ADVANCES IN THE CHEMISTRY OF HETEROCYCLES AND THE PHARMACEUTICAL-CHEMISTRY INDUSTRY OF THE USSR (REVIEW)

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The principal directions in the development of the national economy of the USSR for 1976-1980, which were approved by the 25th Congress of the Communist Party of the Soviet Union (CPSU), specify a new increase in the prosperity of the nation and direct a great deal of attention to the further improvement of public health in our country. "Among our social problems," said General Secretary of the Central Committee of the CPSU L. I. Brezhnev, "there is none more important than our concern for the health of the Soviet people. Our advances here are widely known. However, we must also be aware of the problems that we face in this area. They entail improvement of the organization of public health, expansion of the network of hospitals and polyclinics, and an increase in the production of medical equipment and highly effective drugs" [1].

During 60 yr of Soviet power the health industry in our country has made definite advances that are associated to a considerable extent with the achievements of synthetic organic chemistry and primarily one of its most vigorously developing divisions – the chemistry of heterocyclic compounds.

At the foundation of the Soviet pharmaceutical-chemistry industry one finds prominent chemists such as A. E. Chichibabin, S. N. Reformat-skii, N. D. Zelinskii, N. S. Kurnakov, A. E. Favorskii, V. M. Rodionov, A. P. Orekhov, A. N. Nesmeyanov, A. E. Arbuzov, M. M. Shemyakin, I. L. Knunyants, O. Yu. Magidson, M. V. Rubtsov, N. A. Preobrazhenskii, I. Ya. Postovskii, G. P. Men'shikov, etc.

The Scientific-Research Pharmaceutical-Chemistry Institute, which was organized in 1920 and subsequently was renamed the S. Ordzhonikidze All-Union Scientific-Research Pharmaceutical-Chemistry Institute (ASRPCI), has played an important role; this institute has become the principal scientific center of pharmaceutical chemistry in the country and until the start of World War II ensured the manufacture in the Soviet Union of basic groups of medicinals used in worldwide medical practice [2, 3].

The successful mastery of experience abroad made it possible in the prewar years to begin original research on the creation of new medicinal preparations, including those involving heterocyclic compounds. The search for chemotherapeutic agents in the 4-aminoquinoline series began in this era (M. V. Rubtsov and O. Yu. Magidson) [5] and led to the discovery of a new class of antimalarial preparations, the synthesis of isomers and analogs of hydroquinine (M. V. Rubtsov) [6], the development of the chemistry of pyrolizidine alkaloids (G. P. Men'shikov) [7], the creation of the original medicinal preparations platyphilline (A. P. Orekhov and R. A. Konovalova) [8], pachycarpine (L. P. Orekhov, M. S. Rabinovich, and A. A. Konovalova) [8], salsoline and salsolidine (A. P. Orekhov, and N. F. Proskunina) [8], plasmocid (O. Yu. Magidson and I. T. Strukov) [9], and aminoacrichin (A. M. Grigorovskii) [10].

The most extensively original research was developed in the postwar years. During this period, new centers, in addition to the ASRPCI, for the search for medicinal preparations were developed: institutes of pharmacology, experimental medicine, medicinal parasitology and tropical medicine, the Oncological Center of the Academy of Medical Sciences (AMS) of the USSR, the All-Union Scientific-Research Vitamin Institute (ASRVI), the All-Union Institute of Medicinal Plants (AIMP), the All-Union Scientific-Research Institute of Antibiotics (ASRIA), the Institute of Biophysics, the Kharkov and Novokuznetsk Scientific-Research Pharmaceutical-Chemistry Institute (KNSRPCI), etc. Reserach involving the search for new medicinals was developed in the following institutes of the Academy of Sciences (AS) of the USSR and the academies of sciences of the Soviet republics: the Institute of Organic Chemistry and the Institute of Bioorganic Chemistry of the AS USSR, the Institutes of Organic Synthesis of the AS Latvian SSR and of Fine Organic Synthesis of the AS Armenian

