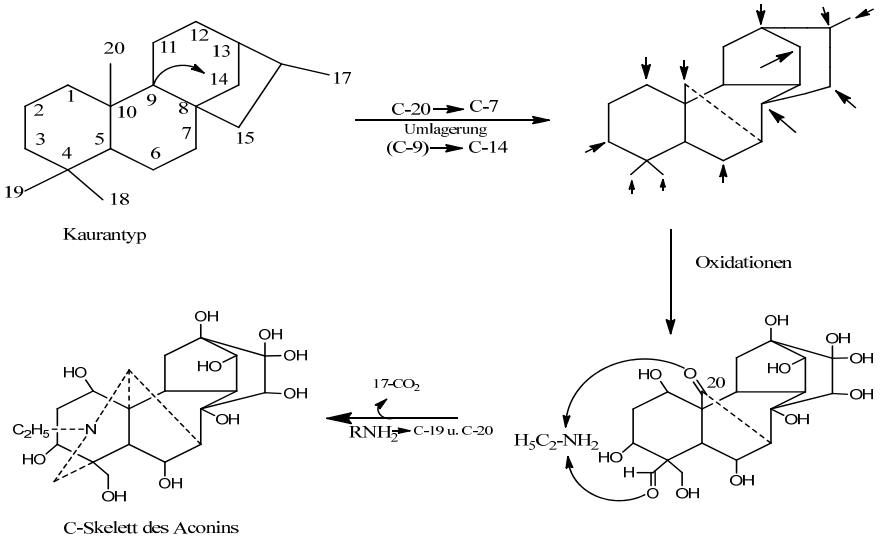
Scientists from Georgia conducted a chemical study of underground organs of*Aconitum orientale* Mill. and *Aconitum nasutum* Fisch. ex Reichenb. It was determined that both species *Aconitum* L. of the flora of Georgia have alkaloids aconitine, lappaconitine, and karakoline. In *Aconitum orientale* Mill., there are bases of ranaconitine, gigactonine, licoctonine, and in *Aconitum nasutum*Fisch. ex Reichenb. talitizamine, cammaconine, aconisine [28-29].

All *Aconitum*diterpene alkaloids are characterized by a high density of oxygen-containing functional groups, but aconitine molecule is an unconditional record holder. It is likely that the highest saturation by these groupsis the reason ofan extreme toxicity of aconitine.

Biosynthesis, pharmacological activity, and also the dynamics of accumulation of diterpene alkaloids of some plant species of the genus *Aconitum*have not been studied in full. Biogenetically, the aconine bases are most likely derived from tetracyclic or pentacyclic diterpenes in which the nitrogen atom of methylamine, ethylamine, or β-aminoethanol binds to C17 and C19 in the C19 diterpenoid skeleton, and to C19 and C20 in the C20 diterpenoid skeleton to form a substituted piperidine ring.That is why the aconitine-type compounds are considered as alkaloids *sui generis*, because their nitrogen is not derived from an amino acidic metabolism. They are defined as pseudo-alkaloids. Little is known about how plants synthesize these alkaloids, and almost nothing is known about how this biosynthesis is regulated.

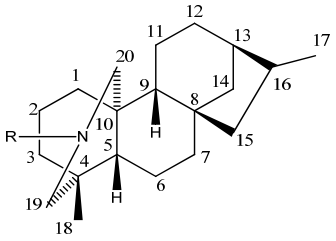


R_1	R_2	
COC_6H_5	$COCH_5$	Aconitine
COC_6H_5	H	Benzoylaconine
H	H	Aconine



Their biogenetic precursors are the diterpenoids of the ent-kauran and atisiran series. In both cases,

during the biosynthesis an additional nitrogen-containing cycle is formed in such a way that the heteroatom becomes a bridge between the C19 and C20 atoms. In this case, two structural subtypes, C20 and C19, which are designated by the number of carbon atoms of the cyclic skeleton, are distinguished. In contrast, C20 alkaloids are derived from two carbon frameworks **11** and **12**. In specific substances, these carbon skeletons are usually framed by oxygen-containing substituents, as in veathine**13** and atizine **14**, giving the names to the corresponding subgroups of the C20 series. In both cases, there are frequent cases of the formation of additional hetero- or carbocycles in addition to those already present in structures **13** and **14**.



