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IN VITRO ANTIOXIDANT ACTIVITY OF COMPOSITIONS BASED ON BIOSURFACTANTS AND AMINO-CONTAINING HETEROCYCLIC DERIVATIVES OF 1,4-NAPHTOQUINONE

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ABSTRACT

Compositions of rhamnolipids (RL) and trehalose lipids (TL) with amino-containing heterocyclic derivatives of 1,4-naphthoquinone were obtained for the first time. The acute toxicity of amino-containing derivatives of 1,4-naphthoquinone was determined by *in silico* method using the GUSAR program. We have studied influence of selected compounds and their rhamnolipid and trehalose lipids compositions on the processes of lipid peroxidation (LPO) and oxidative modification of proteins (OMP) in rat liver tissues upon initiation of free radical oxidation in vitro. It was determined that 1,4-naphthoquinone derivatives have antioxidant activity. RL and TL have a pro-oxidant effect, increase the content of secondary products of lipoperoxidation compared to the control. They have an antioxidant effect in a composition with 1,4-naphthoquinone derivatives. The lead-compound 2-[(6-(4-fluorophenyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)phenyl)amino]naphthalene-1,4-dione (**1**) and its complex with rhamnolipid show high antioxidant activity (which is confirmed by the decrease in the content of carbonyl groups in the side chains of proteins compared to the control).

Keywords: antioxidant activity, amino-containing heterocyclic 1,4-naphthoquinone derivatives, rhamnolipids, trehalose lipids, *GUSAR*

INTRODUCTION

The increase in the processes of free-radical oxidation in the body is observed in many diseases. Their influence in the pathogenesis of various types of cancer, atherosclerosis, hypertension, Alzheimer's disease, Parkinson's disease (**Cassidy**, *et al*., **2020**; **Jiang**, *et al*., **2016**), arthritis, neurodegenerative disorders, diabetes has been proven (**Li**, *et al*., **2016**; **Liu**, *et al*., **2017**). Antioxidants (AO) are the main group of drugs that can resist oxidative stress. They are able to inhibit the development of free-radical reactions, preventing the formation of peroxides that damage the cellular and subcellular membranes of the body (**Karuppagounder**, *et al*., **2021**). That is why the need to find new AO that would be effective in treatment of number of diseases is an important task of scientists for today.

Heterocyclic amino-containing derivatives of 1,4-naphthoquinone and their complexes with TL and RL biosurfactants were choosen for the study of antioxidant activity. Literary sources suggest that 1,4-naphthoquinone derivatives have redox properties. They affect molecular mechanisms of oxygen exchange in tissues and are able to regulate the flow of electrons in the respiratory chain (**Gulcin**, *et al*., **2020**). This indicates the possibility of their use as AO. 1,4-Naphtoquinones are poorly soluble in water, which makes their use difficult. Interfering with the solubilization properties, as well as the ability to increase the permeability of cell membranes, biosurfactants increase the bioavailability and activity of biologically active substances.