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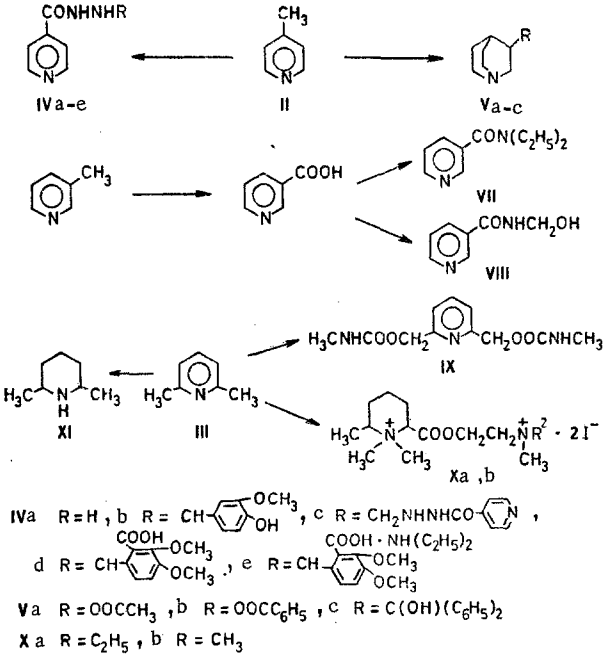
SSR and the Chemistry of Plant Substances of the AS Uzbek SSR, the Institute of Chemistry of the AS Moldavian SSR, the Novosibirsk, Kiev, and Irkutsk Institutes of Organic Chemistry, the Ural Polytechnic and Moscow, Leningrad, and Kazan Chemical-Technological Institutes, the Moscow Institute of Fine Chemical Technology, Moscow, Rostov, Odessa, and Saratov Universities, the Leningrad Pharmaceutical-Chemistry Institute, etc.

It is, of course, impossible to examine all of the numerous studies of the chemistry of heterocycles in our country that have laid the foundation for the creation of new medicinal preparations of this class within a brief review (a considerable number of these studies have been reflected in a review by N. S. Zefirov [4]). Only those studies that have had practical results and have led to the creation of new original medicinal preparations of the heterocyclic series that have successfully passed clinical tests and have been approved for medical application or have resulted in the development and incorporation in the pharmaceutical-chemistry industry of fundamentally new methods for the production of heterocyclic medicinal preparations are therefore examined in the present paper.

The efficient complex utilization in heavy-tonnage industries of the pharmaceutical-chemical preparations of the β-picoline fraction containing β-(I) and γ-picolines (II) and 2,6-lutidine (III) became economically important in the postwar years. A scheme that was developed and incorporated in industry (M. V. Rubtsov, E. E. Mikhlina, E. S. Nikit-skaya, L. N. Yakhontov, V. Ya. Vorob'eva, and A. D. Yanina) was based on the condensation of the unseparated β-picoline fraction with formalin under conditions in which only the γ-picoline fraction undergoes reaction; this fraction gives a mixture of methylol derivatives, from which the β-picoline and 2,6-lutidine are easily removed by steam distillation. Oxidation of the methylol derivatives with nitric acid leads to isonicotinic acid [11], which is used for the industrial production of antituberculous preparations of the isonicotinic acid hydrazide group, including the original medicinals phthivazide (IVb), metazide (IVc), saluzide (IVd), soluble saluzide (IVe) (M. N. Shchukina, G. N. Pershin, O. O. Makeeva, S. A. Vichkanova, S. S. Liberman, and A. I. Polezhaeva) [12], as well as diverse (with respect to medical application) quinuclidine preparations (X) [13]. After additional separation, picoline I is used for the production of nicotinic acid (VI), cordiamin (VII), and nikodin (VIII) (M. V. Rubtsov and L. N. Yakhontov) [14], while 2,6-lutidine (III) is used for the preparation of the antisclerotic agent parmidine (anginine) (IX), the hypotensive preparations dicolin (Xa), dimecolin (Xb), and nanophyn (XI) [15-17] (M. V. Rubtsov, M. D. Mashkovskii, L. N. Yakhontov, E. S. Nikit-skaya, N. A. Serova, I. M. Sharapov, and Yu. I. Syrneva). A new method for the preparation of the neuroleptanalgesic agents phentanyl and droperidol [18, 19] was also developed (É. S. Lavrinovich).

