MAIN STAGES IN THE DEVELOPMENT OF DOMESTIC ALKALOID CHEMISTRY

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The following are considered: 1) the study of alkaloids in Russia before the Great October Socialist Revolution. 2) The development of industry and of scientific investigations in the field of alkaloid chemistry at the end of the XIXth and the beginning of the XXth centuries and the influence of social factors on the development of this part of knowledge. 3) The work of Academician A. P. Orekhov and his school, which opened up a new direction in the development of alkaloid chemistry. 4) The achievements of the modern school of alkaloid investigators in the USSR.

In the historical literature of chemistry, the question of the development of alkaloid chemistry in Russia and the USSR have been considered inadequately. A. P. Orekhov, G. P. Men'shikov, S. Yu. Yunusov, V. M. Rodionov, L. M. Utkin, N. N. Suvorov, and A. S. Sadykov [1-16] have given an account of investigations of alkaloids by XXth-century chemists in individual papers. Of the work of the XIXth century, however, only the discoveries of A. A. Voskresenskii and of Yu. F. Fritsshe are mentioned. A number of papers [17-19] deals with questions of priority. Papers by D. Pavlov [20], A. N. Kost and V. G. Yashunskii [23] have noted the contribution of A. M. Butlerov and A. N. Vyshnegradskii to the study of alkaloids. Individual facts of alkaloid study are discussed in a monograph by Yu. S. Musabekov [24, pp. 243-258] and in other papers [25-28].

In the present paper, an attempt is made to fill the historical literature of chemistry on the study of alkaloids.

Alkaloids Investigations in Russia before the Great October Socialist Revolution

The first work performed in Russia in the field of alkaloid chemistry belongs to the beginning of the XIXth century. Our fellow-countrymen, like the scientists of Europe, attempted to isolate so-called "active principles" from plants possessing medicinal properties.

D. I. Grindel', Professor of Chemistry and Pharmacy at Yur'ev University (1804-1814) occupied himself with the study of the "active principles" of plants. He worked on the base of cinchona bark and also found substances with a similar physiological action, "quinasurrogates" [29-34].

F. F. Reiss, Professor at Moscow University (1804-1832) made an analysis of the "antipyretic action" of cinchona wood [35]. This work of F. F. Reiss was highly valued by the French pharmacologist F. Magendie. F. Magendie stated that the Moscow professor had an influence on the investigations of J. Pelletier and J. Caventou in the field of cinchona alkaloids [36].

Professor F. Gize, who replaced D. I. Grindel', investigated cinchona bark, lichens and coffee extracts. In the fifth volume of "General Chemistry for Teachers and Students" [37], F. Gize described plant and animal substances and gave methods for the isolation of the "active principle" of cinchona bark in the form of crystals.

In 1828, F. Gebel' became Professor of Chemistry and Pharmacy in Yur'ev University. In 1837 he discovered the alkaloid harmaline, which he had detected in the plant Peganum harmala. Both Gebel's paper, and those of Fritsshe, not only those which we have cited but also others relating to the XIXth century or to special historical investigations, state that Gebel' discovered harmaline on December 22, 1837, and Yu. F. Fritsshe discovered harmine in 1841. Yu. F. Fritsshe investigated the chemical properties of both alkaloids with extreme care [19, p. 160; 38-40].

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G. Dragendorf, Professor in the Department of Pharmacy of Yur'ev University (1864-1894) worked fruitfully on the study of alkaloids. His work related to the study of medicinal substances of plant origin. G. Dragendorf studied the following alkaloids:

Alkaloid	Year	References
Morphine and other opium alkaloids	1863-1866	41-43
Strychnine	1866-1879	44-46
Brucine	1866	44
Atropine	1866	47
Hyoscyamine	1866-1870	47-48
Aconitine	1866-1886	47-49
Curarine	1866	50
Narcotine	1868	43
Ergot alkaloids	1876	51
Delphinine	1877	52
Coffee alkaloids	1885	53
Lobelia alkaloids	1889	54

The second chapter of G. Dragendorf's book "The Forensic Chemical Detection of Poisons" is devoted to alkaloids and plant poisons. It describes "the total course of the analysis for the detection of alkaloids" developed by G. Dragendorf and gives an account of methods for detecting and identifying individual alkaloids. He discovered the Dragendorf reagent for alkaloids, $K(BiI_4)$, which is still used at the present time.

During the period of G. Dragendorf's work in Yur'ev University, the number of his students and probationers amounted to 634 persons.

A number of dissertations on the subject of alkaloids was completed under the direction of G. Dragendorf: É. Birsman, "A study of the alkaloids of Coridalis nobilis"; O. Brashe, "The use of spectroscopy for distinguishing the color reactions of poisons for the purposes of forensic chemistry"; K. Pekshen, "A study of the alkaloids of Veratrum album"; Vil'bushevich, "A histological and chemical investigation of yellow cinchona barks"; Khel'mzing, "The detection of cocaine in the animal body"; and others.

Thus, in the XIXth century in the Baltic area, investigations of plant poisons and alkaloids were popular, but the workers concerned (and they were mainly pharmacists and pharmacologists) were interested only in questions of physiological activity and the nature of the action of individual alkaloids on the animal organism.

In 1841, Yu. F. Fritsshe, investigating the plant Peganum harmala, isolated a new alkaloid from it — harmine. Having studied the properties of harmine, including its solubilities in various solvents, and also having obtained and analyzed a number of its salts, Yu. F. Fritsshe determined the composition of this alkaloid, $C_{26}H_{24}N_4O_2$, which corresponds to the modern elementary formula $C_{13}H_{12}N_2O$ [55-57].

In 1841, A. A. Voskresenskii isolated from cocoa beans the alkaloid theobromine* and determined its composition, $C_9H_{10}N_6O_2$ [58]. This formula proved to be wrong and was corrected in 1861 by A. Strecker — $C_7H_8N_4O_2$. It is likely that A. A. Voskresenskii had not isolated a completely pure alkaloid, since the melting point of the preparation that he obtained was 250°C, while pure theobromine melts at 351°C.

A paper published in 1842 by N. N. Zinin, "A description of some new organic bases obtained by the action of hydrogen sulfide on compounds of carbohydrates with nitrous acid" [59], has become well known because of its value for the synthetic dye industry. In this paper, ideas about alkaloids were expanded. At that time, all substances containing nitrogen and exhibiting alkaline properties, i.e., substances capable of salt formation, were regarded as alkaloids. However, in this paper, N. N. Zinin showed the possibility of obtaining alkaloids synthetically. It is just this work that C. Gerhardt had in mind when he wrote in 1848: "In recent years chemistry has succeeded in obtaining synthetically, in addition to urea, many new alkaloids and this induces us to hope that quinine, morphine, and narcotine will no longer be extracted from cinchona or opium but will be obtained by similar processes in our

*θεος (Greek), god; βρῶμα (Greek), food; food of the gods.

laboratories" [59]. This was the first case in the history of alkaloids of their synthetic production. N. N. Zinin's investigation promoted the study of the nature of alkaloids and was necessary for the theoretical considerations developed by C. Gerhardt. In this work, Gerhardt gave a definition of alkaloids for the first time: "Alkaloids is the name given to certain compounds containing hydrogen and nitrogen that are capable of combining directly with hydrogen salts (acids) or with salts of metals and forming definite compounds with them . . . ." In accordance with this definition, Gerhardt assigned ammonia to the type of alkaloids.

