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PRO/ANTIOXIDANT STATUS OF ISOLATED HUMAN BLOOD LYMPHOCYTES TREATED WITH A NEWLY SYNTHESIZED COMPOUND D11-(FURAN-2-YL)-9-HYDROXY-3,11-DIHYDRO-2H-BENZO[6,7]THIOCHROMENO[2,3-D]THIAZOLE-2,5,10-TRIONE

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It is known that 1,4-naphthoquinone derivatives form the basis of a wide range of pharmaceuticals with diverse biological activities. A newly synthesized compound of this group – 11-(furan-2-yl)-9-hydroxy-3,11-dihydro-2H-benzo[6,7]thiochromeno[2,3-d]thiazole-2,5,10-trione, designated by Les-6400 laboratory code, is noteworthy for its drug-like properties. The aim of the study was to determine the parameters of glutathione antioxidant system in isolated human peripheral blood lymphocytes treated with Les-6400. Saponin-permeabilized lymphocytes from the blood samples of healthy male volunteers aged 20–44 years were used in the study. A significant dose-dependent increase in the lipid peroxidation process was observed upon lymphocytes exposure to Les-6400 at concentrations of 10^{-5}–10^{-3} M. At the concentrations studied no effect of Les-6400 on GSH level was observed, while in the 10^{-4}–10^{-3} M concentration range the activity of glutathione antioxidant enzymes was markedly affected: the activity of both glutathione peroxidase and glutathione reductase was increased, while that of glutathione-S-transferase was reduced. Thus, Les-6400 had a pronounced effect on the pro/antioxidant status of blood lymphocytes.

K e y w o r d s: 1,4-naphthoquinone derivative, lymphocytes, lipid peroxidation, glutathione peroxidase, glutathione reductase, glutathione-S-transferase.

Derivatives of 1,4-naphthoquinone represent an important class of biologically active compounds that have attracted considerable attention due to their wide range of applications in medicine and pharmacy. It is well established that derivatives based on 1,4-naphthoquinone form the structural basis of numerous pharmaceuticals and biologically active compounds with diverse biological activities [1]. In this regard, particular interest has been directed toward a newly synthesized compound of this group – 11-(furan-2-yl)-9-hydroxy-3,11-dihydro-2H-benzo[6,7]thiochromeno[2,3-d] thiazole-2,5,10-trione, referred to by the laboratory code Les-6400, due to its drug-like characteristics, especially its impact on the cellular pro-/antioxidant system. Comprehensive studies of its physicochemical properties, pharmacokinetic profile, drug-likeness parameters, and in silico modeling of antitumor activity mechanisms have revealed significant therapeutic potential of Les-6400 [2].

However, there is a lack of studies focused on elucidating the detailed mechanisms underlying the biological activity of this class of compounds. One of the primary mechanisms of cell damage and death caused by reactive oxygen species is currently believed to be lipid peroxidation [3-5]. It is known that lipid peroxidation represents a universal mechanism of cellular membrane damage associated with various pathological conditions [6-9]. The glutathione-dependent antioxidative system plays a central role in neutralizing lipid peroxidation products and other oxidized molecules [10-13]. Through the catalytic activity of glutathione peroxidase (GPx), cells are able to reduce hydrogen peroxide (H_2O_2) and organic hydroperoxides to their corresponding alcohols [14]. This reaction requires reduced glutathione (GSH) as a substrate. The system also includes glutathione reductase (GR), an NADPH-dependent enzyme responsible for reducing oxidized glutathione (GSSG) back to GSH, thereby

maintaining glutathione recycling. Another key enzyme, glutathione-S-transferase (GST), catalyzes the conjugation of GSH with electrophilic compounds (such as lipid peroxides and their reactive aldehydes, some medicines and xenobiotics etc.), serving both a detoxifying and protective function. The pro-/antioxidant system is highly sensitive to oxidative stress, which may be triggered by medications, harmful habits, infectious agents, psychological stress, or various diseases [15, 16].

