SECOND ALL-UNION SYMPOSIUM ON THE DIRECTED SYNTHESIS AND MECHANISM OF THE ACTION OF PHYSIOLOGICALLY ACTIVE AND MEDICINAL SUBSTANCES

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The Second All-Union Symposium on the Directed Synthesis and Mechanism of the Action of Physiologically Active and Medicinal Substances was held on January 17-19, 1977, in Riga. The symposium was devoted to the problems involved in the search for effective antitumorigenic and antivirus chemotherapeutic agents on the basis of the advances in organic and bioorganic chemistry, molecular biology and biochemistry, pharmacology, and chemotherapy.

Approximately 200 specialists from the leading institutes of the country participated in the activities of the symposium, during which 34 papers were presented.

N. I. Perevodchikova ("Medicinal treatment methods in modern oncology") and G. A. Galegov ("Selective inhibition of the reproduction of viruses and practical advances in chemotherapy") presented review papers on the increasing role of medicinal therapy in the struggle against oncological illnesses and virus infections. I. K. Khaetskii devoted his paper to problems of anticarcinogenesis and intracellular regulation of proliferation and differentiation. M. N. Preobrazhenskaya, in her paper, thoroughly analyzed the possibilities of a rational approach to the creation of antitumorigenic preparations and contemplated some methods for increasing the selectivity of the action of antitumorigenic preparations (regulation of enzymes participating in the activation and inactivation of preparations in the organism, the action on the pool of metabolites and the activity of enzyme targets, the direction of transport of a preparation to diseased tissues, the creation of antitumorigenic preparations that can be activated only in the tumor cell and remain inactive in the normal cell, etc.).

I. Ya. Postovskii, Z. V. Pushkareva, et al. examined the synthesis of lipids containing cytotoxic groups, antibiotics with peptide structures, oligopeptides, and analogs in a series of 5-aminoimidazole-4-carboxamide 1-ribonucleotides and 2-azapurine derivatives.

T. S. Safonova reported methods for the preparation of derivatives of pyrimido[4,5-b]-, pyrido[2,3-b]-, and pyrazino[2,3-b]-1,4-thiazines and their transformations.

A paper by A. A. Akhrem and co-workers was devoted to the directed transformation of natural nucleosides and nucleotides to compounds with antivirus and antitumorigenic activity. The authors demonstrated that the use of acetylsalicylyl chloride makes it possible to obtain an entire series of cyclonucleosides and arabinosides from the starting ribosides.

The application of the "indoline–indole" method for the synthesis of 1-glycosylindoles was demonstrated in a paper by I. V. Yartseva, M. N. Preobrazhenskaya, et al. Nucleosides containing a carbohydrate in the pyranose form were obtained by condensation of indoline with a monosaccharide and subsequent acylation. Two methods for the preparation of a new type of nucleoside — 1-glycosylisatins — were proposed: by cyclization of O-acylated N-arylaminoglycosides by means of oxalyl chloride in the presence of $AlCl_3$ or by oxidation of O-substituted 1-glycosylindoles with chromic acid. It was observed that 1-α-arabinopyranosides of substituted indoles constitute a new group of antitumorigenic substances.

E. S. Gubnitskaya demonstrated that the ethyleneimides of phosphorus acids are cleaved by the action of compounds with active chlorine atoms. This made it possible to obtain diverse previously unknown types of 2-chloroethylamides of phosphorus acids in good yields. The reaction was studied in greater detail in the case of the reaction of phosgene and methyl chlorocarbonate with N-substituted ethyleneimines. The synthesis of N-phosphorylated 2-imidazolidones and 2-oxazolidones and the preparation of the previously unknown phosphorylated diaziridines (by the successive reaction of 3,3-pentamethylenediaziridine with dialkylphos-

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phoric acid chlorides in the presence of triethylamine and reaction with phenyl isocyanate) were reported. Bisureas were obtained from diaziridine and isocyanates of dialkylphosphoric acids, and phosphatetraazepines — a new type of heterocyclic compound — were obtained by reaction with diisocyanates.

A number of papers were devoted to the problems involved in the search for new antitumorigenic and antivirus preparations among natural compounds. Thus V. A. Yakovlev and co-workers reported that they have developed new methods for the synthesis of folic acid, as well as the synthesis of S-nucleosylhomocysteines and their sulfoxides from 2,3'-phenylborate esters of 5'tosylnucleosides. The search has also been extended to Co complexes of octadecahydrocorrins, which are structurally related to vitamin B_{12}.

A paper by G. P. Vlasov and V. N. Lashkov was devoted to the synthesis of the antitumorigenic antibiotic actinomycin D and its analogs, a paper by O. K. Kabiev dealt with the use of plant phenolic compounds as the source of new antitumorigenic preparations, and a paper by G. V. Lazur'evskii was devoted to the directed search for anticancer substances in a series of steroid glycosides. M. Yu. Lidak presented a thorough analysis of the prospects in the search for antitumorigenic preparations among biopolymers and their analogs.

A great deal of attention was directed to the problems involved in the establishment of the mechanisms of the action of antitumorigenic and antivirus substances (S. M. Navashin and I. P. Fomina in a paper entitled "Methods for the directed search for antitumorigenic antibiotics and the mechanisms of their action," L. B. Gorbacheva in a paper entitled "Investigation of the molecular mechanisms of the action of nitrosoalkylureas on the transcription level," Yu. V. Dudnik in a paper entitled "Mechanism of the action of anticancer antibiotics," and R. A. Kukain in a paper entitled "Mechanism of the antivirus action of aminoadamantane derivatives").

The problem of the correlation of the structures and physicochemical properties with the antitumorigenic activity and the toxicity of some alkylating agents (diethyleneiminotriazines) was examined in a paper by B. A. Ivina and co-workers, and it was shown that the biological action of the investigated compounds depends substantially on the change in the hydrophilicity. The authors obtained "structure—activity" correlation dependences and concluded that a further search for antitumorigenic preparations in the series indicated above should be made among substances with high hydrophilicity or high lipophilicity.

The symposium adopted a resolution in which the promising character of the development of further research to find effective antitumorigenic and antivirus agents was emphasized.