SOVIET ADVANCES IN THE DEVELOPMENT OF THE CHEMISTRY OF THE ALKALOIDS

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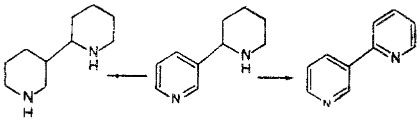
The first alkaloids, theobromine and harmine, were discovered in Russia in the forties of the last century [1]. Then, at the time of the first world war, when Russia was experiencing a shortage of medicaments, the industrial isolation of morphine and codeine from opium, of caffeine from tea dust, of theobromine from cacao pods, etc., was organized, and Prof. A. E. Chichibabin, with his colleagues and pupils, V. M. Rodinov, N. A. Preobrazhenskii, R. A. Konovalova, and others developed a method of obtaining codeine and apomorphine from morphine and other methods. The investigations begun in this period by A. E. Chichibabin and N. A. Preobrazhenskii and their colleagues perfected the synthesis of pilocarpine, cocaine, tropine, scopolamine, arecoline, colchicine, the ipecac alkaloids, yohimbine, cinchonamine, eserine, and the curare alkaloids [2].

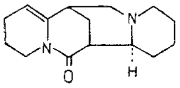
In 1928, an alkaloid division in the Ordzhonikidze All Union Chemical and Pharmaceutical Scientific Research Institute (VNIKhFI) was organized in Moscow under the direction of Academician A. P. Orekhov. Its workers studied mainly the domestic flora in order to find medicinal substances of practical value in it and to establish the structure of newly-isolated alkaloids.

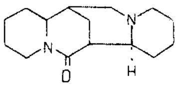
The first Soviet alkaloid, anabasine, was isolated from the central Asiatic plant **Anabasis aphylla** by Academician A. P. Orekhov in 1929 [3]. Anabasine has the composition $C_{10}H_{14}N_2$, gives nicotinic acid on oxidation with potassium permanganate, and loses three molecules of water with the formation of α,β-bipyridyl on dehydrogenation with silver acetate and zinc dust. The catalytic hydrogenation of anabasine forms optically active α,β-bipyridyl. Hence, anabasine has the structural formula of β-(α-piperidyl)pyridine [4, 5].

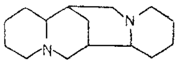


This formula was confirmed by syntheses [6, 7]. This was the first alkaloid, a compound of pyridine with piperidine, that proved to be an effective insecticide, like nicotine.

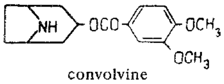
Subsequently, A. P. Orekhov and G. P. Men'shikov [4] isolated lupinine from the low-boiling fraction of the mixture of alkaloids of **Anabasis aphylla**, and the new alkaloids aphylline and aphyllidine from the high-boiling fraction. The catalytic hydrogenation of aphyllidine gave aphylline and the electrolytic reduction of aphyllidine gave dextro sparteine. In view of the loss of optical activity of the des-bases in the repeated Hofmann degradation of aphyllidine, Orekhov ingeniously proposed the following structural formulas for these alkaloids [8]:

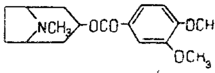

aphyllidine


aphylline


α-sparteine

A. P. Orekhov and R. A. Konovalova [9] isolated from **Convolvulus pseudocantabrica** two new alkaloids, convolvine and convolamine, which proved to be esters of tropine and nortropine with veratric acid:


convolvine


convolamine

In 1932, G. P. Men'shikov isolated heliotrine $C_{16}H_{27}O_5N$ and lasiocarpine $C_{21}H_{33}O_7N$ from the central Asiatic plant **Heliotropium lasiocarpum** [10]. The alkaline hydrolysis of heliotrine gave an optically active amino alcohol, heliotridine, and heliotric acid. In heliotridine, the nitrogen is tertiary and the two oxygens are in the form of hydroxyl groups.