4-Formylpyridine obtained by vapor-phase catalytic oxidation of 4-methylpyridine is used in the production of the cholinesterase reactivator dipyroxime [20] (M. V. Shimanskaya and L. Ya. Leitis).



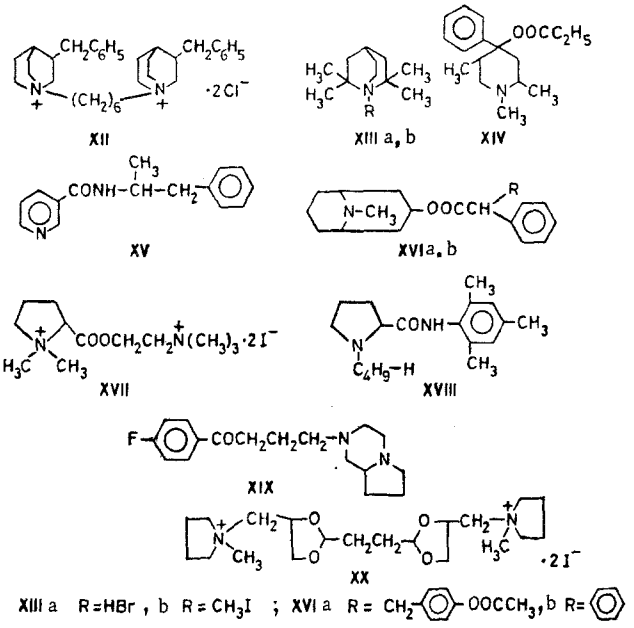
Studies by Soviet scientists made it possible to establish the relationship between the structures, including the stereochemistry and conformation, of quinuclidine compounds and their biological activity [21]; this made it possible to create a series of original preparations — the cholinomimetic aceclidine (Va), the hypotensive and

sedative agent oksilidin (Vb), the antiallergenic preparation fenkarol (Vc), the myelorelaxant kvalidil (XII), the ganglion blocker temekhin (XIIIa), and an agent for controllable hypotonia during surgical operations – imekhin (XIIIb) (M. V. Rubtsov, M. D Mashkovskii, E. E. Mikhlina, L. N. Yakhontov, E. S. Nikit-skaya, V. Ya. Vorob'eva, A. D. Yanina, E. I. Levkoeva, K. A. Zaitseva, F. S. Sadretdinov, I. M. Sharapov, and M. É. Kaminka) [15, 22].

Successful research on the vapor-phase catalytic oxidation [23] (M. V. Shimanskaya and L. Ya. Leitis) and oxidative ammonolysis [24] (B. V. Suvorov and A. D. Kagarlitskii) of alkylpyridines ensures improvement in the technology for the production of a number of pyridine medicinal preparations.

The extensive research of the school of Academician I. N. Nazarov on the synthesis of heterocycles based on acetylenic derivatives, which includes a study of the configuration and conformation of piperidines, resulted in the creation of the effective analgetic promedol (XIV) (I. N. Nazarov, M. D. Mashkovskii, and N. S. Prostakov) [25], which for many years has been produced by the Soviet pharmaceutical-chemical industry. The preparation phenatine (XV), which is a CNS stimulator with vasodilating action, was created on the basis of phenamine and nicotinic acid [26].

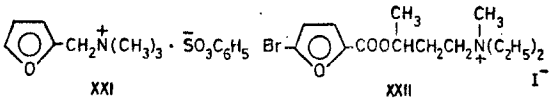
Research on tropine esters led to the development of industrial methods for the preparation of synthetic tropine, atropine (O. Yu. Magidson and N. I. Koretskaya) [27], and homoatropine (R. G. Glushkov, N. I. Koretskaya, and O. Yu. Magidson) [28] and to the creation of the α-adrenolytic tropafen (XVIa) and the central cholinolytic tropacine (XVIb) (O. Yu. Magidson, V. M. Fedosova, M. D. Mashkovskii, and K. A. Zaitseva) [29].