RL and TL belong to low molecular glycolipid biosurfactants (**Jahan**, *et al*, **2020**). Due to the amphiphilic nature of the molecules, biosurfactants contribute to the solubilization of poorly soluble substances, improve the permeability of cell membranes and enhance the effect of biologically active substances when they are used in combination (**Ceresa**, *et al*., **2021**; **Sotirova** *et al*., **2012**) and are low-toxic. RL are products of biosynthesis of *Pseudomonas* bacteria, where rhamnose is attached to the fatty acid tail by a glycosidic bond (**Haba**, *et al*., **2014**). TL are biosynthesis products of actinomycetes bacteria, containing trehalose disaccharide linked to mycolic acids (**Semeniuk**, *et al*., **2022**). The physicochemical properties of biosurfactants contribute to increasing the effectiveness and stabilizing the functional properties of drugs for various purposes (**Shekhar** *et al*., **2015**). Literature sources suggest that biosurfactants can be used in pharmacy (**Naughton**, *et al*., **2019**), in particular, as antimicrobials (**Zhao** *et al*., **2010**; **Abdel-Megeed** *et al*., **2011**; **Sha** *et al*., **2011**) , antiviral (**Singh** *et al*., **2004**; **Akbari** *et al*., **2018**), antitumor (**Pasiar** *et al*., **2016**; **Yuewen** *et al*., **2017**), anti-adhesive drugs (**Rodrigues** *et al*., **2006**; **Bucci** *et al*., **2018**; **Janek** *et al*., **2018**) and as immunological adjuvants (**Al-wazni** *et al*., **2016**). However, most of the compositions are still at the stage of development and research. Thus, it was determined that the bioavailability and biological (antimicrobial) activity of thiosulfonates significantly increased in the composition with RL (**Lubenets** *et al*., **2013**). All this information indicates the feasibility of creating compositions of biologically active compounds with biosurfactants (**Koretska**, *et al*., **2019**). The main goal of creating a composition of synthetic heterocyclic amino derivatives of 1,4-naphthoquinone with biosurfactants is to improve the solubility and reduce the therapeutic dose of the drug. It is known that N-containing heterocyclic derivatives of 1,4-naphthoquinone (**Polish** *et. al*., **2020**) demonstrate high anticonvulsant activity. However, it is known that they are characterized by low solubility in water, which complicates their use. Due to their ability to regulate the permeability of cell membranes, biosurfactants enhance the effect of biologically active substances and increase the bioavailability of sparingly soluble substances (**Banat** *et al*., **2010**; **Salihu**, *et al.*, **2009**). This makes it possible to create new drugs with improved functional properties. We have developed compositions of 1,4-naphthoquinone derivatives with RL, which demonstrate high anticonvulsant activity (**Polish** *et. al*., **2022**). The main goal of the combined use of synthetic naphthoquinone derivatives and biosurfactants is to improve water solubility, bioavailability and reduce the therapeutic dose (inhibitory concentration) of the drug (**Sotirova** *et al*., **2012**; **Koretska** *et al*., **2019**).

MATERIALS AND METHODS

Materials

In this study, we used rhamnolipids, i.e., products of microbial synthesis of *Pseudomonas* sp. PS-17 and TL produced by *Rhodococcus erythropolis* AU-1. Heterocyclic amino-containing derivatives of 1,4-naphthoquinone (**1**, **2**): 2-[(6-(4-fluorophenyl-5-oxo-2,5dihydro-1,2,4-triazin-3-yl)phenyl)amino]naphthalene - 1,4-dione (**1**) was obtained by reacting 1,4-naphthoquinone with a derivative of 1,2,4-triazine by the Michael reaction, ethyl-4-((3-chloro-1,4-dioxo-1,4-dihydronaphthalene-2-yl)amino)-1-phenyl-1H-pyrazole-3-carboxylate (**2**) was

synthesized by nucleophilic substitution of the chlorine atom of 2,3-dichloro-1,4-naphthoquinone with the corresponding amine.
Methods for obtaining heterocyclic amino derivatives of naphthoquinone are described in our previous works (**Polish**, *et al*., **2020**, **Polish**, *et al*., **2021**).

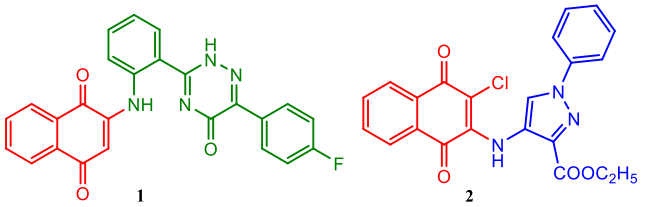

Figure 1 2-[(6-(4-fluorophenyl-5-oxo-2,5dihydro-1,2, 4-triazin-3-yl)phenyl)amino]naphthalene-1,4-dione (**1**), ethyl-4-((3-chloro-1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-1-phenyl-1H-pyrazole-3-carboxylate (**2**)