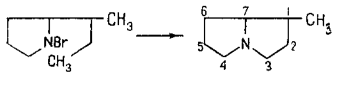
Catalytic hydrogenation of heliotrine in the presence of platinum formed a saturated monohydric amino alcohol, hydroxyheliotridane, and heliotrinic acid. On being heated with concentrated sulfuric acid, the hydroxyheliotridane was dehydrated, forming a base with a double bond, heliotridene, the hydrogenation of which formed the saturated base $C_8H_{15}N$, heliotridane. Consequently, the conversion of heliotrine into heliotridane can be illustrated by the following scheme:

$$\underset{\text{heliotrine}}{C_{16}H_{27}O_5N} \longrightarrow \underset{\text{heliotrinic acid}}{C_8H_{16}O_4} + \underset{\text{hydroxyheliotridane}}{C_8H_{15}ON} \longrightarrow \underset{\text{heliotridene}}{C_8H_{13}N} \longrightarrow \underset{\text{heliotridane}}{C_8H_{15}N}$$

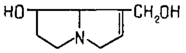
Splitting out of trimethylamine from heliotridane after three successive Hofmann degradations shows that the nitrogen of heliotrine is present at the nodal point between two condensed rings.

The Zelinskii dehydrogenation by means of a palladium-asbestos catalyst of dihydro-des-N-methylheliotridine formed a base which proved to be a pyrrole, These reactions showed that one of the rings of heliotridine is a pyrrolidine ring.

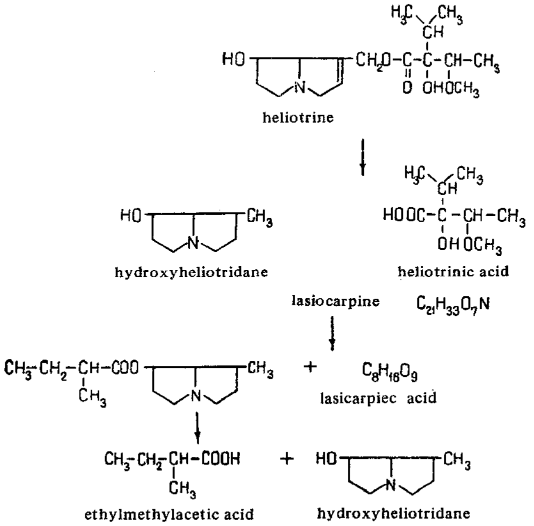
Tetrahydro-des-N-dimethylheliotridane was synthesized. From this work, the structure of 1-methylpyrrolizidine was proposed for heliotridane, and Men'shikov confirmed this by the synthesis of dl-heliotridane.

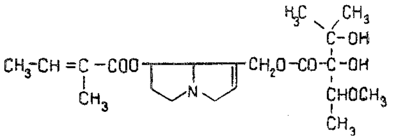


Then, the synthesis of heliotridane was repeated by two other methods and it was possible to obtain both of its diastereomeric forms. Thus, G. P. Men'shikov discovered the existence of the nitrogen heterocyclic compounds of the pyrrolizidine series. At present, more than 120 alkaloids of this series are known. Many of them were isolated from Senecio plants by R. A. Konovalova and A. P. Orekhov. Among them platyphylline has proved to be a valuable medicinal substance. With rare exceptions, the alkaloids of the heliotridane group are esters of mono- and dibasic acids and 1-methylpyrrolyzidine; they have two asymmetric centers and are therefore derivatives of l- and d-heliotridane, pseudoheliotridane, and l-pseudoheliotridane. Men'shikov and Kuzovkov have shown that heliotridine is a diastereomer of retronecine [11].

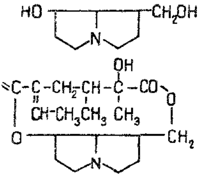


Heliotrine is nothing other than heliotridane in which the primary alcohol group has been esterified with heliotrinic acid, which explains the reductive decomposition of heliotrine well.

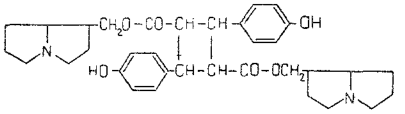




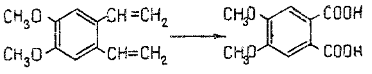
Platyphylline $C_{18}H_{27}O_5N$, like many of the Senecio alkaloids, is a cyclic diester. Both hydroxyl groups of platynecine are esterified by the dibasic cis-senecionic acid [12].

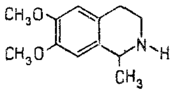


Thezine was isolated by A. P. Arendoruk from Thezium minkwitzianum. The base is saponified by alkaloids and gives two molecules of the amino alcohol 1-hydroxymethylpyrrolyzidine and thezinic acid [13].