In order to determine the constitution (i.e., the structure) of alkaloids, C. Gerhardt and C. Williams studied the influence of alkalis on alkaloids. Attempts were made to elucidate the constitution of some alkaloids by J. Caventou and E. Wilm, O. Hesse, S. Hoogewerff and V. Van Dorp, G. Kerner, H. Weidel, W. Koenigs, and others.

Thus, in 1878-1880 a large amount of experimental material on the properties of alkaloids had been accumulated. In these years, A. M. Butlerov and his pupil A. N. Vyshnegradskii published a series of papers [60-63] which take a prominent place among other investigations in the field of alkaloids performed in this period. A feature of these investigations is that A. M. Butlerov and A. N. Vyshnegradskii, developing ideas of the theory of the chemical structure of organic compounds, dared to extend them to complex compounds. In their own investigations they posed the problem of elucidating the chemical structures of the alkaloids of cinchona bark — quinine and cinchonine. They were in fact the first in the history of the study of these compounds to suggest structural formulas for quinine and cinchonine [20, 60]. In addition, they were the first to express the idea that many alkaloids are derivatives of such heterocyclic nitrogen-containing compounds as pyridine, quinoline, etc. This idea was taken up by chemists, and the intensive study of heterocycles soon led to the formation of the corresponding independent branches of organic chemistry. Unfortunately, the investigations in the field of alkaloid chemistry so fruitfully begun, were brought to an end by the death of A. N. Vyshnegradskii.

Thus, during the whole of the XIXth century, Russian scientists made their contribution to the development of alkaloid chemistry. However, among the investigations the study of the physiological activity of the alkaloids and their use as drugs still predominated. This partially explains the fact that the first generalizing work on alkaloids in Russia, "The Science of Plant Alkaloids, Glucosides, and Ptomaines," was published by E. A. Shatsk, Assistant Professor of Pharmacy and Pharmacognosy at Kazan' University, in 1890-92 [64].

However, in spite of the numerous investigations in the field of alkaloid chemistry, their results found no practical application in the domestic industry, while abroad, particularly in Germany, definite advances were being achieved in this respect.

The weakly developed chemical industry of Tsarist Russia could not stimulate the development of scientific problems and of scientific-technical and engineering investigations, because of which there was no link between scientific discoveries and their introduction into industry. This was shown particularly clearly during the time of the first world war, 1914-1917.

In 1915, A. E. Chichibabin, comparing the industries of Germany and Russia, wrote: ". . .our technical and scientific backwardness has been felt as a burning pair. . .. Such excessive hardships are due to the fact that in Russia the pharmaceutical industry is so feebly developed."

In the first days of the war, however, A. E. Chichibabin acted as an active organizer of the pharmaceutical industry. In the organic chemistry laboratory of the Moscow Higher Technical Institute (MVTU) in 1915, A. E. Chichibabin with his colleagues N. G. Patsukov and V. M. Rodionov began the production of morphine and codeine from opium confiscated by the customs authorities. Methods for the industrial production of these alkaloids were developed in the laboratory, and then morphine and codeine were prepared in large amounts in S. P. Langovii's technical laboratory. The immediate executives of these operations were V. M. Rodionov and N. G. Patsukov.

The success of the operations mentioned permitted the organization of a medicaments shop at MVTU and, simultaneously, of an alkaloid laboratory in the A. L. Shanyavskii University.

In the medicaments shop at MVTU under the direction of student of P. I. Gundovin, about 80 kg of opium was treated every day, which gave 7-8 kg of morphine, and he prepared a total of 2000 kg of this alkaloid and, in addition, a certain amount of codeine and narcotine. Likewise, another student, Korol'kov, mastered the production of atropine from thorn-apple seeds by a method developed by N. G. Patsukov. I. G. Povarnin obtained caffeine from tea dust by the method of Prof. Shustov and on a semifactory apparatus he also obtained caffeine from coffee beans by a method proposed by F. N. Tserevitinov.

The scope and intensity of the work performed in MVTU forced A. E. Chichibabin to present to the government a memorandum on the necessity for setting up in the Technical Institute a factory for chemical and pharmaceutical preparations which would at the same time be a "school for well-informed managers of enterprises of this type." At a meeting of the Council of Ministers on March 1, 1916, a resolution was adopted to assign 300 thousand rubles to the construction of such a factory. However, A. E. Chichibabin did not succeed in creating a training factory at MVTU. Together with N. G. Patsukov and V. M. Rodionov he was instructed to set up the first large alkaloid factory in Moscow. This factory began to produce codeine, caffeine, theobromine, and atropine.

At the beginning of 1917, the production of morphine and of caffeine from tea dust was organized in the factory of the Directorate of the Chief Superintendent of Sanatoria and the Evacuation Section (later Farmzavod No. 1) and N. G. Patsukov began to obtain hyoscyamine from thorn-apple seeds. Morphine hydrochloride, dionin (ethylmorphine hydrochloride), and heroin were manufactured in the "Ars" factory.

To ensure the raw materials basis for the production of alkaloids, A. E. Chichibabin, N. G. Patsukov, and V. M. Rodionov were forced to carry out the planting of the opium poppy in Turkestan. This freed the country from the importation of raw material for obtaining the alkaloids.

Additional scientific investigations were carried out with the aim of intensifying the production of alkaloids. Thus, S. I. Kanevskaya and N. G. Patsukov developed an economically favorable method of obtaining theobromine from cocoa husks. Alkaloids began to be obtained by this method at the Zemskaya pharmaceutical factory.

V. M. Rodionov, with S. I. Kanevskaya and N. G. Patsukov, developed methods for the extraction from opium and purification of five alkaloids; morphine, codeine, thebaine, narcotine, and papaverine. Their method was patented in 1927 [65]. At the same time, V. M. Rodionov developed an original synthesis of codeine using quaternary ammonium salts.

V. M. Rodionov, together with O. A. Zeide, studied the oxidation of narcotine and developed a method for oxidizing narcotine with the isolation of opianic acid and cotarnine. Cotarnine was required for the preparation of the hemostatic stypticin. V. M. Rodionov and P. I. Gundovin proposed a convenient method for isolating narcotine from "opium oil-cake."

At the same time, known methods for the synthesis of morphine derivatives were checked and mastered and original ones were developed. Thus, A. M. Berkengeim suggested a method for the preparation of dionin, V. M. Rodionov developed new methods for obtaining narceine and heroin and R. A. Konovalova for obtaining apomorphine. A. V. Kirsanov developed a procedure for obtaining hydrastine from cotarnine by Pyman's method, and at the beginning of 1917, A. E. Chichibabin developed the technical production of cocaine preparations.

Thus, in concluding a review of investigations in the field of alkaloid chemistry performed in prerevolutionary Russia, it must be stated that at each stage of the development of ideas on alkaloids, Russian scientists performed investigations corresponding to the level of the problems arising and the possibility of their scientific solution.

Thus, the requirements of the first stage of development of ideas on alkaloids determined by the isolation of "active principles" from medicinal plants found expression in the work of D. Grindel', F. Reiss, and F. Gize.