To prepare compositions of RL with the corresponding heterocyclic amine-containing derivative of 1,4-naphthoquinone, 0.01 g of compound **1** or **2** was taken and dissolved in 1 ml of dimethyl sulfoxide. A solution of RL was prepared separately: 0.01 g of RL was dissolved in 49.99 ml of distilled water at pH 7, temperature 20°-25°C with constant stirring and pH control, a solution of the corresponding heterocyclic amine-containing naphthoquinone derivative was added in small portions. Complexes stable at room temperature were obtained (**Polish**, *et al*., **2021**).
To prepare compositions of TL with the corresponding heterocyclic amino-containing derivative of 1,4-naphthoquinone (**Polish**, *et al*., **2021**), equimolar amounts of 2-[(6-(4-fluorophenyl-5-oxo-2,5dihydro-1,2, 4-triazin-3-yl)phenyl)amino]naphthalene-1,4-dione (**1**) or ethyl-4-((3-chloro-1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-1-phenyl-1H-pyrazole-3-carboxylate (**2**), and TL, were ground in a mortar to a homogeneous mass, 1 ml of ethanol was added under constant stirring. The volume was brought up to 50 ml with distilled water. The resulting mixture was placed in an ultrasonic bath for 15-20 minutes. We obtained complexes that are stable at room temperature.

Antioxidant activity

Methods research markers of non-enzymatic link oxidative stress in rat liver homogenate: lipid peroxidation (LPO) and oxidative modification of proteins (OMP)

The antioxidant activity of heterocyclic amino-containing derivatives of 1,4-naphthoquinone and their compositions with RL and TL was determined by their influence on the processes of LPO and OMP. Their alcoholic solutions (ethanol : water, 1 : 3) were used at a concentration of 10^{-6} M. The study was carried out on rat liver tissues.
5 ml of potassium phosphate buffer was added to 0.5 g of crushed rat liver tissue. 0.3 ml of the studied heterocyclic derivatives of 1,4-naphthoquinone was added to 0.3 ml of the obtained homogenate, and the corresponding solvents were added as a control. To induce LPO, 0.3 ml of 2.8% $FeSO_4$ solution was added and after 10 minutes. 0.3 ml of 4% H_2O_2 solution and incubated for 2 hours. The reaction was stopped with 1.2 ml of 40% trichloroacetic acid, which simultaneously precipitated proteins, followed by centrifugation for 10 minutes at 5000g. Determination of both indicators of oxidative stress was carried out in one sample - the content of TBA-active products was determined in the supernatant, and CG - in the sediment according to the method of Lushchak (**Lushchak**, *et al*., **2006**).

Determining methods TBA-active products

The content of TBA-active LPO products was determined in the selected samples by the reaction of MDA with thiobarbituric acid (TBA). At high temperatures in an acidic environment, MDA reacts with TBA, forming a colored trimethine complex with an absorption maximum λ= 532 nm. To 2 ml of the supernatant was added 1.5 ml of a 0.8% solution of TBA in 0.1 M HCl (pH=2.5) and incubated in a water bath at a temperature of 95–100 °C for 60 min. After cooling, 3 ml of butanol was added and centrifuged for 10 minutes at 5000g. Extinction measurements were performed in the upper butanol layer at a wavelength of λ=532 nm (**Molyneux**, *et al*., **2004**). The amount of protein in the samples was determined by the Lowry method (**Michiels**, *et al*., **1991**).

Methods for determining the content of CG proteins

The degree of OMB was determined by the number of formed additional carbonyl groups (CG) in the side chains of amino acids, the content of which was determined by reaction with 2,4-dinitrophenylhydrazine (DNFH) (**Blois**, *et al*., **1958**). For determination the CG of protein, 1 ml of a 1% solution of DNFH in 2M HCl was added to the precipitates after centrifugation of the homogenates. Mixture was triturated and incubated for 1 hour. at room temperature, then centrifuged for 10 min. at 5000 g. The precipitate was washed three times with 1 ml of a mixture of ethanol and ethyl acetate (1:1) and centrifuged in the previous mode. Washed precipitate was dissolved within 45 minutes in 3 ml of 50% urea solution. Undissolved material was separated by centrifugation in the previous mode. In the supernatants, the content of CG proteins was determined on a ULAB 108UV spectrophotometer at a wavelength λ=370 nm (light absorption by 2,4-diphenylhydrazones).

Statistical analysis

All experiments were repeated three times with three parallels in each variant. All data were expressed as mean ± SD. Differences between experimental data were determined using Tukey's one-way analysis of variance (ANOVA), where differences were considered significant at $P<0.05$ (**Morgan** *et. al*, **2012**, **Leech**, *et. al*., **2014**). Biometric processing of all research results data was carried out using the program "Excel-2010" for Windows. Control and experimental groups were compared.