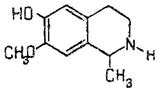


In 1933, A. P. Orekhov and N. F. Proskurnina isolated the new alkaloids salsoline and salsolidine from Salsola richteri. The oxidation of the nitrogen-free substance obtained by the Hofmann degradation of salsolidine formed meta-hemipinic acid [14].





I



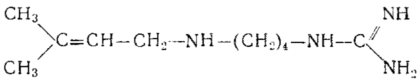
II

Salsoline (II), salsolidine (I), and their isomers were synthesized by A. P. Orekhov and E. Shpet [15]. Salsoline is used in medicine for reducing the blood pressure.

A. P. Orekhov and N. F. Proskurnina also established the structure of ammodendrine, a derivative of α,β-bipiperidyl [16]. The same authors showed that the magnoline and magnolamine that they had isolated from Magnolia fuscata consisted of two molecules of benzyltetrahydroisoquinoline connected through a bridge oxygen in the benzyl part of the molecule [17].

In 1934, A. P. Orekhov, S. Yu. Yunusov, and R. A. Konovalova began the study of the alkaloids of plants of the poppy family (Papaveraceae), which led to the discovery of a series of new alkaloids such as, for example, roemerine (from Roemeria refracta D. C.) and armepavine (from Papaver armeniacum). Their structures were determined completely [18].

M. M. Rubinshtein and G. P. Men'shikov isolated from Sphaerophysa salsula the new alkaloid sphaerophysine, a guanidine derivative [19]:



$$(CH_3)_2C{=}CH{-}CH_2{-}NH{-}(CH_2)_4{-}NH{-}C({=}NH)NH_2$$

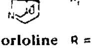
In ten years, a small group of colleagues and pupils of Academician A. P. Orekhov investigated the alkaloid content of more than 900 plants, of which 150 proved to be alkaloid-producing. Sixty-five new alkaloids were isolated and characterized and the structure of more than 20 bases was established.

Along with the investigations of Academician A. P. Orekhov's school described above, we must also mention the work carried out on the same principles in the field of alkaloid chemistry both in Moscow and elsewhere in the Soviet Union. For example, A. D. Kuzovkov et al. studied a series of Aconitum alkaloids (songorine, talatisidine, etc.), the alkaloids of Delphinium (condelphine, eleagnine), sophoramine, and sophocarpine. A. D. Kuzovkov has elucidated the structure of 23 alkaloids completely or partially [20]. Also interesting and important is the work of V. V. Kiselev on the structure of colchamine [21], a valuable medicinal agent against cancer. N. K. Yurashevskii et al. have established the structures of lycorine, girgensonine, dipterine, and leptocladine [22]. Galanthamine was first isolated from Galanthus woronovii and investigated by A. P. Yakovleva and N. F. Proskurnina [23]. A. S. Labenskii and G. P. Men'shikov studied and determined the structure of lindelofine and lindelofamine [24]. The work of L. M. Utkin with A. V. Danilova and N. I. Koretskaya on renardine, onetine, and macrophylline [25] must also be mentioned. A. I. Ban'kovskii established the structure of retamine [26], F. S. Norkina, together with A. P. Orekhov, those of donaxine, thermopsine, and d-lupinine [27], G. V. Lazur'evskii and I. V. Terent'eva that of brevicolline, [28], and A. S. Sadykov et al. the structure of eight alkaloids including anabasamine, isosophoramine and the methyl ester of aphyllic acid [29] and hydroxyaphylline and hydroxyaphyllidine [30].

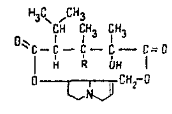
We began our study of alkaloid chemistry in VNIKhFI in Moscow in 1933 under the direction of Academician A. P. Orekhov and have continued this work in Tashkent (since 1943) in the Institute of Chemistry, AS UzSSR, having organized the laboratory of alkaloid chemistry, which was the first special laboratory in Central Asia and which has continued and developed the work begun by A. P. Orekhov on the search for new alkaloid-bearing species and on determining the structure of newly-discovered alkaloids, with the difference that we have begun the study of the dynamics of the accumulation of the alkaloids in the plants and their role and method of formation. For this purpose we have studied different plant organs according to the vegetation periods, and plants from different growth sites.