The work of F. Gebel', G. Dragendorf, Yu. Fritsshe, and A. A. Voskresenskii reflected the demands of the analytical period in the knowledge of alkaloids. These scientists isolated new alkaloids and obtained various derivatives and salts, developed methods for analytical determinations, and established empirical formulas.

The work of N. N. Zinin, A. M. Butlerov, and A. N. Vyshnegradskii had a definite influence on the formation of theoretical views in the field of alkaloid chemistry and thereby promoted the development of organic chemistry as a whole.

And, finally, A. E. Chichibabin and V. M. Rodionov, and many students, developed measures for organizing the domestic alkaloid industry. A powerful factor in the development of the science was the demand of society for valuable drugs, and, what is more, the aggravated critical situation into which Russia fell in the First World War demanded the rapid resolution of technical and scientific problems of alkaloid chemistry.

However, up to the present, a powerful and all-sided development of alkaloid science in Russian has been achieved only since the Great October Socialist Revolution.

Development of Industry and of Scientific Investigations in the Field of Alkaloid Chemistry in Soviet Russia

After the Great October Socialist Revolution the production of pharmaceutical chemicals and alkaloids expanded and investigations on alkaloid chemistry multiplied.

Under the new conditions, A. E. Chichibabin and V. M. Rodionov acquired the possibility of widely developing the activity on the creation of an alkaloid industry that was begun during the First World War. The initiative, energy, and knowledge that they and their numerous pupils devoted to this aim brought considerable advances in the fruitful soil of the socialist system. Thus, in 1927-1928, 3.5 tonnes of alkaloids were produced and in 1932, 39.4 tonnes.

The scientific teaching activity of A. E. Chichibabin and V. M. Rodionov also expanded. In the MVTU, A. E. Chichibabin organized the teaching of the chemical technology of pharmaceutical preparations. V. M. Rodionov, in parallel with work in MVTU (up to 1929), organized in 1920 a department of alkaloids in the 2nd Moscow State University and directed it up to 1930.

Among A. E. Chichibabin's papers — and about 350 of them were published — the main position is occupied by investigations in the field of pyridine and its derivatives. It is also important that A. E. Chichibabin began investigations of alkaloids in Soviet Russia. A. E. Chichibabin himself linked his investigations of pyridine and its derivatives with the study of alkaloids. For example, even in the pre-Soviet period he wrote: "Pyridine homologs containing the benzene nucleus, apart from phenylpyridines, have hitherto been known and studied very little. Nevertheless they present interest both in themselves and in relation to the natural alkaloids. Consequently, I have occupied myself with the application of several methods of obtaining pyridine homologs for the purposes of synthesizing and studying new compounds." A. E. Chichibabin and his pupils developed methods for obtaining several morphine alkaloids. In 1927, A. E. Chichibabin patented a method for purifying crude cocaine [66].

In 1924, N. A. Preobrazhenskii graduated from Moscow State University and began training as a postgraduate student at MVTU under the direction of A. E. Chichibabin, occupying himself with the study of alkaloids isolated from the leaves of the South American plant *Pilocarpus jaborandi*. These investigations were completed by the synthesis of pilopic acid and its stereoisomers, and of pilocarpine, which also served as a definitive proof of the structure of this alkaloid. In 1931, A. E. Chichibabin obtained a patent for a method of isolating optical stereoisomers from optically inactive pilopic acid [67]. Later, N. A. Preobrazhenskii widely developed independent investigations of the alkaloids of *Pilocarpus jaborandi* and others. Together with his students, N. A. Preobrazhenskii successfully developed the synthetic direction in the field of alkaloid chemistry and synthesized cocaine, tropine, scopolamine, arecoline, colchicine, ipecacuanha alkaloids, yohimbine, cinchonamine, eserine, and curare alkaloids.

As already mentioned, even before the revolution V. M. Rodionov was one of the active organizers of the alkaloid industry and in addition to this was fruitfully developing scientific questions connected with the production of alkaloids. Thus, he developed a method for the synthesis of codeine using quaternary ammonium salts as an alkylating agent. This method was immediately taken into use on the industrial scale, but it was necessary to simplify the alkylation of organic compounds. It was found that in addition to trimethylphenylammonium chloride, the production of which was associated with a number of difficulties, it is possible to use trimethylphenylammonium p-toluenesulfonate [68-73]. The needs of the developing alkaloid industry forced V. M. Rodionov with his pupils to find cheap alkylating agents. Such proved to be esters of aromatic sulfonic acids and the products of their addition to tertiary amines. The investigators also developed industrial methods for obtaining the necessary agents. Furthermore, these esters and quaternary bases found wide use in many branches of the chemical industry: the alkaloid industry, and the production of dyes and perfumes.

Working in various branches of science and technology, V. M. Rodionov devoted much attention to alkaloid chemistry. He also attracted other workers to the study of the alkaloid-bearing plants of the central zone of the European part of Russia, especially the celandine and false hellebore. In 1939-1943, V. M. Rodionov, together with Yu. S. Shidlovskaya-Ovchinnikov performed an analytical determination of the combined alkaloids of the plant Chelidonium majus [74]. After the Great Patriotic War [World War II], V. M. Rodionov with N. N. Suvorov and L. V. Shagalov studied the celandine alkaloids. The results of these investigations were published in 1949-52 [75-77], and in 1950 N. N. Suvorov defended a dissertation on "Synthetic investigations in the field of celandine alkaloids."

In 1952 in Tashkent at a combined meeting of the departments of chemical sciences of the Academy of Sciences of the USSR and of the Academy of Sciences of the Uzbek SSR, V. M. Rodionov gave a lecture on "Alkaloid chemistry, its importance, and the next tasks," which was published in "Izvestiya Akademii Nauk SSSR" [8].

In 1953, V. M. Rodionov published a paper [7] in which, speaking of the main factors affecting the development of alkaloid chemistry, he ascribed particular importance to the Great October Socialist Revolution, observing that only in the Soviet period in Russia have the conditions appeared for fruitful activity. The main role in the development of alkaloid chemistry has been played by Academician A. P. Orekhov and his pupils [5].

Contribution of Academician A. P. Orekhov and His School to the Development of Alkaloid Chemistry

After the Great October Socialist Revolution, namely on November 30, 1920, by a Decree of the Main Directorate of Pharmaceutical Chemical Factories, the Institute of Pharmaceutical Chemistry (NIKhFI) was created. It was faced with the following tasks:

1. The development of methods for producing pharmaceutical chemicals not manufactured in the USSR.

2. The solution of questions connected with replacing imported raw material and semi-finished products used in the synthesis of pharmaceutical chemicals by domestic raw materials.

3. The search for new drugs and medicinal forms.

4. The study of the raw materials basis of medicinal and aromatic plants and their use.

5. Scientific and technical aid to industry.

6. The amalgamation of scientific-research work in the field of pharmaceutical chemicals.

Thus, for the first time in our country a scientific institute was created which was called upon to coordinate and direct the activity of all the subdivisions connected with the solution of the scientific and technical problems of the pharmaceutical chemicals industry.

In 1928, an alkaloid division directed by A. P. Orekhov was organized in the NIKhFI.