The immune system, with lymphocytes as its key components, is one of the body's integral systems that responds rapidly to external and internal stimuli. The current understanding considers immune reactivity to be one of the earliest and most sensitive indicators of the negative impact of exogenous and endogenous stressors [17, 18]. Lymphocytes represent a heterogeneous population of cells and play a central role in specific immune responses. They are particularly responsive to oxidative stress, and changes in the activity of their antioxidant defense enzymes can serve as biomarkers of both pathological conditions and the body's adaptive mechanisms [19].

Given that the primary objective of modern medicinal chemistry is the synthesis or identification of compounds as a foundation for the development of new therapeutic agents. However, the identification of compounds with a specific type of activity even if highly potent – is not sufficient on its own. This is due to the fact that highly active compounds must undergo comprehensive investigation, including preclinical and clinical trials, toxicological assessment, and other studies that ultimately determine their potential for implementation in clinical practice.

The aim of the present study was to investigate the effect of Les-6400 on the activity of both enzymatic and non-enzymatic components of the glutathione antioxidant system, as well as on lipid peroxidation processes in human blood lymphocytes.

Materials and Methods

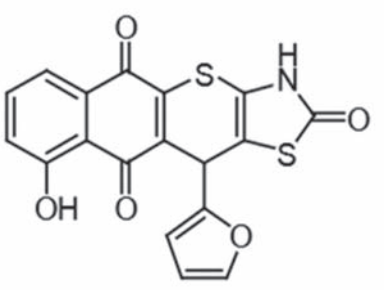
The material for the study consisted of blood samples of apparently healthy male volunteers aged 20–44 years. The samples were collected at the Lviv Regional Clinical Hospital in accordance with a cooperation agreement between Danylo Halytsky Lviv National Medical University and the Lviv Regional Clinical Hospital.

The members of the Ethics Committee for Scientific Research, Experimental Developments, and Scientific Works of Danylo Halytsky Lviv National Medical University did not identify any violations of moral or ethical standards during research (protocol No 11 from 19.12.2022). The submitted materials were deemed scientifically substantiated, and the patient information sheet was found to clearly state all necessary provisions, with which all patients were duly acquainted. Measures were taken to ensure patient health safety, protection of rights, human dignity, and compliance with moral and ethical norms in accordance with the principles of the Declaration of Helsinki on human rights, the Council of Europe Convention on Human Rights and Biomedicine, and relevant legislation of Ukraine.

The compound Les-6400 was synthesized at the Department of Pharmaceutical and Bioorganic Chemistry of Danylo Halytsky Lviv National Medical University.

Peripheral blood lymphocytes were isolated using a modified method by Boyum A. [20]. The content of malondialdehyde (MDA), GSH, GSSG and the activity of glutathione-dependent enzymes was determined in saponin-permeabilized peripheral blood lymphocytes.

The MDA content was determined using the reaction with 2-thiobarbituric acid. 10 mM K, Na-phosphate buffer containing 125 mM KCl (pH 7.4) and 1 mM $KMnO_4$ were added to the experimental sample containing 50 µg of protein. Lipid peroxidation was induced in this sample by adding 500 µl of 10 mM $FeSO_4$ twice at 10-min intervals. After 5 min, the reaction was stopped by the addition of 1 ml of 20% trichloroacetic acid, followed by centrifugation. 250 µl of 1 N HCl and 500 µl of 0.7 mM thiobarbituric acid were added to 1 ml of the supernatant, and the mixture was incubated in a boiling water bath (100°C) for 20 min. After cooling, 3 ml of butanol were added, the mixture was thoroughly shaken, and centrifuged for 10 min at 1500 rpm.



Structural formula of the compound Les-6400

The optical density of the sample was measured at λ = 532 nm against a control (sample without cells), using the molar extinction coefficient of the pink-colored complex ε = $1.56 \cdot 10^5$ $M^{-1} \cdot cm^{-1}$. The results were expressed as μmol/mg protein. Protein concentration was determined by Lowry method.