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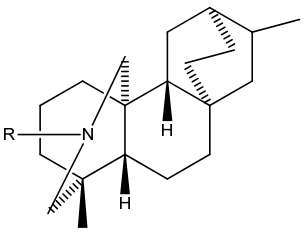

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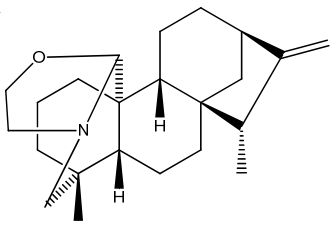

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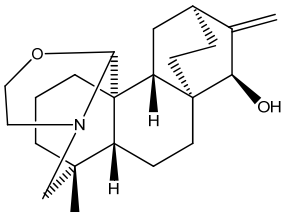
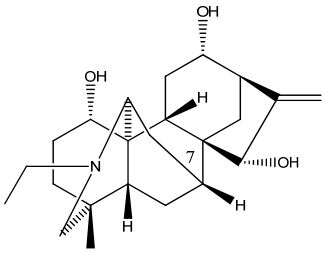


14

R = H, Me, Et

Additional cycles can arise by creating bonds between C20 and C7 atoms, as well as C20and C14 atoms. In the first case, a cyclic system is constructed like in the alkaloids napelline**15** and denudatine**16**. The second variant is realized in the hedagine molecule **17**.In the structures of the latter type, it is possible to form another cycle by binding the nitrogen atom to the C6 carbon as in getisine **18**. All compounds with the carbon-nitrogen skeleton are classified as the getisine group. In a small family of anopterin**19**, C20 and C14 atoms are bound by carbon-carbon bondto the ent-kauran-type skeleton. Alcaloid delnudine**20** also belongs to the C20series. Its molecule is a result of the getisine precursor rearrangement.



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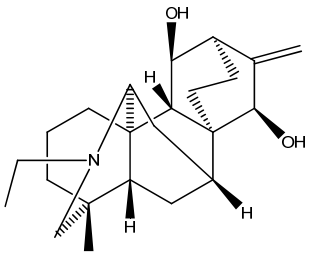

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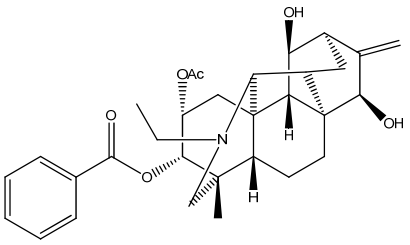

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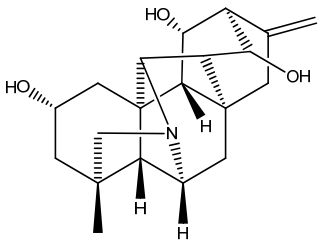

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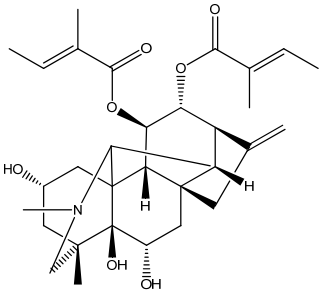

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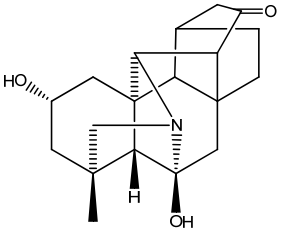
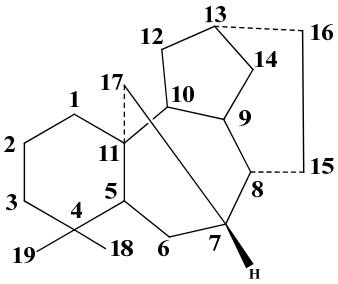


20

The base of the structure of the diterpenoid alkaloids of the C19series is the rearranged carbon skeleton of kauran **21**, also calledaconane. Like in C20 compounds, a nitrogen bridge is formed between the C17 and C19 atoms. By the name of the alkaloid lycoctonine**22**, a carbon-nitrogen skeletonin its base is alsocalled lycoctonane. Within the C19alkaloid family, two main subgroups are distinguished. Having the same carbon-nitrogen skeleton, they differ from each other by the substitution pattern at C6 and C7

atoms. To the lycoctoninesubgroup are referred bases with a hydroxyl substituent at the C7 position and a β-methoxy one at the C6 atom. The presence of an α-glycol moiety is also characteristic for this subgroup of substances. Aconitine is a representative of the other subgroup of C19 alkaloids bearing its name. There are no substituents at the C7 atom, and amethoxy group at the C6 atom has an α-orientation.