We gave an account of the first successes on the questions mentioned in the paper "The dynamics of the accumulation, role, and formation of alkaloids in the plant" (Izvestiya AN UzSSR, ser. khim., no. 4, 1948). In this paper, it was shown that the green part of plant contains the maximum amount of alkaloids at the beginning of the stage of vigorous growth of the plant, and the subterranean part in the roots the smallest amount. In these organs the maximum accumulation of alkaloids is found after the dying off of the green part, in the resting period of the plant. Green seeds contain a smaller amount of alkaloids than ripe seeds. It is clear from this that the alkaloids accumulate in those parts of the plant in which, at a given stage, developments are important and necessary for the creation of the following generation, i.e., the alkaloids play an active role in the vital activity of the plant. However, the alkaloids function differently according to the vegetation period and to the organ in which they are present. For example, in the green parts of a plant the alkaloids are activators and agents transferring oxygen into the peroxy-N-oxide form, and so on. For the same reason, alkaloids are not present in parts of the plant dying off naturally. Thus, in the epigeal part of Trachelanthus korolkovii at the beginning of vegetation when the plant is 10–15 cm high there is 18% of a mixture of alkaloids, and when the plant is 20–30 cm high only 16%. The amount of alkaloid decreases until the epigeal part of the plant dies off and then the content of alkaloids becomes nil. Hundreds of such examples can be given in our laboratory. Because of the characteristics found, the search for alkaloid-bearing plants has been facilitated and alkaloids have become more readily available. A deep understanding of the functions of alkaloids facilitates the search for plant regulators.

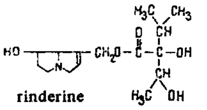
The structural formulas of alkaloids that we have established are given below.



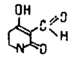
norloline $R = R_1 = H$
loline $R = H;\ R_1 = CH_3$
lolinine $R = COCH_3;\ R_1 = CH_3$



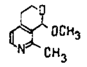
trichodesmine $R = OH$
incanine $R = H$



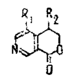
rinderine



gentianaine



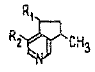
oliveridine



gentianadine $R_1 = R_2 = H$

gentianamine $R_1 = -CH=CH_2$

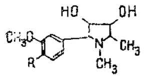
$R_2 = -CH_2OH$



pedicularine $R_1 = COOH$; $R_2 = H$;

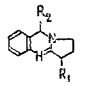
plantagonine $R_1 = H$; $R_2 = COOH$

indicaine $R_1 = H$; $R_2 = CHO$



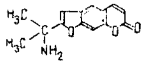
codonopsine $R = OCH_3$

codonopsinine $R = H$

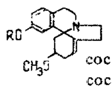


peganidine $R_1 = OH$; $R_2 = CH_2COCH_3$

desoxypeganidine $R_1 = R_2 = H$



prangosine



cocculine $R = H$

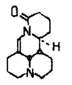
cocculidine $R = CH_3$

Thus, the characteristic feature of our investigation is a consideration of alkaloids as parts of the substances acting in coordination that make up the single whole of the organism.

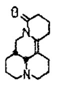
Hitherto, plant substances have been investigated with a view mainly to their agricultural significance, their suitability for foodstuffs, and the presence of essential oils, technical, medicinal, and other substances.

For a correct and rational utilization of plant substances and for the management of the processes taking place in the plant organism and also of heredity, it is necessary to study all the component parts of the plant as a whole and to determine their functions.

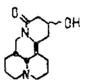
Chemists making use of the advances of all the other sciences, are boldly passing on to the solution of the intricate problem of modern times, the control of life. We consider that for this purpose it is necessary to make a complex study of the changes in plant substances according to the stage of development and the living conditions of the plant. This can be carried out in a single institute with a large number of specialists and laboratories working interdependently in constant contact informing one another and coordinating their work with other institutes. We began to study the changes in plant substances in complex fashion according to the stages of development and the living conditions of the plant in the Institute of the Chemistry of Plant Substances of the Academy of Sciences of the UzSSR, which was created in 1956 on the formulation of the laboratory of alkaloid chemistry. At present, the institute has the following laboratories: for the chemistry of the alkaloids, glycosides, lipids, plant proteins, lactones and acids, plant regulators, carbohydrates, lignin, organic phosphorus-containing plant substances, and flavanoids and coumarins, an analytical laboratory and a laboratory of physical methods of investigation; laboratories for medicinal and technical plants, phytotoxicology, pharmacology, and chemotherapeutics; and a technological laboratory. Subsequently, as highly qualified personnel are trained, laboratories for other basic classes of plant substances will be organized in the institute. In the institute, physicists, botanists, pharmacologists, phytotoxologists, etc., are working in cooperation and successively. This permits results of theoretical and practical importance to be obtained in an extremely short time.