RESULTS AND DISCUSSION

It is known that reactive oxygen species (ROS) and free radical processes initiated by them can lead to various pathological conditions. Under normal physiological conditions, LPO is a vital chain in the regulation of many membrane-dependent processes, and its level in the body is low and maintained by the balance of pro- and antioxidants (**Catalá**, *et. al*, **2016**). However, oxidative stress increases during many diseases (**Honcharuk** *et al*., **2004**; **Polyanska** *et al*., **2002**; **Davis** *et al*., **2014**). As a result, LPO processes are activated, which cause significant changes in the metabolic processes of the cell and the structural and functional integrity of cell membranes, which leads to pathological (inflammatory, neurodegenerative, malignant) tissue changes and, as a result, to their death. It is possible to avoid various complications during the diseases by timely blocking the trigger mechanism of the pathology, that is, by reducing the intensity of POL and OMB in the body with the help of antioxidants. That is why interest in both natural and synthetic antioxidants has recently increased significantly, thanks to their proven positive effect on the course of many diseases. Among natural antioxidants, ginseng and eleutherococcus preparations occupy a prominent place, the active components of which increase the body's resistance to cooling, overheating, various injuries, intoxications, etc. Ascorbic acid as an antioxidant is widely used in the treatment of a number of dental pathologies (periodontitis, gingivitis, stomatitis, caries) (**Steenvoorden** *et al*., **1997**). Rutin and quercetin, as antioxidants of direct action, are used in various heart diseases. Flavonoids are an antioxidant group of compounds consisting of flavonols, anthocyanins, isoflavonoids, flavanones, and flavones. Antioxidant properties of flavonoids are given by phenolic hydroxyl groups attached to ring structures, which can act as reducing agents, hydrogen donors, singlet oxygen absorbers, superoxide radical absorbers, and even as metal chelators. They also activate antioxidant enzymes, reduce a-tocopherol radicals (tocopheroxyls), inhibit oxidases, reduce nitrosative stress, and increase the level of uric acid and low molecular weight molecules. Some of the most important flavonoids are catechin, catechingalate, quercetin and kaempferol (**Dumanović** *et al*., **2021**; **Procházková** *et al*., **2011**).
Phenolic acids have an antioxidant effect and consist of hydroxycinnamic and hydroxybenzoic acids, which act as chelators and absorbers of free radicals with a special effect on hydroxyl and peroxyl radicals, superoxide anions and peroxynitrites. One of the most studied and promising compounds in the hydroxybenzoic group is gallic acid, which is also the precursor of many tannins, while cinnamic acid is the precursor of all hydroxycinnamic acids (**Syahariza** *et al*., **2022**). Synthetic phenolic antioxidants (SPAs), such as 2,6-di-tert-butyl-4-hydroxytoluene (butylhydroxytoluene, BHT) and butylated hydroxyanisole (BHA), have been widely used as antioxidants in some foods, cosmetics, and plastics since the late 1940s. x years (**Wang** *et al*., **2016**). As antioxidants BHT and BHA preserve freshness or prevent spoilage of food and other products are safe at a total content of up to 0.02% wet weight (w/w) of the total fat or oil content of the food (**Joung** *et al*, **2019**). Some synthetic compounds with antioxidant activity are known from literature sources, including phenylcarbamoylbenzoic acid derivatives (**Irfan** *et al*., **2021**), 4-phenyl hydroxycoumarin (**Veselinovic** *et al*., **2014**), Schiff bases (**Xing** *et al*., **2022**), phthalimide derivatives (**Shankar** *et al*., **2000**), hydrazides (**Tchekalarova** *et al*., **2020**) and pyridoxal isonicotinoyl hydrazone (**Sarkar** *et al*., **2022**), as well as natural phenolic compounds isolated from *Acacia confusa* (**Tung** *et al*., **2007**), isoeugenol derivatives (**Findik** *et al*., **2011**) and resveratrol, which are beneficial for human health (**Gulcin** *et al*., **2010**). The antioxidant activity of new phenolic compounds derived from resorcinol (1,3-dihydroxybenzene) was studied through the design, synthesis and *in vitro* antioxidant evaluation of selected compounds for the formation of amides from 2-acetyl-4-aminoresorcinol and anhydrides (**Guerra-Vargas** *et al*., **2018**).
Considering the fact that 1,4-naphthoquinone derivatives can have antioxidant properties, the study of their effect on the processes of POL and OMB and the effect of their compositions with biosurfactants is an important task. The method of obtaining the composition of heterocyclic amino-containing derivatives of 1,4-naphthoquinone with RL (**Polish**, *et al*., **2021**) and TL (**Polish**, *et al*., **2022**) is described above. The compounds have high biological activity.