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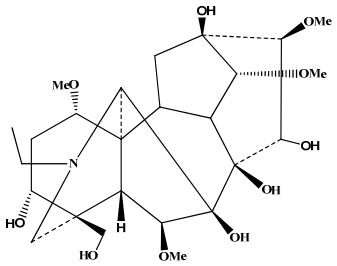


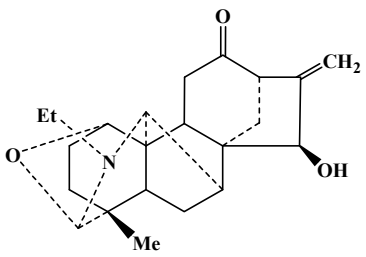
22

The group of C19 diterpenoid alkaloids is quite numerous. By 1987, 175 natural representatives of this group had been known. Over 150 of themwere isolated from plants of the genera *Aconitum* L. and *Delphinium* L.

C19 and C20 diterpenoid bases in their majority are highly poisonous substances. Thus, LD 50 of aconitine is only 0.22 mg/kg. Due to this fact, *Aconitums* and *Delphiniums*are among the deadliest plantsof the middle latitudes. The toxic effect of their nitrogen metabolites is realized in a disruption of the nervous system activityand a heart function. In small doses, many of these substances exhibit anti-inflammatory, analgesic, antiarrhythmic, anti-epileptic properties. Moreover, different alkaloids have their own spectrum of physiological effects. For instance, aconitine is astrong analgesic agent, whilelycoctonine is completely deprived of this action. The practical application of diterpenoid alkaloids as drugs is restricted due to thepoisoning hazard in case of an overdose. Despite this fact, *Allapinin* (lappaconitine hydrobromide) is produced in Russia and is known as one of the best antiarrhythmic drugs.

For a number of years, JSC International Research and Production Holding "Phytochemistry" have been working on isolation and study of alkaloids from plant species of the genus *Aconitum* L. A general production technology of alkaloids from plant raw materialshas been developedusing conventional extraction techniques and a column chromatography. The isolation methodsare specificfor each alkaloid and have their own peculiarities, which makes it possible to obtain alkaloids with 95-99.9% purity according tothe HPLC analysis results [30, 31].

During the chemical study of roots of *Aconitum monticola* Steinb. we have isolated and identified alkaloids songorine **4** (yield 0.1%), the accompanying alkaloid songoramine **22**, monticamine **23**, delcosine **24**. Delcosine has been isolated from *Aconitum monticola*for the first time. The chemical composition of *Aconitum leucostomum* Worosch.has been studied and four main compounds have been isolated, they are as follows:mesaconitine **25**, lappaconidine **26**, sepaconitine **27**, lappaconitine**1**. X-ray diffraction analysis has been carried out for the first time to determine the spatial structure of a lappaconitine molecule [32-34].



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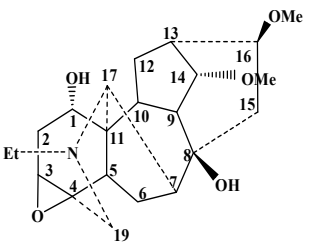

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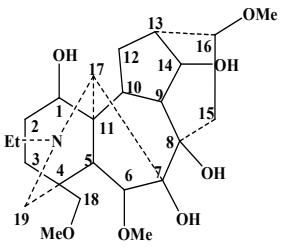

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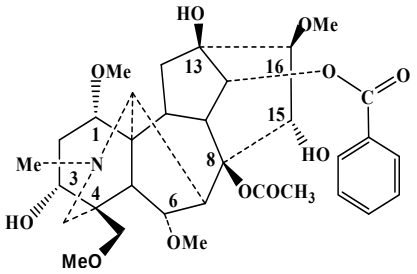

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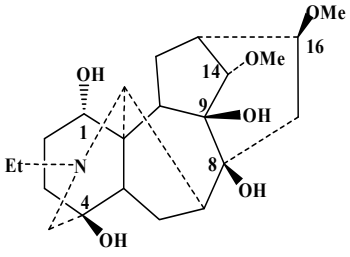

