Antineoplastic Chemotherapy and Radioprotectives

Volume II

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Radioprotectives

New Antineoplastic Chemotherapeutics:
Alkylating Agents

T. S. Safonova[1]

On Some Directions in Search of Antitumour Substances

For the purpose of searching for antitumour substances a series of di-(2-chloroethyl)- amines of bicycle compounds (A), cyclophosphazotriene derivatives (B), diethylene imides of phosphoric acid (C) and condensed systems of 1,4-thiazine (D) have been obtained and studied biologically (*T. S. Safonova, V. A. Chernov,* 1970).

It was noted that antitumour activity and toxicity of the derivatives (A) (Fig. 1) containing di(2-chloroethyl) amino group is influenced by the presence of the substituent, by the cytotoxic group position and by a number of carbon atoms in the alicycle part of the molecule.

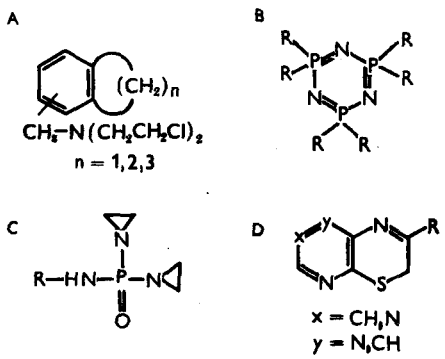

Fig. 1.

Of cyclophosphazotriene group (B) (Fig. 1) the compounds containing residues of various amine were subjected to biological study. Esters of amino acids, morpholin, piperidine, pyrrolidine and ethylene amine were used as amines.

The biological study of the compounds belonging to this group has shown that an antitumour action is exerted only by the substances containing an ethylene imine cycle. It is ascertained that the degree of antitumour effect is determined by the character of the amine in the cycle. It should be noted that cyclotriphosphazene derivatives containing 5-ethylen imine groups and a heterocyclic residue, in addition to a considerable antitumour effect with respect to rat sarcoma 45 and mouse sarcoma 180, are capable of increasing the duration of mouse life with leukaemia.

Investigations in the field of ethyleneimine derivatives (C) came mainly to the preparation of a series of phosphoric and tiophosphoric acid diethylene imides.

These works have resulted in preparing drugs dipin and thiodipin which have proved to be effective for the treatment of some hemoblastoses. Dipin is used for the treatment of patients with a tumour-like form of chronic lympholeucoses. The effectiveness of this drug has been also noted in laryngeal cancer and hypernephroid tumour.

Thiodipin shows a therapeutic effect in patients with chronic lympholeucosis, chronic myeloleucosis and lymphogranulomatosis. It is administered per os.

At present much material has been collected which allows the comparison of the structure of the substances and their reactivity with biological action. The antitumour action of the substances belonging to this group depends on the heterocyclic nature, position of the diethylene imino phosphoramide group in the cycle and on the electron-donor and acceptor properties of the substituents.

The alkylating properties of the compounds (C) (Fig. 1.) can be characterized in the simplest way by the ability of ethylene imine groups to hydrolytic splitting. Therefore, the study of the hydrolysis rate of the said compounds could characterize quantit-

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