A. P. Orekhov was born in 1881 in Nizhne Novgorod. In 1899, having graduated from the modern school in Astrakhan, Aleksandr Pavlovich became a student at the St. Petersburg Institute of Means of Communication, and in 1901 he transferred to the Ekaterinoslav Mining Institute. However, for participating in the student revolutionary movement he was excluded from the Institute and was first sent abroad where he studied chemistry and worked in the University of Jena in Prof. L. Knorr's laboratory, and from 1907 in Prof. A. Nauman's laboratory in Giessen.

In 1909, having submitted a dissertation "Einwirkung von Phosphorpentasulfid auf aromatische Amine" [78] and having passed his doctoral examination, A. P. Orekhov obtained the degree of Doctor of Philosophy. For the following 10 years he worked in the laboratories of Giessen and Jena Universities and from 1918 to 1928, with a small interruption during which A. P. Orekhov was a chemist on the production of alkaloids and pharmaceutical preparations, he worked in Paris, managing M. Tiffeneau's laboratory.

In one of his letters, A. P. Orekhov, evaluating his position, wrote "I had gotten tired of making sacrifices for science, but I now see that I am ready to sacrifice a hundred times more rather than to live as I am doing now. The conclusion from this is clear: as soon as a quieter time arrives I shall immediately leave the factory and travel to Moscow in order to acquire the possibility of occupying myself in the university" [79, p. 7].

In 1928, at the invitation of the directors of the All-Union Institute of Pharmaceutical Chemistry (VNIKhFI), A. P. Orekhov returned to Moscow and to the end of his days he directed the work of the alkaloid division of the Institute. In January 1939, for his outstanding contribution to the development of science, A. P. Orekhov was elected an Academician of the Academy of Sciences of the USSR.

Thus, a new and most fruitful stage in the history of domestic alkaloid science began in 1928. Here is how A. P. Orekhov evaluated his approach to alkaloid chemistry: "The external factor that led me to working with these substances was the proposal of the Directorate of VNIKhFI to organize an alkaloid division in this Institute. Although in my previous activity I had performed no research work in the field of alkaloids, this field was not completely new to me. When a student at the University of Jena, I worked on organic chemistry in the laboratory of a very great specialist on alkaloid chemistry (especially that of morphine) Prof. Knorr, and the first of my supervisors leading me in this direction was Prof. Rabe — a well-known worker on quinine. Thus, my initial teaching in organic chemistry took place in a laboratory which had lived mainly in the range of interests of alkaloid chemistry. Furthermore, in the University of Jena the closest neighbor of our laboratory was Professor A. Pictet, who had also worked in the alkaloid field. Contact with him and his assistants confirmed my interest in this field and I studied it seriously in its theoretical aspects. Switching to this new field of research work did not present me with particular difficulty, particularly in view of the fact that when working in the "Poulenc" factory (near Paris) I had become acquainted in practice with the procedure of working with alkaloids" [79, p. 8].

The direction created by Academician A. P. Orekhov in the field of alkaloid chemistry was distinguished by the fact that he was the first person in the world to begin the complex study of alkaloids. It included the search for new alkaloid-bearing plants, development of methods of isolating and determining alkaloids, the establishment of structures and the performance of syntheses, the solution of stereochemical problems and problems of biosynthesis, and the study of physiological properties and questions relating to the industrial preparation of substances necessary for the national economy.

The alkaloid division carried out a series of expeditions to collect and study plant raw material. The work of the expeditions* was led by P. S. Massagetov, L. A. Utkin, and M. N. Varlamov. Areas of Kazakhstan, Kirghizia, Turkmenia, Georgia, Abkhasia, Adzharia, Zabaikal'ya (Aginskaya steppe), and Nizhnie Sayany (Tunkinskaya valley) were investigated. In the expeditions, 800 species of previously unstudied plants of the USSR were collected and then investigated, and more than 100 alkaloid-bearing representations were found. Detailed chemical investigations enabled A. P. Orekhov and his pupils and successors to isolate about 100 new previously undescribed vegetable bases and to determine the complete structures of 40 of them:

Alkaloid	Year	References
Anabasine	1929–1937	81–95
Aphyllidine	1932–1955	96–101
Aphylline	1932–1955	96–101
Heliotrine	1932–1950	102–107
Lasiocarpine	1932–1950	102–109
Pachycarpine	1933–1937	110–114
Salsoline	1933–1939	115–121
Salsolidane	1933–1939	115–121
Convolvine	1933–1947	122–127
Convolamine	1933–1947	122–127
Ammodendrine	1935–1938	113–129

*A detailed account of these expeditions has been given by P. S. Massagetov [80].

Alkaloid	Year	References
Armepavine	1935-1940	130-133
Oripavine	1935-1937	130-131
Platyphylline	1935-1965	134-141
Seneciphylline	1935-1965	134-141
Trichodesmine	1935-1959	142-146
Salsamine	1937	120
Magnolamine	1938-1946	147-149
Magnoline	1938-1946	147-149
Roemerine	1938-1948	150-155
Dipterine	1939-1940	156-157
Leptocladine	1939-1941	158-161
Trachelanthamine	1941-1947	161-164
Trachelanthine	1941-1947	161-164
Halostachine	1943-1947	165-166
Gentianine	1944-1949	167-170
Sphaerophysine	1944	170-172
Girgensonine	1946	173
Viridiflorine	1946-1948	163-164, 174
Galanthine	1947-1953	175-176
Smirnovine	1947-1949	177-178
Lindelofamine	1948	179
Lindelofine	1948	179
Isoammodendrine	1949	180
Supinine	1949	181
Cocculidine	1950-1970	182-185
Cocculine	1950-1970	182-185
Thalicmidine	1950-1968	186-192
Thalicmine	1950-1968	186-192
Macrotomine	1952	193

As early as 1929, at the very beginning of the development of scientific investigations, A. P. Orekhov succeeded in achieving success. In a study of the Central Asian plant Anabasis aphylla he isolated the alkaloid anabasine, which has acquired importance to the national economy as an excellent insecticide. Subsequently, from the low-boiling fraction of the mixture of alkaloids of Anabasis aphylla A. P. Orekhov and G. P. Men'shikov isolated lupinine and from the high-boiling fraction the new alkaloid aphylline and aphyllidine.

In 1932, G. P. Men'shikov isolated the alkaloids heliotrine and lasiocarpine from the plant Heliotropium lasiocarpum. At the present time, more than 120 alkaloids of this series are known. Many of them were found by A. P. Orekhov and R. A. Konovalova in a study of plants of the genus Senecio, among them being platyphylline and seneciphylline, discovered in 1935 and studied for many years. As the investigations showed, platyphylline has proved to be a valuable drug.

In 1933, A. P. Orekhov and N. F. Proskurnin isolated the new alkaloids salsoline and salsolidine from the plant Salsola richteri. In 1934, salsoline, salsolidine, and their isomers were synthesized by A. P. Orekhov and E. Shpet. Salsoline has been used in medicine as a drug lowering the blood pressure.

In 1933, A. P. Orekhov and R. A. Konovalova isolated the alkaloids convolvine and convolamine from the plant Convolvulus pseudocanhabrica and demonstrated their structure. The discovery of these alkaloids gave a new source for the production of tropine and nortropine, which are valuable starting materials for the preparation of a number of drugs.