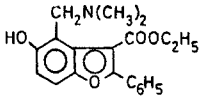
Systematic studies of lactim esters [30] and acetals of lactams [31] and other modified cyclic amides [32] (R. G. Glushkov and V. G. Granik) made it possible to develop and incorporate in industry original methods for the production of corazole [33], allopurinol, and klofelin [34].

The brief-action gangliolytic gigronii (XVII) (A. P. Skoldinov, V. V. Zakusov, A. M. Likhosherstov, and D. A. Kharkevich) [36], the local anesthetic pyrromekain (XVIII) (A. P. Skoldinov, A. M. Likhosherstov, and N. G. Pryanishnikova) [37], and the neuroleptic azabutiron (XIX) (A. P. Skoldinov, A. M. Likhosherstov, and K. S. Raevskii) [38] were created on the basis of the development of methods for the synthesis of derivatives of pyrrolidine-2-carboxylic acid and condensed azabicyclic pyrrolidinopiperazine systems by aminolysis of α,ω-dihalo carboxylic acids (A. P. Skoldinov and A. M. Likhosherstov) [35]. The original muscle relaxant with mixed activity dioksonii (XX), which initially induces a depolarization phase and then has an antidepolarizing effect, was created in a series of quaternary pyrrolidine derivatives (S. A. Giller, A. A. Kimenis, and G. P. Sokolov) [39].

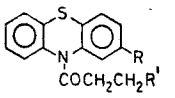
Research on a number of furan compounds led to the original preparations benzamon (XXI), a cholinomimetic used for the treatment of glaucoma (N. V. Khromov-Borisov) [40], and fubromegan (XXII), which has cholinomimetic action (A. L. Mndzhoyan and R. A. Aleksanyan) [41]. An original spasmolytic and coronary dilating agent – fenikaberan (XXIII) – was found in the benzofuran series (A. N. Grinev and V. G. Stolyarchuk [42].



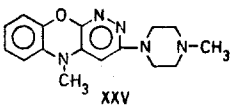
XXI XXII



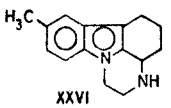
XXIII



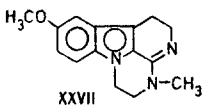
XXIVa-d



XXV

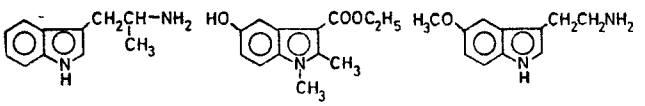


XXVI

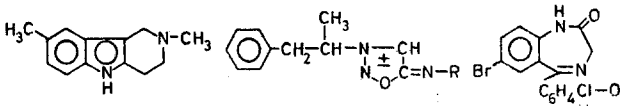


XXVII

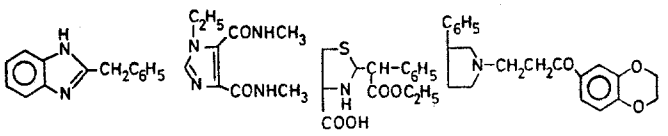
XXIVa R = NHCOOC$_2$H$_5$, R' = morpholino; b R = CF$_3$, R' = N(C$_2$H$_5$)$_2$; c R = Cl, R' = N(C$_2$H$_5$)$_2$; d R' = N⟨N⟩; R = Cl