The total GSH content was determined in a cell suspension after complete reduction of GSH by GR using Ellman's reagent [21]. The reaction mixture contained potassium phosphate buffer (100 mM, pH 7.5), EDTA (1 mM), NADPH (0.2 mM), 5,5′-dithio-bis-2-nitrobenzoic acid (DTNB, 0.6 mM), and the cell suspension in a final volume of 1.0 ml. The enzymatic reaction was initiated by the addition of glutathione reductase (1.9 U; 0.037 ml of a 50 U/ml solution). The formation of 5,5′-dithio-bis-2-nitrobenzoic acid was monitored spectrophotometrically λ = 412 nm. To determine the content of oxidized glutathione (GSSG), 2-vinylpyridine was added to the incubation mixture to a final concentration of 2% 60 min prior to the assay. The GSH content was calculated as the difference between total and oxidized glutathione concentrations.

GPx activity was determined by the rate of GSH oxidation in the presence of tert-butyl hydroperoxide. Samples containing 50 μg of protein were incubated at 37°C for 10 min with 830 μl of 0.1 M Tris–HCl buffer (pH 8.5) containing 6 mM EDTA, 12 mM sodium azide (NaN_3), and 4.8 mM GSH. Subsequently, 70 μl of 20 mM tert-butyl hydroperoxide were added, and the samples were incubated for an additional 5 min. The reaction was stopped by the addition of a 200 μl 20% trichloroacetic acid solution, followed by centrifugation at 10000 rpm for 10 min. Control samples were prepared by adding trichloroacetic acid prior to the addition of tert-butyl hydroperoxide. For the determination of residual GSH, 20 μl of Ellman's reagent (0.01 M solution of 5,5′-dithiobis-2-nitrobenzoic acid in methanol) and 2 ml of 0.1 M Tris–HCl buffer (pH 8.5) were added to 20 μl of the supernatant and incubated for 5 min. The absorbance was measured at λ = 412 nm. The GPx activity was expressed as μmol GSH per minute per 1 mg of protein.

GR activity was determined spectrophotometrically by the decrease in optical density as a result of NADPH oxidation. The reaction was initiated by adding 50 μL of the corresponding sample suspension (protein content did not exceed 50 μg/ml) to 2 ml of the incubation medium consisting of 0.01 M K,Na-phosphate buffer (pH 7.4), 0.008 M oxidized glutathione prepared in 0.01 N NaOH, and 0.002 M NADPH prepared in 1% $NaHCO_3$. Enzyme activity was calculated based on the decrease in NADPH content, which was monitored spectrophotometrically at λ = 340 nm for 10 min. GR activity was expressed as nmol NADPH per minute per 1 mg of protein.

GST activity was assessed by the rate of formation of the conjugate with 1-chloro-2,4 dinitrobenzene [22]. The incubation medium containing 2.5 ml of 0.1 M potassium phosphate buffer (pH 6.5), 0.03 ml of a 300 mM reduced glutathione solution and 0.1 ml. 0.1 ml of sample suspension (protein content did not exceed 50 μg/ml) was added to the incubation medium. The 0.1 ml of 0.1 M potassium phosphate buffer (pH 6.5) was added to the control sample instead of the protein fraction. The reaction was initiated by adding 0.2 ml of 0.015 M 1-chloro-2,4-dinitrobenzene to both cuvettes, and after 3 min the optical density was measured against the control at a λ = 340 nm. GST enzyme activity was calculated using the extinction coefficient of the complex (9.6 $mM^{-1} \cdot cm^{-1}$) and expressed as μmol of GSH per minute per 1 mg of protein.

Experimental data were processed by methods of variation statistics using MS Excel. Results are presented as mean ± standard error of the mean (SEM). The statistical significance of differences between groups was assessed using Student's *t*-test. Differences were considered statistically significant at $P < 0.05$.