In 1934, O. P. Orekhov, S. Yu. Yunusov, and R. A. Konovalova began investigations on the plants of the Papaveraceae family, discovered the alkaloids roemerine and aremepavine and others and determined their structures completely.

In 1935-1938, A. P. Orekhov together with N. F. Proskurnin studied the plant Ammodendron conollyi. They isolated a series of new alkaloids and demonstrated the structure of ammodendrine. In 1937, studying the plant Magnolia fuscata they isolated the alkaloids magnolamine, the structures of which were also deciphered completely. The structure of magnolamine was refined in 1977 [231].

TABLE 1

Year	No. of publications	Including		Publications on alkaloids	Including		Percentage of the total number
		papers	brief communications		papers	brief communications	
1965	98	82	16	17	13	4	17,3
1966	128	87	41	21	11	10	16,4
1967	159	75	84	44	16	28	27,6
1968	210	62	148	62	14	48	29,5
1969	275	107	168	59	19	40	21,4
1970*	337	150	187	80	42	38	23,7
1971	316	145	171	65	30	35	20,5
1972	303	151	152	60	36	24	19,8
1973	295	124	171	55	22	33	18,6
1974	383	131	252	76	25	51	19,8
1975	342	136	206	74	25	49	21,6
1976	358	142	216	83	36	47	23,4
1977	283	141	142	64	31	33	22,6
1978	266	137	129	42	22	20	15,8
Total	3753	1670	2083	802	342	460	21,4

*The size of the journal was increased from 36 quires to 72.

The investigations of 1928-1939 put our country at the head of the world for the study of alkaloids, since during this period in the USSR alone, 100 new alkaloids were described while the number for all the other countries of the world was only 175.

It is worth mentioning that A. P. Orekhov and his pupils, developing the complex study of alkaloids, simultaneously succeeded by chemical investigations in developing the technology of the production and the introduction into industry of such drugs as platyphylline, salsoline, salsolidine, sphaerophysine, convocaine, tsititon [cytisine], pachycarpine, tropacine, colchamine, galanthamine, condelphine, elatine, diplacine, and melliktin [mellictine], and also the insecticide anabasine.

A. P. Orekhov published about 120 scientific papers. His monograph "The Chemistry of the Alkaloids" [194] went through two editions. The second edition, revised and supplemented by his pupils, was published in 1955 [195]. A. P. Orekhov's most considerable investigation in the field of alkaloid chemistry was a separate publication in 1965 [196].

Academician A. P. Orekhov passed away in 1939, but the work that he had begun was continued by numerous pupils and successors. Thus, in the period from 1938 to 1946 N. K. Yurashevskii and his colleagues determined the structures of the alkaloids lycorine, girgensonine, dipterine, and leptocladine.

In 1944, M. M. Rubinshtein and G. P. Men'shikov isolated from the plant Sphaerophysa salsula the alkaloid sphaerophysine, which proved to be a guanidine derivative.

In 1948, A. S. Labenskii and G. P. Men'shikov studied the alkaloids lindelofine and lindelofamine and determined their structures. In 1952-1955, N. F. Proskurnina and A. P. Yakovleva, studying the plant Galanthus woronowii, isolated the new alkaloid galanthamine and studied it [197-198].

From 1953 to 1961, A. D. Kuzovkov et al. studied a series of aconite alkaloids and the alkaloids of the delphinium [199-208]. A. D. Kuzovkov deciphered the structures of a total of 26 alkaloids.

The work of V. V. Kiselev performed in the period from 1952-1957 to determine the structure of colchamine, a valuable anticancer agent, must be mentioned [209-211].

In the period from 1950 to 1965, A. V. Danilova, L. M. Utkin, and N. I. Koretskaya performed a series of investigations on such alkaloids as macrophylline, renardine, and onetine [212-217].

In 1957, A. I. Ban'kovskii et al. established the structure of retamine [218].

In the period from 1957-1969, G. V. Lazur'evskii et al. undertook a study of the plant Carex brevicollis. They succeeded in isolating several alkaloids and establishing their structures: for example, the structure of brevicolline [219-225], which has found use in medicine.

However, the most fruitful study of alkaloids was developed in Central Asia. The investigations begun on the initiative and under the direction of A. P. Orekhov have given rise to a modern school of alkaloid researchers in the USSR of S. Yu. Yunusov and A. S. Sadykov.

Modern School of Alkaloid Researchers in the USSR

"In 1934, as a student in the chemical faculty of the V. I. Lenin Central Asian State University [SAGU] I began, under the direction of Orekhov, an investigation of the alkaloids of *Sophora alopecuroides.* I defended the diploma work completed, in which I had discovered six new alkaloids, in the chemical faculty of SAGU in 1935.

The warm paternal relationship to us of the Russian Soviet scientist Academician Aleksandr Pavlovich Orekhov and the interesting new field of alkaloid chemistry that had been successfully developed aroused the great love and interest of many young organic chemists of the Central Asian State University. In 1936, in the chair of the chemical faculty of SAGU G. V. Lazur'evskii and A. S. Sadykov began to work in contact with and under the direction of A. P. Orekhov," — so writes the founder of the modern school of alkaloid study, S. Yu. Yunusov [6, p. 228].

From this time, under the direction of A. S. Sadykov the study of alkaloids was contained in Tashkent State University. The results of investigations of the alkaloids of *Anabasis aphylla* lasting many years were generalized by A. S. Sadykov in a monograph [226] devoted to the memory of A. P. Orekhov. In the same year, 1956, together with O. S. Ostroshchenko, he published a work "Results of the chemical study of the subshrub *Anabasis aphylla* growing in the Turkmen SSR" [227].

During the study of the alkaloids it transpired that many of them belong to the group of quinolizidine bases, and therefore the chemical study of this group of alkaloids and also their stereochemistry and biogenesis, formed one of the main directions of the scientific work of the chemists of Tashkent State University. The results of these investigations were generalized in the monograph "Alkaloids of the quinolizidine series" [228] and in papers by A. S. Sadykov [12-15, 232].*

In 1943, a laboratory of alkaloid chemistry was organized in the Institute of Chemistry of the Academy of Sciences of the Uzbek SSR. It was directed by the pupil and successor of Academician A. P. Orekhov, S. Yu. Yunusov, who had worked with A. P. Orekhov for about 10 years and had performed a series of cooperative investigations with him.

The program drawn up by the scientists consisted in the continuation and development of the comprehensive investigations of alkaloids begun by A. P. Orekhov. The comprehensiveness consisted in the search for new alkaloid-bearing plants, the development of methods for the isolation and determination of new alkaloids, the establishment of the chemical structures of newly discovered alkaloids, the search for improved methods of synthesis, the solution of stereochemical problems and problems of vegetation and biosynthesis, and the study of the physiological properties of the alkaloids and the dependence of these properties on chemical structure, and in perfecting the technology of the industrial preparation of valuable substances.

The successful development of the investigation of alkaloids required the creation of a special institute, and in 1956, on the basis of the laboratory of alkaloid chemistry of the Institute of Chemistry of the Academy of Sciences of the Uzbek SSR, the Institute of the Chemistry of Plant Substances of the Academy of Sciences of the Uzbek SSR was created, and this is a coordinating center for the development of this scientific discipline; it is directed by S. Yu. Yunusov.