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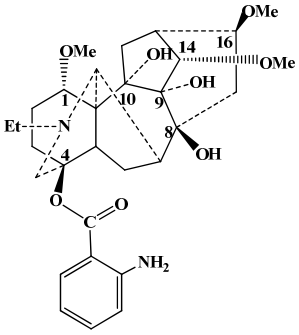

27

The optimal conditions for separation and analysis of alkaloids songorine, lappaconitine, and associated components have been determined by HPLC. Themethod of quantitative analysis of the investigated compounds has been developed for the plants of*Aconitum soongaricum* Stapf., *Aconitum anthoroideum* DC.,and *Aconitum villosum* Reichenb., growing on the territory ofKazakhstan. The content of alkaloids in plants under study varies according to HPLC data, i.e.songorine from 0.01% to 0.23%, lappaconitine from 0.01% to 0.04% of the air-dry raw materials [35].

Phytochemical screening of the harvestedwild samples from the genus *Aconitum* L., allowed us to establish the pronounced antibacterial activity of the cumulative extract from*Aconitum anthoroideum* DC., an analgesic activity of the cumulativeextract from*Aconitum leucostomum* Worosch. and *Aconitum villosum* Reichenb., and a cytotoxic activity of extracts from*Aconitum monticola* Steinb., *Aconitum anthoroideum* DC*., Aconitum leucostomum* Worosch., and *Aconitum villosum* Reichenb. Fl. Alt. The expressed antiviral activity of lappaconitine and the sum of alkaloids from*Aconitum monticola* Steinb. and *Aconitum anthora*have been determined for the first time against the carnivore plague virus and infectious rhinotracheitis, which makes them promisingingredients for the development of a new drug [36].

It has been revealed that the main components of *Aconitummonticola* Steinb. are songorine**4**and songoramine **22**;*Aconitum soongaricum* Stapf. - aconitine **3** anddelcosine**24**;*Aconitum leucostomum* Worosch. - lappaconitine **1**.

In the herbarium fund of JSC International Research and Production Holding"Phytochemistry",there are collections of 9 species from the genus *Aconitum*, the most common of which are *Aconitum leucostomum* Worosch. and *Aconitum monticola* Steinb.forming large thickets in the wild.

We have conducted a cameral treatment of herbarium materials of *Aconitum* species in the herbarium fund of JSC IRPH «Phytochemistry» (KG) to identify the specific habitats of plants from this genus in the flora of Kazakhstan.

***Aconitum monticola* Steinb**. in Fl. URSS. 7 (1937) 730, 209. - Gamajun. in Fl. Kazakh. 4 (1961) 52, tab. 6, fig. 1. - Vorosch. in Bull. Main bot. garden, 72 (1969) 37. - A. pallidum auct. non Rchb .: Kar. et Kir. in Bull. Soc. Nat. Mosc. 15 (1842) 138. - A. lycoctonum auct. non L.:O. et B. Fedtsch. in Tr. Society nat. Kazan. Univ. 33, 3 (1899) 79, quoad var. pallidum. - O. et B. Fedtsch. Consp. Fl. Turk. 1 (1906) 22, quoad var. pallidum. Type in Leningrad.

Herbarium collections: East Kazakhstan region, the Koksuridge, a forest meadow. 14.VIII.2014; Almaty region, Zhungarsky Alatau, in the vicinity of Lepsinsk village, the lower part of the ravine Rusachka. 10. VII.2000.

***Aconitum leucostomum* Worosch.** Bull. Main. bot. garden, 11 (1952) 62. - A. excelsum p. p. non Rchb. Fl. USSR, VII (1937) 201; Kryl. Fl. West. Sib. V (1931) 1151. - A. vulparia C.A. Mey. ex Ldb. Fl. Alt. II (1830) 287, non Rchb. Type in Vienna.