Results and Discussion

Glutathione-dependent intracellular detoxification pathways of lipid peroxidation products play a key role in modulating the effects of antibiotics, cytostatics, and other drugs on cell viability [12-14, 19]. We conducted a comparative study of lipid peroxidation processes and the glutathione system in peripheral blood lymphocytes under the action of the compound Les-6400. Analyzing the functional state of the glutathione system and lipid peroxidation allows for a more detailed understanding of the mechanism of action of this compound.

Oxidative stress, which was presumably induced by Les-6400, was triggered by adding the compound to the incubation medium at concentrations ranging from 10^{-6} to 10^{-3} M. The intensity of oxidative stress was assessed by measuring the content of MDA, a final product of lipid peroxidation. An increase in lipid peroxidation was observed at

different concentrations of Les-6400 (Fig. 1). In the control group, the concentration of MDA in blood lymphocytes was (61.2 ± 5.3) μmol/mg protein. Upon exposure to different concentrations of Les-6400 in the incubation medium (10^{-6}–10^{-3} M), this value increased. Specifically, MDA level was twice higher ($P < 0.001$) at Les-6400 concentration compared to control. Thus, a statistically significant increase in lipid peroxidation processes was observed in blood lymphocytes under the influence of Les-6400 at concentrations above 10^{-5} M.

Another indicator of oxidative processes is the content of oxidized glutathione (GSSG). It was found that the GSSG level in blood lymphocytes of male donors tended to increase; however, these changes were not statistically significant compared to the control group (Fig. 2).

Along with the increase in lipid peroxidation, changes in the activity of enzymes in the glutathione system were detected. It was shown that in the control group glutathione peroxidase activity in blood lymphocytes was 156.3 ± 14.5 nmol GSH/min·mg protein. Under the influence of compound Les-6400, enzyme activity tended to increase in an almost dose-dependent manner at all studied concentrations, reaching its maximum value at 10^{-3} M – 196.0 ± 18.6 nmol GSH/min·mg protein (Fig. 3).

However, the concentration of reduced glutathione under the influence of Les-6400 at concentrations ranging from 10^{-6} to 10^{-3} M remained virtually unchanged compared to the control values and ranged between 19.3 and 23.7 nmol GSH/mg protein (Fig. 4).

The activity of glutathione peroxidase (GPx) in the cell depends on the function of glutathione reductase (GR), which catalyzes the reduction of oxidized glutathione (GSSG) back to its reduced form (GSH). Therefore, alongside GPx activity determination, the activity of glutathione reductase was also examined. In the control group GR activity was 51.9 ± 5.1 nmol NADPH/min·mg protein. Under the influence of compound Les-6400 enzyme activity significantly increased, reaching its highest value 81.3 ± 8.4 nmol NADPH/min·mg protein at a concentration of 10^{-4} M which is 1.48-fold higher compared to values (Fig. 5).

Glutathione reductase prevents the accumulation of secondary lipid peroxidation products; however, it cannot neutralize them, unlike glutathione-S-transferase (GST). In the control group GST activity was 96.9 ± 9.2 nmol GSH/min·mg protein. Adding compound Les-6400 to the incubation medium at concentrations of 10^{-6} to 10^{-3} M dose-dependently reduced the activity of this enzyme to 70.1 ± 8.2 nmol GSH/min·mg protein, with a 1.4-fold decrease observed at a concentration of 10^{-3} M (Fig. 6).