To create compositions with biosurfactants, new biologically active compounds were selected, for which predictions of acute toxicity for rats by different routes of administration of substances (intra-abdominal, intravenous, oral and subcutaneous) were made in the GUSAR program using QSAR models (**Lagunin**, *et al*., **2011**, **Krishna**, *et al*., **2014**). This parameter is one of the most important in the development of medicines. Acute toxicity is an adverse effect (or death) that occurs shortly after the onset of action of a substance after a single dose. The LD_{50} value is an important characteristic of acute toxicity, the dose of which causes 50% mortality 24 hours after the introduction of the compound. The results of the study are given in **table 1**.

Table 1 Predicted acute toxicity of new heterocyclic amino-containing derivatives of 1,4-naphthoquinone to rats

Substance	Intraperitoneal route of administration		Intravenous route of administration		Oral route of administration		Subcutaneous route of administration	
	LD_{50} (mg/kg)	Classification of toxicity of substances*	LD_{50} (mg/kg)	Classification of toxicity of substances*	LD_{50} (mg/kg)	Classification of toxicity of substances*	LD_{50} (mg/kg)	Classification of toxicity of substances*
1	760.600	Class 5	113.600	Class 4	672.200	Class 4	753.600	Class 4
2	727.200	Class 5	215.600	Class 4	1879.000	Class 4	1024.000	Class 5

Note: * Classification of acute toxicity to rodents according to the OECD project (Organization for Economic Cooperation and Development).

The obtained results of the forecast of acute toxicity give grounds for asserting that 2-[(6-(4-fluorophenyl-5-oxo-2,5dihydro-1,2,4-triazin-3-yl)phenyl)amino]naphthalen-1,4 -dione (**1**) and ethyl 4-((3-chloro-1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-1-phenyl-1H-pyrazole-3-carboxylate (**2**), probably, it can be classified as low-toxic drugs (toxicity class 4, 5). Therefore, they can be used for obtaining compositions with biosurfactants and for further studies of their biological activity.

Antioxidant activity

The antioxidant activity of 2-[(6-(4-fluorophenyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)phenyl)amino]naphthalene-1,4-dione (**1**), ethyl- 4-((3-chloro-1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-1-phenyl-1H-pyrazole-3-carboxylate (**2**) and their compositions with RL and TL were determined by their influence on the processes of lipid peroxidation and oxidative modification of proteins in rat liver tissues under initiation of free-radical oxidation *in vitro*.