Herbarium collections: Karaganda region, the Karkaraly mountains, in the vicinity of Lake Pashennoe, in the floodplain by the stream. 16.VI.1976 (KG); East Kazakhstan region, in the

neighborhood of Leninogorsk, Ivanovsky ridge, larch planting site. 21.VII.1976 (KG); Karaganda region, Karkaralinsk district, the surroundings of Shaitan-kul lake, the shore by the stream. 7.VII. 1984 (KG); East Kazakhstan region, in the vicinity of Leninogorsk, the linear albumen of the field pit, the sole of the mountain 23.VIII. 1985 (KG); East Kazakhstan region, the road Ust-Kamen - Leninogorsk, in the vicinity of Bystruha village, the slopes of the mountains. 23.VIII.1985 (KG); Semipalatinsk region, near the village Alekseevka, the Tarbagatai mountains. 10.VII.1994 (KG); Almaty region, Aksai gorge of Zailiysky Alatau 2200 m, along the Aksay river, 12.VII.2000 (KG); East Kazakhstan region, Listvyaga ridge, the Upper Katun district,herb meadowsat foothills, 2100 m abovesea level. 26.VII.2004 (KG); East Kazakhstan area, Western Altai, Ivanovsky ridge, thinned larch-cedar forest. H=1800 m. 11. VIII.1997 (KUZ); Kazakhstan, East Kazakhstan region, Western Altai, Ivanovskiy range. Fir-birch forest. H=1700 m. 08.VII.1997 (KUZ); East Kazakhstan region, Western Altai, Ivanovsky range, a temporary watercourse side. A high-grass alpine meadow. H=1900 m. 11.VIII.1997 (KUZ); East Kazakhstan region, Western Altai, Ivanovsky range, 4 km north-east. peaksof Vysheyvanovsky Belok. Alpine meadow. H=1900 m. 08.VII.1997 (KUZ); East Kazakhstan region, Western Altai, Ivanovsky ringe, a temporary watercourse side. A high-grass alpine meadow. H=1900 m. 27.VII.1997 (KUZ).

***Aconitum septentrionale* Koelle.** 1786, Spicil. Observ. Acon. : 22; Friesen, 1993, Fl. Sib. 6..: 138.

Herbarium collections: Kazakhstan, Pavlodar region, Bayanaul mountains, glades at the foothills. 08.VIII.2006. (KUZ).

***Aconitum anthoroideum* DC.** in Syst. nat. 1 (1818) 366. - Gamagun. in Fl. Kazakh. 4 (1961) 53, tab. 7, fig. 3. - Vorosch. in Bull. Main Bot. garden of the Academy of Sciences of the USSR. 72 (1969) 37. A. Anthora var. anthoroideum Rgl. in Ind. Sem. Hort. Petropol. (1861) 41. - Kryl. Fl. Sib. Occid. 5 (1931) 1147. - A. anthora auct. non L .: O. et B. Fedtsch. in Tr. Society Nat. Kazan. Univ. 33, 3 (1899) 79. - O. et B. Fedtsch. Consp. Fl. Turk. 1 (1906) 22. - Steinb. in Fl. URSS.7 (1937) 190, quoad pl. ex Dshung. et Tarb. Type in London.

Herbarium collections: East Kazakhstan region, in the vicinity of Leninogorsk down the road to Bogdanicha. 06. VIII.1963 (KG); East Kazakhstan region, Alpine meadows near the Topolovka river (near Katun village) 28. VII.2004 (KG); East Kazakhstan region, in the vicinity of Zavodinka village. 01.VIII.2012 (KG); East Kazakhstan region, Western Altai, Ivanovsky ridge, eastern foothills ofthe peaksVysheyvanovsky Belok. Moraine. H=2000 m. 26.VII.1997. VII (KUZ); East Kazakhstan region, Western Altai, Ivanovsky ridge, northern spurs of Vysheyvanovsky Belok peak, tundra. H=2100 m. 22.VII.1997 (KUZ).

