ANALYSIS OF THE DEPENDENCE «STRUCTURE-ANTIAMNESTIC ACTION» IN A SERIES OF NEW DERIVATIVES OF 4-AMINOBUTANOIC ACID

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Pharmacocorrection of cognitive disorders is becoming increasingly important today in connection with the increasing requirements for effective intellectual activity in all spheres of society. In order to pharmacocorrection of cognitive disorders, various nootropic drugs are widely used, which normalize the metabolism of cells of the central nervous system, activate energy and protein metabolism, facilitate the transmission of nerve impulses, increase the brain's resistance to hypoxia and toxic effects. Among the various agents of nootronic action, GABA-ergic drugs are today the most widely used and economically available, but do not always meet the requirements of efficacy and safety. Given the above, it is important to search for new nootropic drugs, in particular among GABA derivatives, conducted by a number of scientists. Promising in this aspect are new derivatives of 4-aminobutanoic acid, synthesized at the National University of Pharmacy.

The aim of the study was to screen 11 newly synthesized 4-aminobutanoic acid derivatives for the presence of antiamnestic activity and to identify the structure-antiamnestic effect relationship in the passive avoidance conditional response test (PACRT).

Analysis of the structure-antiamnestic effect relationship for the synthesized series of compounds showed that the most active are 4-aminobutanoic acid derivatives containing a hydroxymethyl radical (compounds KGM-1 and KGM-2). The introduction of a methyl radical into the molecule KGM-2 leads to a decrease in antiamnestic activity (KGM-3). It was found that the replacement of one of the hydroxymethyl radicals in the molecule KGM-2 also helps to reduce the antiamnestic effect. Methylation of the basic structure (4-aminobutanoic acid) increased the activity only in cases when methyl and benzyl radicals were present in the molecule (compounds KGM-5 and KGM-6). The introduction of only methyl radicals (compounds KGM-9; KGM-10 and KGM-11) enhances the antiamnestic activity compared to the basic structure, and in the studied series of compounds they show high antiamnestic activity only at the highest study dose of 50 mg/kg.

Thus, combination in the structure of both benzyl and methyl radicals provides a high antiamnestic effect. The results of the analysis of the dose-effect relationship, including taking into account the proportion of animals in the group with fixed passive avoidance conditional response, give grounds for choice for further study of compounds KGM-5 and KGM-2.