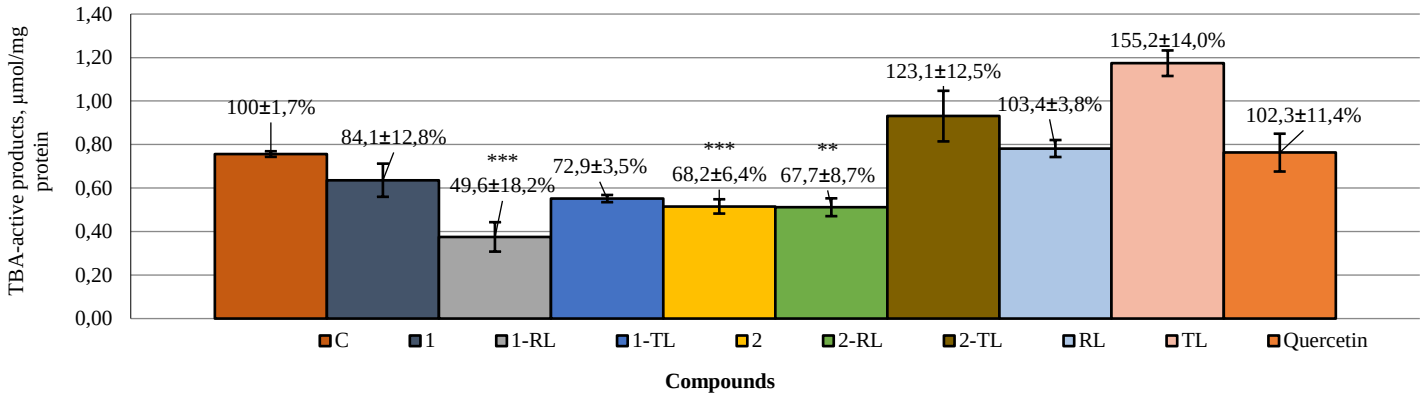

Figure 2 The content of TBA-active products in the rat liver tissues under effect of 2-[(6-(4-fluorophenyl-5-oxo-2,5dihydro-1,2,4-triazin-3-yl)phenyl)amino]naphthalene-1,4-dione (**1**), ethyl 4-((3-chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)amino)-1-phenyl-1H-pyrazole-3-carboxylate (**2**), RL, **TL** and composite preparations based on them **1-RL**, **1-TL** та **2-RL**, **2-TL** ($p \leq 0.001$ - ***; $p \leq 0.01$ - **; $p \leq 0.05$ - *).

It was established that amino-containing derivatives of 1,4-naphthoquinone exhibit antioxidant activity in LPO processes due to a decrease in the content of TBA-active products compared to the control (**Fig. 2**): by 30-35% for compound **2** and its composition with RL. It should be noted that compound **2** (**Fig. 2**) reduces the content of secondary LPO (TBA-active products) by 16%, and in the complex with rhamnolipids (**1-RL**) by approximately 50% compared to control.

Thus, the complex of RL with **1** actively prevents the occurrence of free radical processes also in proteins, where we can see a decrease in the content of CG of proteins by 40.4%. Composition **1-TL** (**Fig. 3**) also shows significant antioxidant activity in the processes of OMP, where the content of CG proteins show decrease by 36.6% relative to the control.

Under the influence of **RL, TL**, and **2-TL** (**Fig. 2**), the content of secondary products of lipoperoxidation increased by 3.4%, 55.2%, and 23.1%, respectively, relative to the control, i.e., they have a pro-oxidant effect. Therefore, TL and the 2-TL composition showed significant pro-oxidant activity in the processes of lipid peroxygenation.