The Institute has clearly defined its scientific direction — the comprehensive investigation of plant substances and of all plant organs according to the vegetation period and the growth site with the aim of:

1) developing methods of isolating plant substances;

2) determining their chemical structures; and

*The structures and configurations of 28 alkaloids were established [229] (Ed.).

3) establishing the mutual transitions and interrelationships as component processes of a single plant organism.

An important stage in the development of the domestic science of alkaloids consists of investigations with the application of modern physical and biochemical methods: NMR, ESR, IR, and mass spectroscopies, x-ray structural analysis, the ORD method, chromatography, ionophoresis, artificial mutagenesis, and the labelled-atom method. With the aid of these methods it has been possible in a short time to obtain new scientific results permitting a deeper understanding of the chemical processes taking place in plants and therefore bringing near the time when scientists will be capable of directing the vital activity of the plant organism for the purpose of obtaining the required substances. The work of the laboratory of alkaloid chemistry of the Institute of Chemistry of the Academy of Sciences of the Uzbek SSR and of the Institute of the Chemistry of Plant Substances of the Academy of Sciences of the Uzbek SSR has been considered in more detail in publications by S. Yu. Yunusov [16].

The investigations of Soviet alkaloid workers have been generalized in S. Yu. Yunusov's book "Alkaloids" [229]. However, the achievements had grown considerably by 1979. Thus, S. Yu. Yunusov and his colleagues have studied 4000 species of plants and have systematically investigated 460 of them; they have isolated 1095 alkaloids and, using modern physical methods in combination with chemical methods, have demonstrated the chemical structures of 326 alkaloids, the stereochemistry of the majority of them having also been established [229].

Since 1965, the results of investigations on alkaloids have been widely published in the journal "Khimiya Prirodnykh Soedinenii" ["Chemistry of Natural Compounds"] created by a decree of the Presidium of the Academy of Sciences of the USSR. Its chief editor is S. Yu. Yunusov. In the period from 1965 to 1978, alone, 3753 papers and brief communications have been published in the journal, 802 of these publications, or 21.4% of the total number, relating to alkaloids (Table 1).

At the present time, alkaloid chemistry as a scientific discipline has achieved its maturity. This is shown by the fact that more than 100 individual alkaloids have found use in medicine thanks to a comprehensive study [230].

One is forced to recall the words of A. P. Orekhov delivered in 1936 in the Academy of Sciences of the USSR: ". . .when in 1928 the Alkaloid Division was organized in NIKhFI there were three of us — R. A. Konovalova, who had had some experience of working with alkaloids, G. P. Men'shikov, and I. There was no trained staff at all" [3].

Now, as we see, much has changed. Even the geography of the investigations has expanded. Thus, not only has the book "Alkaloid-bearing Plants of the USSR" (S. A. Sokolov, 1952) appeared, but also the collections "Alkaloid-bearing Plants of Moldavia" (1960), "Investigations on the Flora of Kirghizia for Alkaloid Content" (1965), "Physiologically Active Compounds from the Plants of Kirghizia" (1970), and "Alkaloid-bearing Plants of Kirghizia" (1975) and the writing of the monograph "Alkaloid-bearing Flora of Central Asia" is being completed.

And yet, in spite of the considerable amount of work performed in the Soviet Union on the study of plant raw material, many regions have not yet been studied in a planned manner for the presence of alkaloid-bearing plants. This relates primarily to the extremely rich region of Siberia.

LITERATURE CITED

1. Khim.-Farm. Prom., No. 6, 3 (1934).
2. Khim.-Farm. Prom., No. 1, 9 (1935).
3. Izv. Akad. Nauk SSSR, Ser. Khim., No. 6, 935 (1936).
4. In: XX Years of the Work of VNIKhFI im. S. Ordzhonikidze [in Russian], Moscow—Leningrad (1941), p. 51.
5. Jubilee Collection Devoted to the 30th Anniversary of the Great October Socialist Revolution [in Russian], Moscow—Leningrad, Part 1 (1947), p. 683.
6. Jubilee Collection Devoted to the 25th Anniversary of the Uzbek SSR (1924-1949) [in Russian], Tashkent (1949), p. 223.
7. Usp. Khim., 22, No. 5, 628 (1953).
8. Izv. Akad. Nauk SSSR, Ser. Khim., 385 (1953).

9. In: The Main Directions of the Work of VNIKhFI (Review of Activity during 1920-1957) [in Russian], Moscow (1959), p. 369.
10. In: Chemistry in Uzbekistan [in Russian], Tashkent (1965), p. 26.
11. In: The Development of Organic Chemistry in the USSR. Soviet Science and Technology over 50 Years [in Russian], Moscow (1967), p. 571.
12. Nauchn. Tr. Tashk. Gos. Univ., 3, No. 341, 3 (1968).
13. Khim. Prir. Soedin., 149 (1970).
14. In: Science in Uzbekistan [in Russian], T. I. Estestvennye Nauki, Tashkent (1974), p. 192.
15. In: Science in Uzbekistan [in Russian], T. I. Estestvennye Nauki, Tashkent (1974), p. 205.
16. Order of the Red Banner of Labor Institute of the Chemistry of Plant Substances [in Russian], Tashkent (1976).
17. P. A. Charukhovskii, Voen.-Med. Zh., No. 1, part 13, 64 (1829).
18. P. P. Saksonov, Priroda, No. 10, 72 (1950).
19. U. V. Pal'm, Proceedings of the Thirteenth International Congress of the History of Science, Sec. VII [in Russian], Moscow (1974), p. 159.
20. Zh. Russ. Riz.-Khim., 13, 370 (1881).
21. Usp. Khim., 21, No. 2, 260 (1952).
22. Vestn. Mosk. Univ., Khimiya, No. 2, 95 (1952).
23. Zh. Prikl. Khim., 25, No. 7, 681 (1952).
24. Yu. S. Musabekov, The History of Organic Synthesis in Russia [in Russian], Moscow (1958).
25. N. A. Figurovskii, V. N. Ryzhikov, and T. A. Komarova, in: Questions of the History of Science and Technology of the Baltic Area [in Russian], Tartu (1977), p. 125.
26. V. N. Ryzhikov, N. A. Figurovskii, and T. A. Komarova, RZhKhimiya, No. 21, 21 A2 Dep. (1978).
27. V. N. Ryzhikov, N. A. Figurovskii, and T. A. Komarova, RZhKhimiya, No. 21, 21 A3 Dep. (1978).
28. V. N. Ryzhikov, N. A. Figurovskii, and T. A. Komarova, RZhKhimiya, No. 21, 21 A7 Dep. (1978).
29. Russ. Jahrb. Pharm., 6, 172 (1808).
30. Huffeland's J. Prakt. Heilkunde, 29, No. 6, 99 (1809).
31. Huffeland's J. Prakt. Heilkunde (1809).
32. Huffeland's J. Prakt. Heilkunde, 29, No. 7, 116 (1809).
33. Huffeland's J. Prakt. Heilkunde, 21, No. 10, 112 (1810).
34. D. H. Grindel, Chinasurrogat oder ein neues Arzneimittel. Dorpat (1809); Leipzig (1809).
35. J. Pharm., 1, 488 (1815).
36. F. Magendie, Pharmacie [Russian translation], Moscow (1840).
37. F. Gize, General Chemistry for Teachers and Students [in Russian], Kharkov, Parts 1-5 (1813-1817).
38. Ann. Chem., 38, 363 (1841); J. Pharm., 1, 159 (1842).
39. J. Prakt. Chem., 16, 81 (1839).
40. Kastner's Arch. Natürl., 7, 263 (1826).
41. Pharm. Z. Russl., 2, 451 (1863-1864).
42. Pharm. Z. Russl., 4 (1866).
43. Pharm. Z. Russl., 7, 233 (1868).
44. Pharm. Z. Russl., 2, 27 (1866); 5, 85 (1866).
45. Pharm. Z. Russl., 6, 663 (1867).
46. Virchov's Arch., 76, 373 (1879).
47. Pharm. Z. Russl., 5, 92 (1866).
48. Pharm. Z. Russl., 8, 460 (1870).
49. Pharm. Z. Russl., 23, 311, 329, 345, 361, 377 (1884).
50. Pharm. Z. Russl., 5, 153 (1866).
51. Arch. Exp. Path. Pharmacol., 6, 153 (1876).
52. Arch. Exp. Path. Pharmacol., 7, 55 (1877).
53. Pharm. Z. Russl., 24, 116 (1885).
54. "The alkaloids of Lobelia inflata," Lecture [in German] at a meeting of the Medical Faculty of St. Petersburg; Med. Wochenschr. (1889).
55. J. Prakt. Chem., 31, 56 (1847); 42, 275; 43, 144 (1848); 44, 370; 48, 175 (1849).
56. St. Petersb. Acad. Bull., 6, 49, 241 (1848); 7, 129 (1849); 8, 81 (1850).
57. Ann. Chem., 64, 360 (1848); J. Prakt. Chem., 60, 358 (1853); St. Petersb. Acad. Bull., 12, 17 (1854).

