CREATING OF NOVEL OXIDANTS RELATED TO STRUCTURAL ANALOGUES OF N-CHLOROTAURINE: THEIR MOLECULAR PROPERTIES AND ACTION ON THE BLOOD PLATELETS

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Features of changes in the functions of blood cells and coagulation system components during their covalent modification by structural analogues of taurine chloramine which are moderate reactive oxidants have been established.

With usage of the computational data, a new structural analogue of chloramine of taurine (N-acetyl-N-chloro-2,2-dimethyltaurine) was created. It is established that N-acetyl-N-chloro-2,2-dimethyltaurine is an inhibitor of blood platelets functions. It exhibits specific pharmacological activity in platelet rich plasma and in human whole blood. In the blood, the action of the created inhibitor is selective, inhibition of platelets occurs in the absence of hemolytic damage to red blood cells.

The rate constant of N-acetyl-N-chloro-2,2-dimethyltaurine reaction with sulfhydryl group in dithiothreitol that served as a model of biologically significant thiols, was determined. The obtained constant (2.53×10^4 1/(M c)) is two orders of magnitude higher than the constant for the known monochloramine derivatives of amino acids. This constant is also several orders of magnitude greater than the rate constant for reaction with methionine. Thus, the created inhibitor of the platelets has the property of highly selectively modifying cysteine residues in protein targets. This selectivity can determine the action of the inhibitor on the purine receptor P2Y12 in platelets, in which there is a sulfhydryl group near the binding site of ADP.