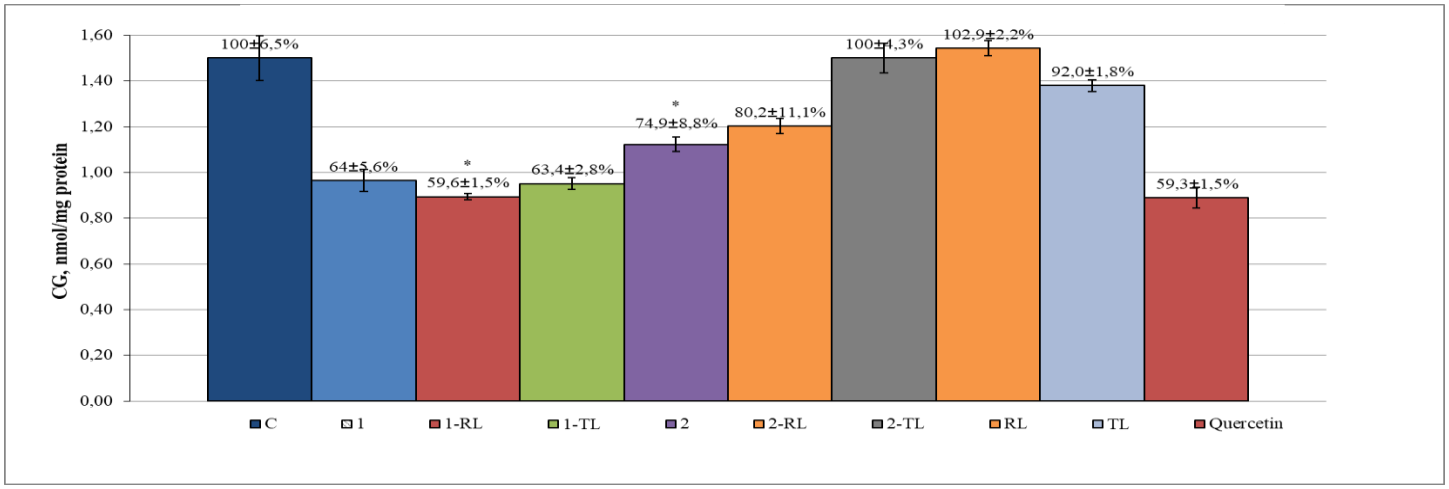

Figure 3 The content of additional CG in the rat liver tissues under effect of 2-[(6-(4-fluorophenyl-5-oxo-2,5dihydro-1,2,4-triazin-3-yl)phenyl)amino]naphthalene-1, 4-dione (**1**), ethyl 4-((3-chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)amino)-1-phenyl-1H-pyrazole-3-carboxylate (**2**), **RL**, **TL** and composite preparations based on them **1-RL**, **1-TL**, **2-RL** та **2-TL** ($p \leq 0.001$ - ***; $p \leq 0.01$ - **; $p \leq 0.05$ - *).

Heterocyclic amino-containing derivatives of 1,4-naphthoquinone showed an effect on the processes of OMP (**Figures 2, 3**). Thus, high antioxidant activity was shown by substance 1 and its complex with RL due to the fact that the content of CG decreases by 36% and 40%, respectively, compared to the control. Compound 2 and its complex with RL show less antioxidant activity in OMP processes due to a decrease in CG content compared to the control by 25% and 20%, respectively.

To compare the studied compounds and their compositions with RL, studies were conducted with the well-known AO. i.e. quercetin (**Figures 2, 3)**. Thus, under the influence of quercetin, the content of TBA-active products show increase by 2.3%, that is, its effect was within the control limits, and in the OMP processes, the content of CG proteins decreased by 40.7% compared to the control, which proves the antioxidant properties of quercetin. Composite preparation of 2-[(6-(4-fluorophenyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)phenyl)amino]naphthalene-1,4-dione (**1**) with **RL** (**Fig. 3**) shows the same antioxidant activity in OMP processes as quercetin. This confirms antioxidant properties.

The main goal of the simultaneous use of synthetic naphthoquinone derivatives and biosurfactants, which have antioxidant activity important for pharmacy, is to reduce the therapeutic dose of the drug. It was determined that under the influence of the studied heterocyclic derivatives of 1,4-naphthoquinone results in increase of content of products of free radical oxidation of lipids and proteins, intensification of processes of LPO and OMP, which, most likely, can lead to a significant disruption of cellular metabolism. Under the action of the above-mentioned complexes, there is a certain decrease in the level of TBA-active products and the formation of additional carbonyl groups in comparison with the control, which shows a decrease in the intensity of the processes of LPO and OMP, which confirms their antioxidant activity. This is explained by the solubilization ability of poorly water-soluble compounds and the effect of biosurfactants on the permeability of cell membranes of rat liver hepatocytes.

As a result of experimental biological studies, it was found that biosurfactants exhibit pro-oxidant activity, especially TL in OMP processes. However, in a complex with heterocyclic amine-containing derivatives of 1,4-naphthoquinone, biosurfactants show antioxidant activity. The antioxidant activity of four composite preparations based on heterocyclic amino-containing derivatives of 1,4-naphthoquinone and biosurfactants was determined in comparison with the original compounds. It was determined that the composition of 2-[(6-(4-fluorophenyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl) phenyl) amino]naphthalene-1,4-dione with RL **1-RL** showed the highest antioxidant activity in the processes of **LPO** and **OMP.**

CONCLUSIONS

Compositions of biosurfactants - trehalose lipids and rhamnolipids with new heterocyclic amino-containing derivatives of 1,4-naphthoquinone were obtained. The antioxidant effect of the obtained biologically active compounds and their composite preparations with rhamnolipids and trehalose lipids under initiation of free radical oxidation in vitro in rat liver tissues was established.

Biosurfactants showed a pro-oxidant effect in the processes of lipid peroxidation, however, in their compositions with heterocyclic amine-containing derivatives of 1,4-naphthoquinone, an increase in antioxidant activity was found.

It was determined that the composition of 2-[(6-(4-fluorophenyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)phenyl)amino]naphthalene-1,4-dione with rhamnolipids exhibits high antioxidant activity. The presence of antioxidant properties of the developed compositions allows them to be considered as potential objects for further in vivo studies of their biological activity, as well as prospects for their use.

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