XXVIII XXIX XXX



XXXI XXXIIa, b XXXIII



XXXIV XXXV XXXVI XXXVII

XXXIIa R = H, b R = CONHC$_6$H$_5$

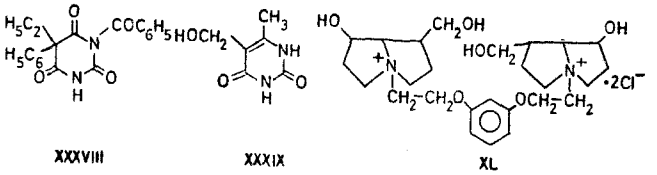
A large amount of research has been devoted to the systematic study of phenothiazine derivatives. Methods have been developed for the synthesis of these compounds by thionation of the corresponding diarylamines or Smiles rearrangement of substituted diphenyl sulfides. In addition, the principles of the relationship between the structure and biological activity have been uncovered [43], and the industrial production of the most important psychotropic phenothiazine preparations aminazine [44], triphthazine [45], etaperazine [46], propazine [47, 48] etc. has been organized (M. N. Shchukina, A. P. Skoldinov, S. V. Zhuravlev, and N. V. Savitskaya). This research subsequently led to the creation of the antiarhythmic agent etmozin (XXIVb) [49] and the antianginal preparations chloracizine (XXIVc) [50] and nonakhlazine (XXIVd) [51] (A. P. Skoldinov, S. V. Zhuravlev, V. V. Zakusov, N. V. Kaverina, and Yu. I. Vikhlyaev), as well as to the discovery of the antidepressant azafen, which is a diazaphenoxazine derivative (XXV) (M. N. Shchukina, M. D. Mashkovskii, T. V. Gortinskaya, and A. I. Polezhaeva) [52, 53].

New antidepressants with four ring structures – pirazidol (XXVI) [54] (A. N. Grinev, I. D. Mashkovskii, V. I. Shvedov, L. B. Altukhova, and N. I. Andreeva) and inkazan (XXVII) (R. G. Glushkov, M. D. Mashkovskii, and N. I. Andreeva) – have recently been created.

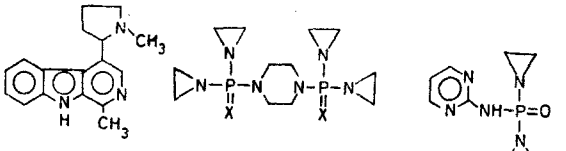
Diverse studies of indole compounds have undergone extensive development in the USSR (A. N. Kost, N. N. Suvorov, A. N. Grinev, M. N. Preobrazhenskaya, I. I. Grandberg, V. P. Mamaev, Yu. P. Kitaev, N. F. Kucherova, et al.). A practical result of these studies was the creation of a CNS stimulator with an antidepressive effect – indopan (XXVIII) (N. N. Suvorov, M. N. Preobrazhenskaya, M. D. Mashkovskii, and T. K. Trubitsyna) [55] – the hypotensive agent dimekarbin (XXIX) (A. N. Grinev, A. P. Terent'ev, and K. S. Shadurskii) [56], the radiological protective substance mexamine (XXX) (N. N. Suvorov) [57], the neuroleptic karbidin (XXXI) (N. F. Kucherova, N. K. Kochetkov, V. V. Zakusov, and N. K. Barkov) [58], and the antihistamine preparation dimebon (A. N. Kost and K. S. Shadurskii) [56, 59], and a method for the synthesis of serotonin adipate has been developed and incorporated in industry (N. N. Suvorov and L. B. Shagalov) [60].

The creation of the effective psychostimulators sidnofen (XXXIIa) [61] and sidnokarb (XXXIIb) [62] is intimately associated with research on sydnoneimines (V. G. Yashunskii, L. E. Kholodov, M. D. Mashkovskii, and R. A. Al'tshuler) [63]. Methods have been developed for the preparation of the individual threo isomer of the psychostimulating preparation meridil (L. N. Yakhontov and E. I. Levkoeva) [64]; methods suitable for use in industry for the preparation of the neuroleptics nitrazepam (K. Yu. Novitskii and N. I. Koretskaya) and oxazepam (V. N. Gorbunov) have also been developed, and the new neuroleptic fenazepam (XXXIII) (A. V. Bogat-skii, V. V. Zakusov, and Yu. I. Vikhlyaev) [65] was created.

Research on a series of derivatives of imidazole and its condensed systems (A. M. Simonov, B. A. Porai-Koshits, N. V. Khromov-Borisov, L. S. Éfros, A. F. Pozharskii, P. M. Kochergin, B. A. Tertov, et al.) resulted in the practical utilization of the spasmolytic and hypotensive agent dibasole (XXXIV) (S. V. Anichkov, B. A. Porai-Koshits, O. F. Ginzburg, and L. S. Éfros) [66] and the respiratory analeptic etimizol (XXXV) (S. V. Anichkov and N. V. Khromov-Borisov) [67]. A new leucopoeisis stimulator – leikogen (XXXVI) – was found in the thiazolidine derivative series (I. T. Strukov) [68], and a new adreno-blocking agent – pirroksan (XXXVII) – was found in the benzodioxane series (A. V. El'tsov and S. N. Golikov) [69].