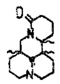
leontalbine



leontalbinine

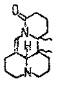


altertine

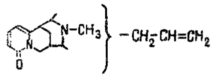


albertine

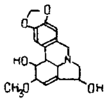
d-sophoridine



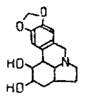
darvasine



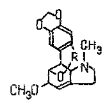
alteramine



ungminorine

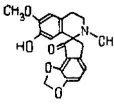


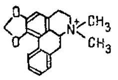
ungminoridine

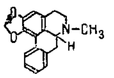


ungerine $R = CO$

unsevine $R = CHOH$


parfumine


remrefidine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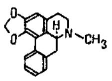
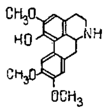

isoroemerine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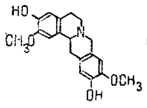
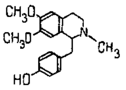
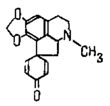

koramine


armepavine


fugapavine

In the Soviet Union about 300 species of alkaloid-bearing plants belonging to more than 40 families have been subjected to detailed chamical investigation. Exactly 518 alkaloids have been isolated of which 368 have proved to be new. The structures of 221 alkaloids have been established. Eighty alkaloids have found use in medicine: opium and the opium alkaloids (morphine, codeine, papaverine, etc.), caffeine, pilocarpine, tropine, homotropine, hyosoyamine, bellagerbine (hyosyamine, atropine, scopolamine), atropine, scopolamine, convocaine, theophylline, colchicine, platyphylline, thezine, salsoline, salsolidine, sphaerophysine, ephedrine, brevicolline, pachycarpine, colchamine, lycorine, dihydrolycorine, cytisine, galanthamine, apochlorine (methylapogalanthamine hydrochloride), sarracine, echinopsine, lobeline, peganine, harmine, harmaline, l-tetrahydropalmatine (hyndarin hydrochloride), berberine, tetrahydroberberine, β-allocryptopine, tetrandrine, dauricine, cycleanine, securinine, triacanthine, emetine, ergometrine, ergotamine, reserpine, ajmaline, delsemine, elatine, condelphine, mellictine, (methyllicaconitine), lutenurine, salasodine, salasonine, protopine, narwedine, gentianine, gentianidine, dubinidine, haplophyllidine, perforine, foliosidine, vincanine, vincametrine (vincamine hydrochloride), ervinine (copsinine), metvine (vincamine hydrochloride), akummidine, foetidine, thalisopine, thalsimine, thalicsimine, thalicmidine, sanguinarine, glaucine, and stephoglabrine.

Since the alkaloids fulfil an active function in the plant organism, with a correct elucidation of the physiologically active properties of the plant substances they should find use in medicine and veterinary practice, in agriculture, and other fields of the national economy.

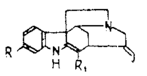
In general, all alkaloids are relatively poisonous, as for example, the alkaloids of **Heliotropus**, **Trichodesma**, **Sophora**, **Thermopsis**, **Aconitum**, **Convolvulus**, and many others. When they are present in food products and forage, they cause poisoning and disease in man and animals. Consequently, particularly with the mechanization of harvesting, poisonous weeds must not get into the grain, and the grain must not be wetted with the juice of alkaloid-giving plants.

The elucidation of the connection between the activity of the substance in the plant and in the human and animal organisms is one of the routes for the creative search for medicinal plant substances.

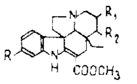
The alkaloid derivatives obtained hitherto have not so far given important medicinal agents and have not revealed regular relationships between the chemical structures of the substances and their physiological activity.

Since the initial organization of our laboratory, 3589 species of plants from various growth sites have been analyzed for their alkaloid content. The vegetative organs were analyzed separately. Of them, 1912 species proved to be alkaloid-bearing. A quantitative determination of alkaloids has been carried out on 650 individual organs of 250 species of plants. From 119 species, 228 alkaloids have been isolated of which 128 were new. Of the total number of 221 alkaloids with established structure in the USSR, we have shown the structure of 126.

