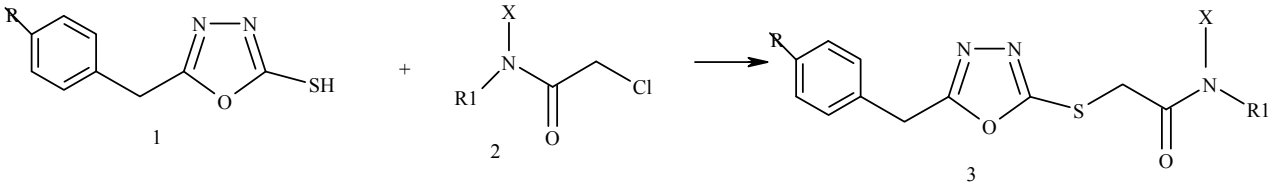
SEARCH FOR POTENTIAL DIURETICS AMONG THE DERIVATIVES OF 1,3,4-OXADIAZOLE

D. P. Chumatchenko, D. V. Bondarenko, L. O. Perekhoda
The National University of Pharmacy, Kharkiv, Ukraine
perekhodalina@ mail.ru

Purpose. Purpose of the work is synthesis of potential biologically active substances the derivatives of 1,3,4-oxadiazoles and the study of their diuretic activity. Analysis of the literature shows that among the derivatives of 1,3,4- oxadiazole, there are a lot of promising compounds in terms of pharmacy, but at the same time, their biological properties have been insufficiently studied.

Materials and Methods. In order to search for new bioactive substances - potential diuretics, aryl(heteryl) amides of 5-R-benzyl-1,3,4-oxadiazol-2-yl-thioacetic acid were synthesized. The high reactivity of initial substances of 5-R-benzyl-2-mercapto-1,3,4-oxadiazoles(1) makes it possible quite easy modify their structure by alkylation, which extends the probability of finding new effective compounds in this series. To study the difference in activity depending on the presence of anilide or heteryl fragment, alkylation was performed by aryl (heteryl) amides of chloracetic acid (2) under the conditions of basic catalysis. The structure of obtained aryl(heteryl) of 5-R-benzyl -1,3,4-oxadiazole-2-yl- thioacetic acid (3) is proved by modern physical and chemical methods of UV, IR and ^{1}H NMR- spectroscopy, the purity is confirmed by the method of thin-layer chromatography.



Diuretic activity of new compounds were studied by E.B. Berkhin's method on white male rats weighing of 180.0-200.0 g. Hypothiazide was used as comparator preparation. Tested compounds and hypothiazide were introduced intragastrically in a state of fine dispersed aqueous suspension stabilized by Twin-80, in a dose of 40 mg/kg.

Results and conclusions. New aryl-and heterylamides of 5-R-benzyl-1,3,4-oxadiazole-2-yl- thioacetic acid were synthesized. The structure of substances synthesized were proved by spectral methods. Received experimental data show that all 20 synthesized substances have moderate diuretic activity, and 2 compounds exceed hypothiazide activity. For promising compounds studied the toxicity *in vitro* (in a model test - system of rat bone marrow cells) and acute toxicity *in vivo*. The research results of cytotoxic activity *in vitro* and acute toxicity *in vivo* showed that the compounds synthesized are slightly toxic. Performed researches have allowed to select two compounds for in-depth study.