58. Ann. Chem., 1, 125 (1842); St. Petersb. Acad. Bull., 8, No. 13, 206 (1841).
59. J. Prakt. Chem., 27, 140 (1842).
60. Zh. Russ. Fiz.-Khim. Ova, 10, No. 6, 244 (1878).
61. Zh. Russ. Fiz.-Khim. Ova, 11, 183 (1879).
62. Zh. Russ. Fiz.-Khim. Ova, 11, 321 (1879).
63. Zh. Russ. Fiz.-Khim., Ova, Section 2, Nos. 1-2, 16 (1880).
64. E. A. Shatskii, The Science of Plant Alkaloids, Glucosides, and Ptomaines [in Russian], Kazan', Parts 1 and 2 (1890-1892).
65. Patent No. 3254, cl. 12p, 14 (1927).
66. Patent No. 2542 (1927).
67. Patent No. 21,132 (1931).
68. In: Communications on Scientific and Technical Investigations in the Republic [in Russian], Moscow, March-April (1920), p. 11.
69. Zh. Nauchn. Khim.-Farm. Inst. VSNKh, No. 2, 46 (1921).
70. Bull. Soc. Chim. Fr., 39, No. 4, 305 (1926).
71. Bull. Soc. Chim. Fr., 45, No. 4, 109 (1929).
72. Bull. Soc. Chim. Fr., 45, No. 4, 121 (1929).
73. Zh. Khim. Prom., 7, 11 (1930).
74. Zh. Prikl. Khim., 16, 152 (1943).
75. Dokl. Akad. Nauk SSSR, 69, 189 (1949).
76. Dokl. Akad. Nauk SSSR, 75, 43 (1950).
77. Dokl. Akad. Nauk SSSR, 82, 731 (1952).
78. Diss. Giessen (1909).
79. A. P. Orekhov, Intramolecular Rearrangements. Investigations in the Field of Theoretical Organic Chemistry [in Russian], Moscow (1965), p. 5.
80. P. S. Massagetov, Sacred Herbs. Journeys. Adventures. Search [in Russian], Moscow (1973).
81. Compt. Rend., 189, 945 (1929).
82. Byull. NIKhFI, No. 1, 1; No. 2, 33 (1931).
83. Byull. NIKhFI, No. 12, 299 (1931).
84. Ber., 64, 266 (1931).
85. Ber., 65, 232 (1932).
86. Ber., 65, 724 (1932).
87. Ber., 65, 1126 (1932).
88. Khim.-Farm. Prom., No. 4, 188 (1933).
89. Ber., 66, 466 (1933).
90. Ber., 67, 289 (1934).
91. Ber., 67, 1157 (1934).
92. Ber., 67, 1398 (1934).
93. Ber., 67, 1606 (1934).
94. Ber., 69, 496 (1936).
95. Zh. Obshch. Khim., 7, 951 (1937).
96. Khim.-Farm. Prom., No. 1, 10 (1932).
97. Ber., 65, 234 (1932).
98. Ber., 67, 1845 (1934).
99. Ber., (1974).
100. Zh. Obshch. Khim., 7, 2048 (1937).
101. Dokl. Akad. Nauk SSSR, 102, 755 (1955).
102. Ber., 65, 974 (1932).
103. Ber., 66, 875 (1933).
104. Ber., 68, 1051 (1935).
105. Izv. Akad. Nauk SSSR, Ser. Khim., No. 6, 969 (1936).
106. Zh. Obshch. Khim., 19, 1702 (1949).
107. Dokl. Akad. Nauk UzSSR, No. 1, 3 (1950).
108. Ber., 69, 1110 (1936).
109. Ber., 69, 1799 (1936).
110. Ber., 66, 621 (1933).
111. Ber., 66, 625 (1933).
112. Khim.-Farm. Prom., No. 3, 5 (1934).
113. Ber., 68, 1807 (1935).
114. Zh. Obshch. Khim., 7, 743 (1937).
115. Ber., 66, 841 (1933).