Permeabilized human peripheral blood lymphocytes were chosen as an experimental model since the use of primary human cells increases the physiological relevance of the obtained data compared to animal cell lines. In addition, permeabilization of the plasma membrane allows to control the

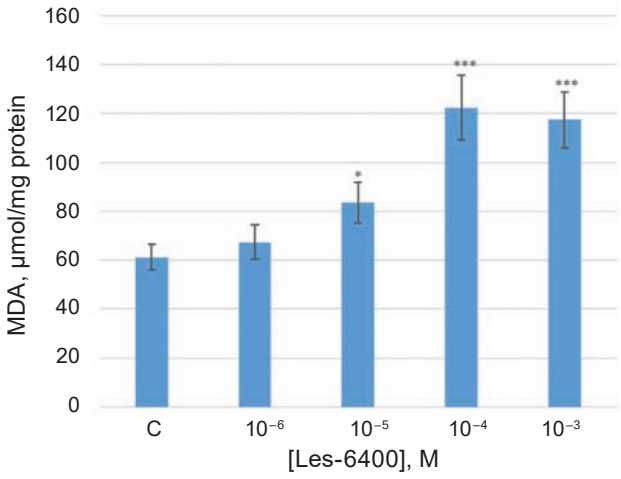


*Fig. 1. Effect of compound Les-6400 on lipid peroxidation in peripheral blood lymphocytes (M ± m, n = 8), *P < 0.05, ***P < 0.001*

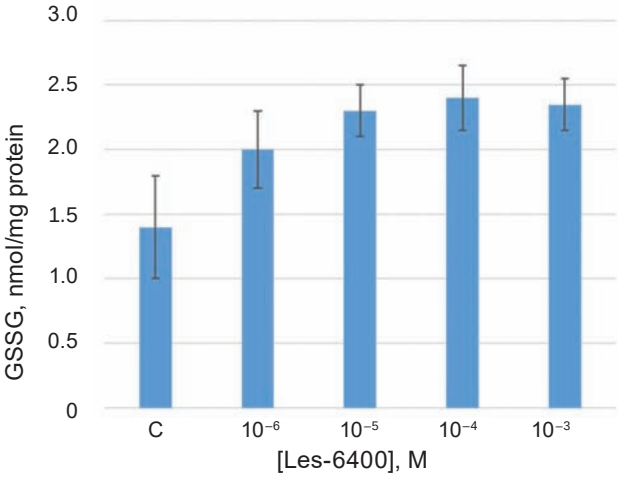


Fig. 2. Effect of compound Les-6400 on the concentration of oxidized glutathione in peripheral blood lymphocytes (M ± m, n = 8)

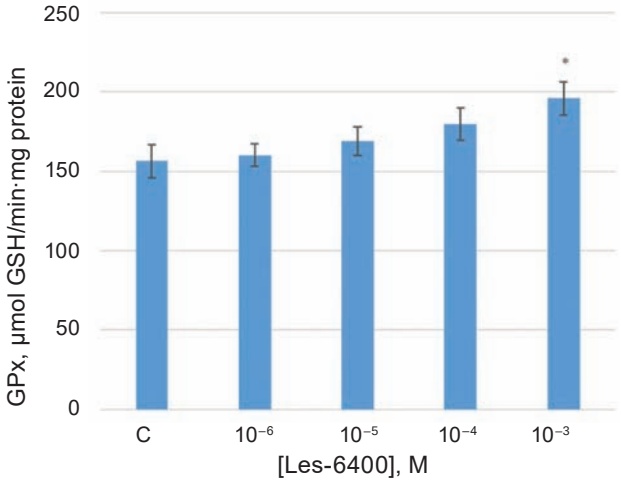


*Fig. 3. Effect of compound Les-6400 on glutathione peroxidase activity in peripheral blood lymphocytes (M ± m, n = 8), *P < 0.05*