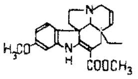
In connection with the determination of the chemical structures of alkaloids, we have studied the mechanism of many reactions and have revealed some general features (DAN UzSSR, no. 8, 12, 1948). For example, the majority of alkaloids of the aporphine group with an established structure are derivatives of 2, 3, 5, 6- and 3, 4, 5, 6-tetrahydroxyaporphine, a smaller number are derivatives of 3, 5, 6- and 4, 5, 6-trihydroxyaporphine, and a still smaller number are derivatives of 5, 6-dihydroxyaporphine, the phenolic hydroxyls of which are partially substituted by methoxyl or methylenedioxy groups. The first two types of compound can be formed from one and the same tetrahydroxy-N-methylbenzyltetrahydroisoquinoline, which can also be detected in the plant organism.



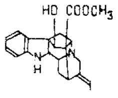
vincamine $R = H;\ R_1 = CHO$
vincanidine $R = OH;\ R_1 = CHO$
vinervine $R = OH;\ R_1 = COOCH_3$
vinervinine $R = OCH_3;\ R_1 = COOCH_3$
vincanicine $R = OCH_3;\ R_1 = CHO$



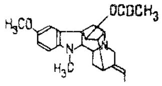
ervamine $R = R_1 = R_2 = H$
ervincinine $R = OCH_3; R_1 + R_2 = -O-$
ervinceine $R = OCH_3;\ R_1 = R_2 = H$
ervinidinine $R = H;\ R_1 + R_2 = -O-$



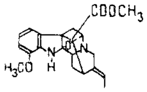
ervamicine



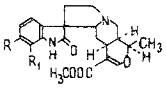
vincarine



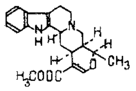
majdinine



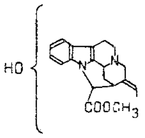
vincaricine



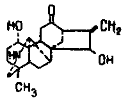
vinerine, vineridine,
and ericinine $R = OCH_3,\ R_1 = H$
majdine $R = R_1 = OCH_3$



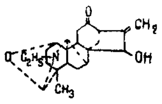
ervine



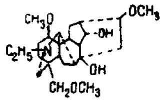
hydroxypleiocarpamine



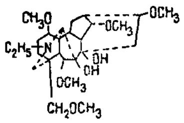
norsongorine



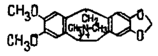
songoramine



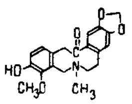
talatisamine



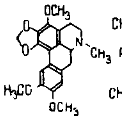
delphatine



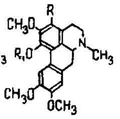
roemrefine



thalictrisine

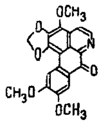


thalicmine

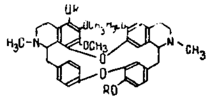


thalicmidine $R=R_1=H$

thalicsimidine $R=OCH_3$ $R_1=CH_2$



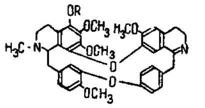
thalicminine



thalisopine $R=CH_3$; $R_1=H$

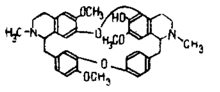
thalisopidine $R=R_1=H$

o-methylthalisopine $R=R_1=CH_3$

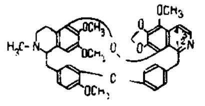


thalsimine $R=CH_3$

thalsimidine $R=H$

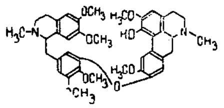


thalmine

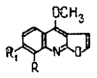


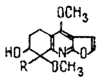
thalfine

thalfinine = 1,2,3,4- tetrahydro-2-methylthalfine



foetidine





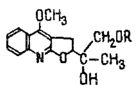
haplopine $R_1 = OH;\ R = OCH_3$

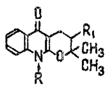
robustine $R_1 = H;\ R = OH$

folifinine $R_1 = -CH_2-CH_2-\overset{CH_3}{\underset{OH}{C}}-CH_3;$ $R = OH$

haplophyllidine $R = -CH_2-CH=C\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}$

perforine $R = CH_2-CH_2-\overset{CH_3}{\underset{OH}{C}}-CH_3$



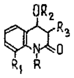


dubinidine $R = H$

dubinine $R = COCH_3$

haplofoline $R = R_1 = H$

folifine $R = CH_3;\ R_1 = OH$



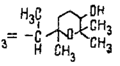
foliosidine $R = R_2 = CH;\ R_1 = -OCH_2-\underset{OH}{CH}-\overset{CH_3}{\underset{OH}{C}}-CH_3;\ R_3 = H$

folifidine $R = R_2 = CH_3;\ R_1 = H;\ R_3 = H$

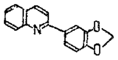
robustinine $R = R_3 = H;\ R_1 = OCH_3;\ R_2 = CH_3$

bucharaine $R = R_1 = R_3 = H;\ R_2 = -CH_2-CH=\underset{CH_3}{C}-CH_2-CH_2-\underset{OH}{CH}-\overset{CH_3}{\underset{OH}{C}}-CH_3$