***Aconitum soongaricum* Stapf.** in Ann. Bot. Gard. (Calcutta) 10 (1905) 141. - Steinb. in FL. URSS.7 (1937) 232. - Gamagun. in Fl. Kazakh. 4 (1961) 54, tab. 7, fig. 6, excl. pl. e Alat. Transil. - Gamajun in Vorosch. in Bull. Main Bot. garden, 72 (1969) 39, pro max. p. (excl. plantis floribus et pedunculis appressi pubescentibus). A. alatavicum Vorosch. in. Bot. Journ. 30, 3 (1945) 137, fig 11, b; fig. 12, a. - Vorosch. in Bull. Main Bot. garden, 72 (1969) 38. - A. Napellus auct. non L .: Trautv. in Bull. Soc. Nat. Mosc. 33, 1 (1860) 83 (incl. formae 1,2,3). - O. et B. Fedtsch. in Tr. Society Nat. Kazan. Univ. 33, 3 (1899) 80, quoad pl. e Tarb. Alat. Dshung., p.p. et Tian-Schan, p.p. - O. et B. Fedtsch. Consp. Fl. Turk. 1 (1906) 23, quoad pl. e Tarb., Alat. Dshung., p.p. et Tian-Schan, p.p. et e excl. syn. - A. karakolicum auct. non Rapcs .: Vorosch. in Bull. Main Bot. garden 72 (1969) 39 pro min. p. (quoad plantas floribus et pedunculus patenter pilosis). Cotype in Leningrad.

Herbarium collections: Almaty region, Zailiysky Alatau, Kaskelen gorge, 1955m. above sea level N= 43º00'38.8" E = 076 º37'21,8". 8.X.2017 (KG); Almaty region, Zailiysky Alatau, Aksai gorge, along the Aksai river. 1800-2000 m. above sea level. A herbal and shrubs community. 12. VII.2000 (KG); Almaty region, Zhungarsky Alatau, the gorge Uigentas. 2200m. above sea level. 26.VIII.2014 (KG); Kazakhstan, Almaty region, Alakol district, Zhongar-Alatau State National Natural Park (SNNP), the upper reaches of the river Sarymsakty, the subalpine zone. 45 ° 24.229'NL, 80 ° 49.662'EL, A=2226. 24.VIII.2014 .; Kazakhstan, Almaty region, Alakol district, Zhongar-Alatau SNNP, the upper reaches of the river Sarymsakty, moraine lakes, alpine meadow. 45 ° 21.175'NL, 80 ° 48.442'EL, A=2600. 25.VIII.2014.

***Aconitum villosum* Reichenb.** Fl. Alt. II, 282; Ldb. Fl. Ross. I, 68. - A. ciliare β. polytrichum DC. Syst. I (1818) 378.-A. flaccidum Rchb. Uebers. (1819) 39 nom nud. - Fl. USSR, VII (1937) 213. - A. volubile var. villosum Rgl. Ind. Sem. Horti Bot. Petropol (1861) 43; Kryl. Fl. West. Sib. V (1931) 1150. Type in Vienna.

Herbarium collections: East Kazakhstan region, Listvyagaridge, 15 km down the village Kegi, a shrubby herbal forest edge. 02.08.2004.

***Aconitum altaicum* Steinb.** Fl. USSR, VII (1937) 731, 222. - A. napellus var. alpinum Rgl. Ind. Sem. Hort. Bot. Petropol. (1861) 45 p.p .; Kryl. Fl. West. Sib. V (1931) 1149. Type in Leningrad.

Herbarium collections: East Kazakhstan region,Narymsky ridge, in the neighborhood of village Novoberezovka, vally of theriver Terekty. 1120 m. above sea level. 26.VIII.1976 (KG); East Kazakhstan region, in the vicinity of Leninogorsk. 09.IX.1982 (KG).

***Aconitum volubile* Pall.** ex Koelle, Spicil. Acon. (1788) 21; Fl. USSR, VII (1937) 213; Kryl. Fl. West. Sib. V (1931) 1150. Type in London. - A. tortuosum Willd. Enum. Hort. Berol. (1809) 576.

Herbarium collections: East Kazakhstan region, branch of the state farm Ulanovskiy, natural boundary Katre.27.VIII.1985 (KG); East Kazakhstan region, Ridder,in the neighborhood of the village Kedrovka. 05.VIII.2012 (KG); East Kazakhstan region, Western Altai, northern foothills of Ivanovsky ridge, stow Gray Meadow, floodplain of the river White Uba. H=1200 m. 14.VIII.1997 (KUZ).