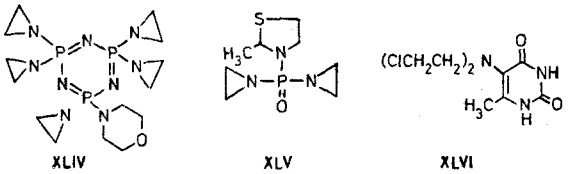


XXXVIII XXXIX XL

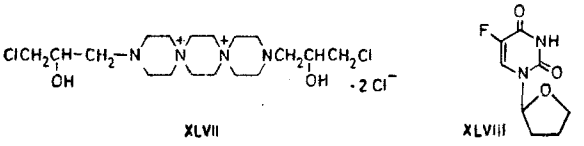


XLI XLIIa, b XLIII

XLIIa R=O; b R=S



XLIV XLV XLVI



XLVII XLVIII

Research on the chemistry of pyrimidines (V. M. Rodionov, O. Yu. Magidson, V. P. Mamaev, Yu. P. Shvachkin, L. S. Éfros, K. A. Chkhikvadze, R. G. Glushkov, M. Yu. Lidak, A. V. El'tsov, S. I. Zav'yalov, et al.) led to the creation of the antispasmodic agent benzonal (XXXVIII) (L. P. Kulev and V. G. Stolyarchuk) [70] and the leucopoeisis stimulator and antiphlogistic agent pentoxyl (XXXIX) (N. V. Lazarev) [71] and to the development and incorporation in industry of new methods for the production of orotic acid (O. Yu. Magidson, K. A. Chkhikvadze, S. I. Zav'yalov, and V. I. Gunar) [72].

Research on alkaloids and the products of their transformations on the basis of semisynthesis has led to the creation of the original curare-like preparations diplatsin (XL) [73], melliktin, and kondel'fin [74] (A. D. Kuzovkov, M. D. Mashkovskii, G. P. Men'shikov, A. V. Danilova, R. A. Konovalova, M. S. Rabinovich, P. M. Dozortseva, A. I. Briskin, and P. S. Massagetov), the tonic securinine (A. I. Ban'kovskii, A. D. Turova, V. I. Murav'eva, and Ya. A. Aleshkina) [75], the cholinesterase inhibitor galanthamine (N. F. Proskurnina, M. D. Mashkovskii, and R. P. Kruglikova-L'vova) [76], the uterine agent brevicolline (XLI) (G. V. Lazur'evskii and I. V. Terent'eva) [77], and the hypotensive vinkarin (S. Yu. Yunusov) [78] and to the development of industrial methods for the preparation of the tranquillizer gindarin (T. N. Il'inskaya [79] and the antitussive agent glaucine (L. D. Yakhontova and T. N. Il'inskaya) [80].

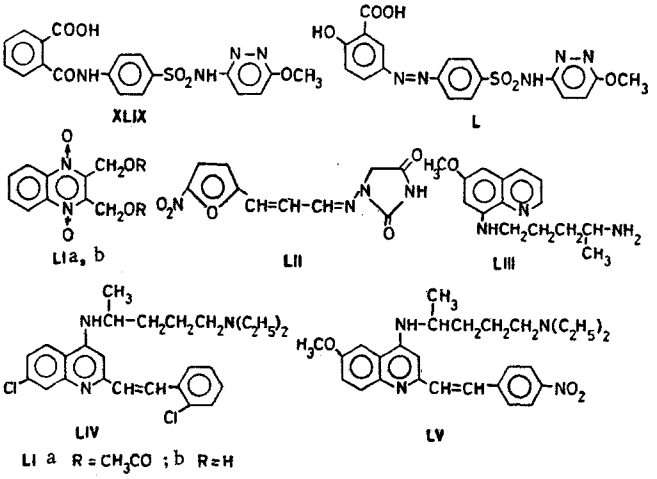
The total syntheses, accomplished for the first time by Soviet chemists, of the natural alkaloids pilocarpine (N. A. Preobrazhenskii) [81], emetine (R. P. Evstigneeva) [82], and curare alkaloids (N. A. Preobrazhenskii,