116. Khim.-Farm. Prom., No. 2, 8 (1934).
117. Ber., 67, 1214 (1934).
118. Izv. Akad. Nauk SSSR, Ser. Khim., No. 6, 957 (1936).
119. Zh. Obshch. Khim., 7, 1999 (1937).
120. Bull. Soc. Chim. Fr., 1265 (1937).
121. Zh. Obshch. Khim., 9, 415 (1939).
122. Khim.-Farm. Prom., No. 2, 52 (1933).
123. Arch. Pharm., 271, 145 (1933).
124. Ber., 67, 1153 (1934).
125. Zh. Obshch. Khim., 7, 646 (1937).
126. Zh. Obshch. Khim., 9, 41 (1939).
127. In: Proceedings of the All-Union Scientific-Research Institute of Medicinal Plants [in Russian], Moscow, No. IX (1947), p. 3.
128. Zh. Obshch. Khim., 8, 308 (1938).
129. Bull. Soc. Chim. Fr., 29 (1938).
130. Ber., 68, 2158 (1935).
131. Zh. Obshch. Khim., 7, 1791 (1937).
132. Zh. Obshch. Khim., 7, 1797 (1937).
133. Zh. Obshch. Khim., 10, 641 (1940).
134. Ber., 68, 650 (1935).
135. Ber., 68, 1886 (1935).
136. Ber., 69, 1908 (1936).
137. Zh. Obshch. Khim., 8, 273 (1938).
138. Zh. Obshch. Khim., 8, 391 (1938).
139. Zh. Obshch. Khim., 8, 396 (1938).
140. Zh. Obshch. Khim., 18, 1198 (1948).
141. Zh. Obshch. Khim., 35, 584 (1965).
142. Ber., 68, 2039 (1935).
143. Dokl. Akad. Nauk UzSSR, No. 4, 28 (1953).
144. Dokl. Akad. Nauk UzSSR, No. 4, 31 (1957).
145. Dokl. Akad. Nauk UzSSR, No. 6, 19 (1957).
146. Zh. Obshch. Khim., 29, 677 (1959).
147. Bull. Soc. Chim. Fr., 1357 (1938).
148. Zh. Obshch. Khim., 9, 126 (1939).
149. Zh. Obshch. Khim., 16, 129 (1946).
150. Bull. Soc. Chim. Fr., 811 (1939).
151. Zh. Obshch. Khim., 9, 1356 (1939).
152. Zh. Obshch. Khim., 9, 1507 (1939).
153. Zh. Obshch. Khim., 9, 1868 (1939).
154. Bull. Soc. Chim. Fr., 70 (1940).
155. Dokl. Akad. Nauk UzSSR, No. 8, 12 (1948).
156. Zh. Obshch. Khim., 9, 2203 (1939).
157. Zh. Obshch. Khim., 10, 1781 (1940).
158. Zh. Obshch. Khim., 9, 595 (1939).
159. Zh. Obshch. Khim., 11, 157 (1941).
160. Zh. Obshch. Khim., 11, 207 (1941).
161. Zh. Obshch. Khim., 11, 209 (1941).
162. Zh. Obshch. Khim., 15, 225 (1945).
163. Zh. Obshch. Khim., 16, 1311 (1946).
164. Zh. Obshch. Khim., 17, 343 (1947).
165. Zh. Obshch. Khim., 13, 801 (1943).
166. Zh. Obshch. Khim., 17, 1569 (1947).
167. Zh. Obshch. Khim., 14, 1148 (1944).
168. Farmatsiya, No. 5, 10 (1946).
169. Zh. Obshch. Khim., 18, 1510 (1948).
170. Dokl. Akad. Nauk SSSR, 66, No. 3, 437 (1949).
171. Zh. Obshch. Khim., 14, 161 (1944).
172. Zh. Obshch. Khim., 14, 172 (1944).
173. Zh. Obshch. Khim., 18, 1736 (1948).
175-176. Zh. Obshch. Khim., 17, 1216 (1947).*
177. Zh. Obshch. Khim., 17, 2265 (1947).

*As in Russian Original — Publisher.

178. Dokl. Akad. Nauk SSSR, 61, 317 (1948).
179. Zh. Obshch. Khim., 18, 1836 (1948).
180. Zh. Obshch. Khim., 19, 1396 (1949).
181. Zh. Obshch. Khim., 19, 1382 (1949).
182. Zh. Obshch. Khim., 20, 368 (1950).
183. Zh. Obshch. Khim., 20, 1514 (1950).
184. Tr. Inst. Khimii Akad. Nauk UzSSR. Tashkent, No. III, 3 (1952).
185. Khim. Prir. Soedin., 74 (1970).
186. Zh. Obshch. Khim., 20, 1151 (1950).
187. Dokl. Akad. Nauk UzSSR, No. 2, 23 (1951).
188. Zh. Obshch. Khim., 22, 1047 (1952).
189. Dokl. Akad. Nauk UzSSR, No. 10, 24 (1953).
190. Khim. Prir. Soedin., 426 (1966).
191. Khim. Prir. Soedin., 202 (1968).
192. Khim. Prir. Soedin., 196 (1968).
193. Zh. Obshch. Khim., 22, 1457 (1952).
194. A. P. Orekhov, The Chemistry of the Alkaloids [in Russian], Moscow (1938).
195. A. P. Orekhov, The Chemistry of the Alkaloids [in Russian], 2nd ed., Moscow (1955).
196. A. P. Orekhov, The Chemistry of the Alkaloids of Plants of the USSR [in Russian], Moscow (1965).
197. Zh. Obshch. Khim., 22, 1899 (1952).
198. Zh. Obshch. Khim., 25, 1035 (1955).
199. Dokl. Akad. Nauk SSSR, 91, 1145.
200. Zh. Obshch. Khim., 23, 504 (1953).
201. Zh. Obshch. Khim., 25, 2006 (1955).
202. Zh. Obshch. Khim., 28, 558 (1958).
203. Zh. Obshch. Khim., 28, 2283 (1958).
204. Zh. Obshch. Khim., 29, 1728 (1959).
205. Zh. Obshch. Khim., 30, 1727 (1960).
206. Zh. Obshch. Khim., 26, 3220 (1956).
207. Med. Prom. SSSR, No. 9, 12 (1959).
208. Zh. Obshch. Khim., 31, 1389 (1961).
209. Dokl. Akad. Nauk SSSR, 87, 227 (1952).
210. Zh. Obshch. Khim., 26, 3218 (1956).
211. Dokl. Akad. Nauk UzSSR, No. 9, 33 (1957).
212. Zh. Obshch. Khim., 25, 831 (1955).
213. Zh. Obshch. Khim., 30, 345 (1960).
214. Zh. Obshch. Khim., 20, 1921 (1960).
215. Zh. Obshch. Khim., 31, 3815 (1961).
216. Khim. Prir. Soedin., 22 (1965).
217. Zh. Obshch. Khim., 32, 647 (1962).
218. Med. Prom. SSSR, No. 12, 23 (1957).
219. Zh. Obshch. Khim., 27, 3170 (1967).
220. In: Alkaloid-Bearing Plants of Moldavia [in Russian], Kishinev (1960), pp. 21, 35.
221. Khim. Prir. Soedin., 249 (1967).
222. Khim. Prir. Soedin., 98 (1968).
223. I. V. Terent'eva, G. V. Lazur'evskii, and P. A. Vember, Brevicolline — an Alkaloid of Carex brevicollis. The Experience of Chemical and Clinical Study [in Russian], Akad. Nauk Mold. SSR, Kishinev (1969), p. 97.
224. Khim. Prir. Soedin., 39 (1969).
225. Khim. Prir. Soedin., 397 (1969).
226. A. S. Sadykov, The Chemistry of the Alkaloids of Anabasis aphylla [in Russian], Tashkent (1956).
227. A. S. Sadykov and O. S. Otroshchenko, Results of a Chemical Study of the Subshrub Anabasis aphylla Growing in the Turkmen SSR [in Russian], Tashkent (1956).
228. A. S. Sadykov, Kh. A. Aslanov, and Yu. K. Kushmuradov, Alkaloids of the Quinolizidine Series [in Russian], Moscow (1975).
229. S. Yu. Yunusov, Alkaloids [in Russian], Tashkent (1974).
230. M. D. Mashkovskii, Drugs [in Russian], Moscow (1977).
231. O. N. Tolkachev, Khim. Prir. Soedin., 234 (1977).
232. A. S. Sadykov, The Development of Bioorganic Chemistry in Uzbekistan [in Russian], Tashkent (1978).