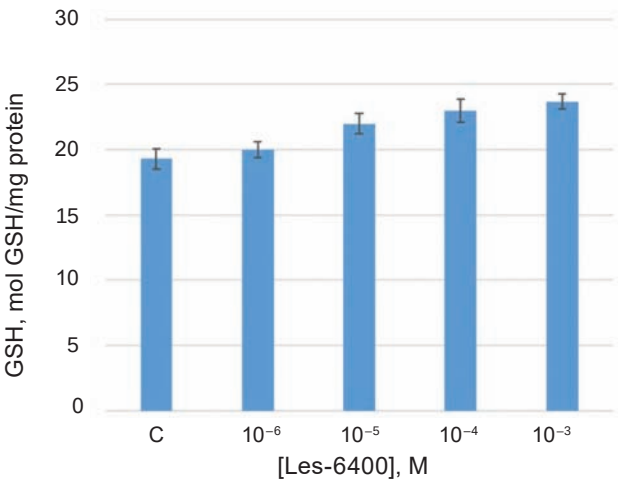


Fig. 4. Effect of compound Les-6400 on the concentration of reduced glutathione in peripheral blood lymphocytes (M ± m, n = 8)

intracellular environment and directly assess the effect of Les-6400 on enzyme activity, minimizing the impact of membrane transport.

Researchers at the Department of Pharmaceutical, Organic, and Bioorganic Chemistry of Danylo Halytsky Lviv National Medical University have tested the use of 1,4-naphthoquinone derivatives as dienophiles in the synthesis of biologically active polycyclic thiopyrano-thiazoles. During the study of the newly synthesized compound Les-6400, potential molecular-biological mechanisms of its antitumor action were outlined, including the inhibition of tumor growth factor β (TGF-β). High apoptotic ability of compounds synthesized from 1,4-naphthoquinone derivatives was established, which occurs through the activation of caspases 3/7, 8, and 9, and changes in mitochondrial potential in MDA-MB-231 breast cancer cells. A strong interaction with DNA was found for the 1,4-naphthoquinone derivatives, as confirmed by a high level of competitive displacement of methyl green from its complex with DNA (42.5-66.4%) and the ability to alter the net absorption (NetAbs) in the oxidation reaction of $KMnO_4$ with pyrimidine bases in DNA damage regions. Two compounds from this class were shown to reduce the level of reduced glutathione by forming

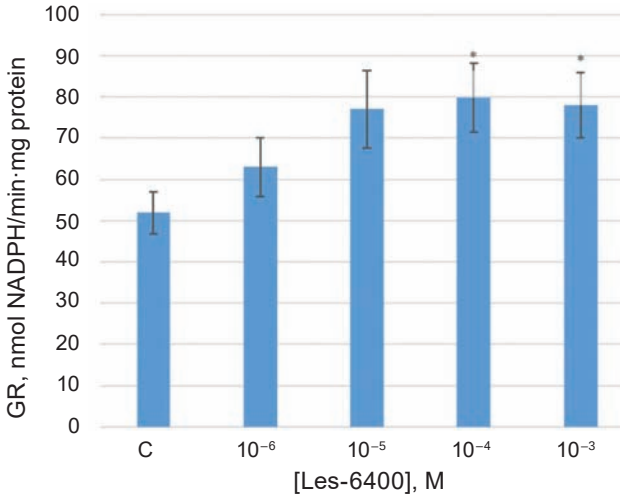


*Fig. 5. Effect of compound Les-6400 on glutathione reductase activity in peripheral blood lymphocytes (M ± m, n = 8), *P < 0.05*

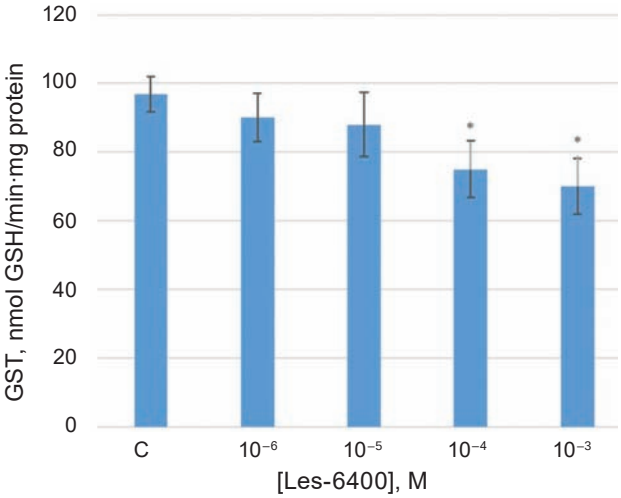


*Fig. 6. Effect of compound Les-6400 on glutathione-S-transferase activity in peripheral blood lymphocytes (M ± m, n = 8), *P < 0.05*