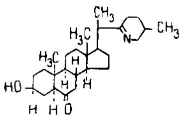
bucharidine $R_3 =$



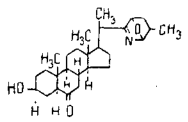
$R = R_1 = R_2 = H$



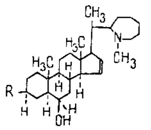
dubamine

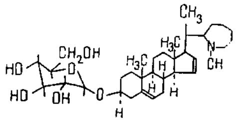


petiline



korsevinine

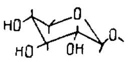


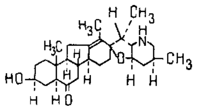


edpetilidinine R = βOH

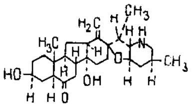
sevkorine

edpetilinine R =

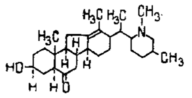




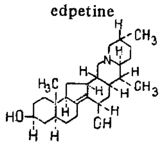
peumisine



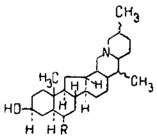
edpetine



korsevine

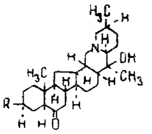


korseveridine

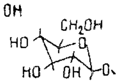


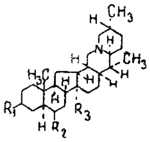
edpetilidine R = β OH + H

eduardine R = O



imperialine $R = \beta\,OH$

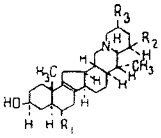
edpetiline $R =$ 



petilinine $R_1 = R_2 = \alpha OH + H,\ R_3 = \alpha H$

petilidine $R_1 = \beta OH + H,\ R_2 = \alpha OH + H,\ R_3 = \alpha H$

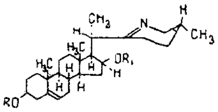
korseviline $R_1 = \alpha OH + H,\ R_2 = \beta OH + H,\ R_3 = \alpha OH$

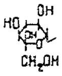


korseverine $R_1 = O;\ R_2 = H;\ R_3 = \beta CH_3 + H$

korsinine $R_1 = \beta OH + H;\ R_2 = H;\ R_3 = \beta CH_3 + H$

korsine $R_1 = \beta OH + H,\ R_2 = \beta OH;\ R_3 = \alpha CH_3 + H$



veralosine $R_1 = COCH_3$ $R =$ 

veralosidine $R_1 = R = H$

Depending on which of the two hydrogens (in position 1 or 5 of the benzene ring A) takes part in cyclization, aporphine bases of the first or second type are formed. They are related not only by their structure but also by the configuration at the asymmetric carbon center. These alkaloids rotate the plane of polarization of light to the right. Bases of the first type have a specific rotation several times smaller (from 40 to 100°), than bases of the second type (from 200 to 300°). Derivatives of 3, 5, 6- and 4, 5, 6-trihydroxyaporphines whose structures have been shown definitely rotate to the left. Alkaloids substituted in position 4 have angles of rotation several times larger than those substituted in position 3. Aporphines substituted in positions 5 and 6 are likewise characterized by very small angles of rotation. These facts show that a change in the optical properties of the aporphine alkaloids is caused not only by a change in the substituting groups but also by the spatial arrangement of the individual rings relative to the asymmetric carbon. Thus, the angle of rotation of these bases is being used successfully to establish the positions of the substituting groups.

These investigations enabled us to predict the structures of the alkaloids thalicmidine and thalicmine and these were confirmed by the results of our and other investigations.

The search for alkaloid-bearing species and alkaloids must be carried out in different organs and in plants from different growth sites according to the vegetation period and then the alkaloids will become more accessible and far-reaching biological tests broader.

If it is borne in mind that 20, 000 plants grow in the territory of the USSR and 200,000 plants throughout the world, it becomes clear what unlimited possibilities lie open before us.

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