***Aconitum barbatum* Pers.** Syn. Pl.II (1807) 83; Fl. USSR, VII (1937) 204; Kryl. Fl. West. Sib. V (1931) 1153 - A. sibiricum Poir. Encycl. meth. Suppl. I (1810) 113-A. hispidum DC. Syst. Nat. I (1818) 367. - A. Gmelini Rchb. Uebers. Gatt. Aconitum (1819) 63. - A. ochranthum C. A. M. in Ldb. Fl. Alt. II (1830) 285. - A. lycoctonum var. barbatum Rgl. Bull. Soc. Nat. Mosc. XXXVI, 3 (1861) 77. Type in London.

Herbarium collections: Semipalatinsk region, the neighborhood of the village Yuzhny, the southern slope of the hill. 08. VII.1994 (KG).

Thus, based on the results of cameral treatment of herbarium materials in the herbarium fund of JSC IRPH “Phytochemistry” (KG), ithas been established that most herbarium collectionswereharvested in mountainous floristic regions of the flora of Kazakhstan, which highlights the need to study samples from the genus *Aconitum*in these floristic areas. The herbarium fund contains herbarium materials of 9 species of the genus *Aconitum*, of which the most common are *Aconitum leucostomum* Worosch. and *Aconitum monticola* Steinb. forming large thickets in the nature.

The conducted analytical review will serve as a ground for phytochemical studies of plants of the genus *Aconitum*. In the course offuture research,we plan to extract alkaloids from some plants of the genus *Aconitum* and carry out chemical transformations of these alkaloids to obtain new substances with the improved physico-chemical properties, a more pronounced biological activity, a lower toxicity, and a prolonged action as compared to the original natural analogues. The promising sources for production of biologically active alkaloids, including aconitine, are*Aconitum soongaricum* Stapf., *Aconitum monticola* Steinb., and *Aconitum leucostomum* Worosch., growing in the territory of Kazakhstan.

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ACONITUM L. ТУЫСТАС ӨСІМДІКТЕРДІҢ АЛКАЛОИДТЫ ТҮРЛЕРІ

Аннотация. *Aconitum* L. туыстас өсімдіктердің алкалоидты түрлеріне талдамалы шолу жүргізілді. Алынған деректер *Aconitum* L. туыстас өсімдіктердің бірқатар түрлерін ғылыми зерттеу, сондай-ақ жаңа дәрілік зат жасауға арналған алкалоидтарды, соның ішінде тазалығы жоғары аконитинді бөліп алу үшін негіз болады.

Аталған өсімдік түрлерінің Қазақстан флорасындағы нақты өсу орындарын анықтау бойынша кеппешөп материалдарының басым бөлігі Қазақстан флорасының таулы флоралық аудандарында жиналғаны белгілі болды. Бұл аталған флоралық аудандардағы *Aconitum* L. туыстас өсімдіктердің үлгілерін зерттеу қажеттілігін көрсетеді. «Фитохимия» халықаралық ғылыми-өндірістік холдингі» АҚ-да (KG) *Aconitum* L. туыстас 9 өсімдік түрінің кеппешөп материалдары бар, олардың ішінде табиғатта үлкен тоғайларды құрайтын *Aconitum leucostomum* Worosch. және *Aconitum monticola* Steinb. өсімдік түрлері неғұрлым жиі кездеседі.

Түйін сөздер: *Aconitum* L., алкалоидтар, химиялық зерттеу, кеппешөп материалдары, камералық өңдеу.

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АЛКАЛОИДОНОСНЫЕ ВИДЫ РОДА *ACONITUM* L.

Аннотация. Проведен аналитический обзор алкалоидоносных растений рода *Aconitum* L. Полученные данные послужат основой для научных исследований некоторых видов растений рода *Aconitum* L., выделению алкалоидов, в том числе аконитина высокой чистоты для создания нового лекарственного вещества.

По выявлению конкретных мест произрастания видов данного рода во флоре Казахстана, установлено, что большинство гербарных материалов собраны в горных флористических районах флоры Казахстана, что свидетельствует о необходимости изучения образцов рода *Aconitum* L. из указанных флористических районах. В гербарном фонде АО «Международный научно-производственный холдинг «Фитохимия» (KG) имеется гербарные материалы 9 видов рода *Aconitum* L., из них наиболее часто встречаются виды рода *Aconitum leucostomum* Worosch. и *Aconitum monticola* Steinb., образующие большие заросли в природе.

Ключевые слова: *Aconitum* L., алкалоиды, химическое изучение, гербарные материалы, камеральная обработка.

МАЗМҰНЫ

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