O. N. Tolkachev, L. V. Volkova, and V. G. Voronin) [83], which are used as medicinal preparations, are of great value. The total synthesis of ephedrine, caffeine, theobromine, theophylline, and papaverine has been made operable on an industrial scale in the USSR. Important research in this area has been accomplished by O. Yu. Magidson, E. S. Golovchinskaya, K. A. Chkhikvadze, V. A. Mikhalev, V. A. Zasosov, M. I. Dorokhova, N. I. Koretska, et al.

The search for antitumorigenic agents among heterocyclic derivatives has been carried out and is still being carried out in the country on an extensive scale under the supervision of such prominent scientists as N. N. Blokhin, I. L. Knunyants, I. Ya. Postovskii, A. F. Larionov, S. A. Giller, V. A. Chernov, T. S. Safonova, M. N. Preobrazhenskaya, N. M. Émmanuél', Z. V. Pushkareva, S. N. Sergievskaya, A. Ya. Berlin, E. S. Golovchinskaya, et al. Of the original preparations with an action of the alkylating type one should note dipine (XLIIa) [84] and thiodipine (XLIIb) [85] (S. I. Sergievskaya, A. A. Kropacheva, and V. A. Chernov), which are active in chronic lympholeucosis, fosfemid (XLIII) (T. S. Safonova and V. A. Chernov) [86], which is effective in hemodermias and cancer of the uterus and ovaries, fotrin (XLIV) (T. S. Safonova, and V. A. Chernov) [86], which is used in chronic lympholeucosis, erythremia, hemodermias, and some other tumors, and imifos (XLV) (S. A. Giller and M. Yu. Lidak) [87], which is used in the treatment of painful erythremias. Dopan (XLVI) – 5-[bis-(2-chloroethyl)amino]-6-methyluracil – is used for the treatment of lymphogranulomotosis, myeloleucosis, and lympholeucosis (L. F. Larionov, and V. G. Nemets) [88].

An original class of antitumorigenic agents – dispiropiperazinium derivatives – was found by Soviet researchers (V. A. Mikhalev, M. I. Dorokhova, and V. A. Chernov). The most effective preparation of this class is prospidin (XLVII) [91], which is characterized by great therapeutic breadth, effectiveness in the treatment of cancer of the larynx, lungs, bladder, lymphogranulomotosis, and skin retikulezakh. In contrast to the previously known antitumorigenic preparations of the alkylating type, prospidin does not have a depressive effect on hemopoiesis.

Methods for the synthesis of derivatives of pyrimido[4,5-b]-, pyrido[2,3-b]-, and pyrazino[2,3-b][1,4]-thiazines have been developed in order to search for new antitumorigenic agents among folic acid antagonists, and their transformations and biological activity have been investigated. The highest activity with respect to dihydrofolate reductase was displayed by 6-aminopyrido[4,5-b][1,4]thiazines and pyrimido[4,5-b][1,4]thiazin-6-ones, which differ from the known folic acid antagonists – aminopterine and methotrexate – with respect to their additional ability to inhibit aminopterine reductase. Tomizin, a preparation from this group, is being subjected to clinical testing (T. S. Safonova and V. A. Chernov) [86]. Research on unique analogs of nucleosides – N_1-furanidylpyrimidines and N_9-furanidylpurines – has been developed extensively. As a result of these studies, the original preparation ftorafur (XLVIII), which is the latent form of 5-fluorouracil and is being used successfully for cancer of the stomach, mammary gland, and rectum, was created (S. A. Giller, R. A. Zhuk, M. Yu. Lidak, and A. A. Zidermane) [92, 93].



