

НАПРЯМ 1. ФАРМАЦЕВТИЧНІ НАУКИ

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RESEARCH OF ANTIOXIDANT PROPERTIES OF XANTHINYL-8-PROPIONIC ACID DERIVATIVES

Reactive oxygen species (ROS) are continuously made in a living cell as products of its normal metabolism [1, p. 216-284]. They also play a role of mediators of important intracellular signaling pathways [2, p. 593-615]. During evolution the cell acquired protective mechanisms to limit hyperproduction of ROS, both via enzymes (superoxide dismutase, catalase, glutathione peroxidase) [3, p. 110-181].

Accumulation of ROS and NO derivatives in the cell exerts damaging effects on its constituents, such as carbohydrates, proteins, lipids, and nucleic acids [4, p. 315-370]. The consequences of interactions of ROS and NO derivatives with their targets manifest in formation of oxidative and nitrosative stress products, undesirable for normal cell metabolism.

The search for antioxidant compounds capable of interrupting the pathological biochemical processes at various steps of oxidative and nitrosative stress development, and thus exerting prophylactic and therapeutic effects, is a priority for medical and pharmaceutical sciences.

In continuation of this research we investigated the effects of newly synthesized derivatives of xanthinyl-8-propionic acids on late markers of oxidative and nitrosative stresses.

For study antioxidant properties we used next methods in vitro:

– inhibition of NO[•]-radical (The method is based on photoinduction of Sodium nitroprusside, which is accompanied by the accumulation of NO[•]-radical)

– inhibition of oxidative modification of protein, that were initiated by Fentone's reactive;

– inhibition of non enzymatic initiation of free radical lipid peroxidation. The statistical data analysis was carried out with the help of the software STATISTICA® for Windows 6.0 [5, p. 216-270]. The data is presented as the sample mean ± the standard error of the mean. The fidelity of differences between experimental groups was estimated with the help of Student's t-test and Fisher's exact test.

In vitro study of derivatives of xanthinyl-7-propionic acids have been shown that almost all compounds exhibit antioxidant properties. Obtained results also help us to establish some patterns of structure-activity relationship.

Thus, we found that insertion of hydrazine group in the structure of xanthinyl-8-propionic acids increased antioxidant properties, especially by NO[•]-radical inhibition. So, we assume that their expressed NO scavenger properties caused by the presence of hydrazide fragment in the structures of the compounds.

Obtained results of the estimation of AOA could be used for further search of NO scavengers among hydrazides of xanthinyl-8-alkanic acids.

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