A large amount of research has been carried out in the Soviet Union with respect to making the production of better prolonged-action sulfanilamides of the heterocyclic series – sulfapyridazine, sulfadimethoxine, sulfamonomethoxine, and sulfalene – an industrially operable process (M. N. Shchukina, V. A. Zasosov, T. V. Gortinskaya, V. N. Sokolova, T. N. Nikulina, L. E. Kholodov, et al.); an original prolonged-action sulfamide preparation for the treatment of intestinal infections – ftazin (XLIX) – (M. N. Shchukina, T. V. Gortinskaya, G. N. Persin, E. N. Padeiskaya, and L. M. Polukhina) [94] and an original preparation for the treatment of nonspecific ulcerative colitis – salazopyridazine (L) – (M. N. Shchukina, T. V. Gortinskaya, G. N. Persin, and E. N. Padeiskaya) [95] have been created.

Preparations for the treatment of acute bacterial infections – khinoksidin (LIa) and dioksidin (LIb) – have been created [96] on the basis of a systematic study of N-oxides of the quinoxaline series [96].

A systematic study of nitrofuran derivatives led to the development and incorporation in industry of the chemotherapeutic preparations furazolidone, furacilin, furazoline, and furadonine (S. A. Giller, K. K. Venter, and R. Yu. Kalnberga) [97-99].

An original preparation of the nitrofuran series – furagin (II) – and its soluble salt solafur have displayed high activity with respect to suppression of most antibiotic-resistant strains of bacteria, including resistant staphylococci (S. A. Giller and K. K. Venter) [100]. A systematic study of nitrofuran derivatives as antitumorigentic substances and radiosensitizers was recently begun (M. Yu. Lidak and N. M. Sukhova) [101].

Research on quinoline derivatives, particularly 4- and 8-aminoquinoline derivatives, has resulted in the creation of quinocide (LIII), an antimalarial preparation with gamontocidal action that also affects paraerythrocyte schizonts (M. B. Braude, A. F. Bekhli, and V. I. Stavrovskaya) [102] and the development of an industrial method for its synthesis [103], as well as an original method for the preparation of the known antimalarial preparation khingamin (A. F. Bekhli) [104].

Systematic studies of 2-styryl-4-aminoquinolines and quinazolines (M. V. Rubtsov, L. N. Yakhontov, G. N. Pershin, N. Yu. Moskalenko, N. A. Novitskaya, L. A. Pelenitsyna, N. A. Yanbukhtin, and G. P. Zhikhareva) made it possible to ascertain the antimicrobial, antiprotozoa, antituberculous, and antivirus activity of these substances and to create the preparations aminoquinol (LIV) and trikhomonatsid (LV), which have found application for the treatment of lambliasic and trichomona infections [105]. New methods for the synthesis of the antitrichomona agents metranidazol (P. M. Kochergin) [106] and nitazol (M. O. Kolosova) [107].

In summing up the results of 60 yr of development of medicinal chemistry and the pharmaceutical-chemical industry in the area of creation of new original medicinal preparations of the heterocyclic series, Soviet scientists are judiciously evaluating the great problems and tasks that the health industry faces. Further expansion of research on the search for new effective medicinals and primarily for the treatment of cardiovascular and nervous and psychic illnesses, virus and bacterial infections, malignant neoplasms, and tuberculosis is necessary.

According to the 1976-1980 five-year plan, a 44-46% increase in the production of the medicinal industry, including synthetic medicinal preparations (a 46-48% increase), is planned in the Soviet Union, and 220 new medicinal preparations are to be produced [108]; the task of researchers engaged in the search for new medicinals and the technology for their production is to ensure the successful fulfillment and surpassing of this five-year plan.

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LUMINESCENCE AND PHOTOCHEMISTRY OF AZOLES (REVIEW)

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A review of the luminescence and photochemical properties of azoles and their relationship to their structures is given. The mechanism of the deactivation of the excited states of the molecules is discussed.

Azoles have recently found extensive application as dyes, effective luminophores [1, 2], scintillators [3-5], and active media for lasers [6, 7]. At the same time, their structural peculiarities are responsible for the interest in these molecules as models with which it is expedient to study the specific character of processes involving the deactivation of the electronically excited states of a broad class of compounds containing a C = N group [8, 9].

These circumstances have stimulated the development, particularly in the last decade, of intensive research on the luminescence and photochemistry of azoles.

The aim of the present review was to critically examine the most important, from the point of view of the authors, problems associated with the deactivation of the excited states of azole molecules.

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