covalent GS-6 adducts, confirming their antioxidant properties. *In vivo* studies of acute toxicity Les-6400 demonstrated significantly lower toxicity on C57BL/6 mice compared to the reference drug doxorubicin [2].

Earlier, we demonstrated that a completely different class of compounds fluoroquinolones - dose-dependently stimulate lipid peroxidation and slightly affect GPx activity, while having almost no impact on the concentration of reduced glutathione [23]. Increased lipid peroxidation was also observed with the antitumor agent mitomycin C [24, 25].

Indeed, at first glance the obtained results may appear contradictory. However, they indicate not a purely pro- or antioxidant effect of Les-6400, but rather its biphasic mode of action. It was shown that exposure to Les-6400 leads to a significant increase in MDA levels, indicating the induction of oxidative stress. This effect may result from an initial pro-oxidant action of the compound or from a disturbance of the cellular redox balance at early stages of exposure. At the same time, other experiments demonstrate activation of antioxidant defense mechanisms, as evidenced by increased GPx and GR activities, allowing the effects of Les-6400 to be interpreted as indirectly antioxidant. Most likely, the initial elevation of lipid peroxidation serves as a trigger for an adaptive cellular response. Moderate increases in reactive oxygen species levels or lipid peroxidation products induce the synthesis of antioxidant enzymes and enhance cellular resistance to subsequent oxidative challenges. Thus, the observed 2-fold increase in MDA does not contradict the antioxidant effects of Les-6400 rather reflects the stage-dependent and concentration- and time-dependent nature of its action.

An interesting effect of the compound Les-6400 on GST activity was observed. GSTs are the major class of metabolic enzymes playing a key role in the detoxification of xenobiotics. In addition to their important role in detoxification, GSTs also have diverse biological activity in the onset and progression of various diseases. Mammalian GSTs form a large family that can be divided into three classes: cytosolic GSTs, mitochondrial GSTs, and microsomal GSTs, based on their cellular localization. Among them, cytosolic GSTs are likely the most studied and are widely expressed in various cell types [26]. Cytosolic GSTs are widely expressed in human tissues and comprise approximately 40% of total GSTs [27, 28]. Since our studies were conducted on saponin-permeabilized blood lymphocytes, it is likely that the activity observed was primarily from the cytosolic fraction of GSTs. It is important to note that cytosolic GSTs perform a variety of biological functions: (1) catalyzing the conjugation of reduced glutathione with electrophilic compounds (including drugs), electrophilic drug metabolites, and endogenous electrophiles [29]; (2) catalyzing the reduction of organic hydroperoxides; (3) regulating various cell signaling pathways, such as the mitogen-activated protein kinase (MAP) pathway, which regulates apoptotic signaling (ASK1) [30]; (4) post-translational modification of proteins through S-glutathionylation or deglutathionylation [31]; and (5) contributing to multidrug resistance to chemotherapeutic agents and protecting cancer cells from apoptosis [32].

In recent decades, significant attention has been given to studying the mechanisms of excessive GST expression in various pathological conditions and drug resistance in tumors. As a result, many GST inhibitors have been developed and applied, either alone or in combination with chemotherapeutic agents, for the treatment of multidrug-resistant tumors. Moreover, in recent years, new properties of GST have been discovered in other diseases, such as pulmonary fibrosis and neurodegenerative disorders, although the exact regulatory mechanisms remain unclear. Given the observed overexpression of GST in various diseases, there is an ongoing search for specific inhibitors of this enzyme. Some of them are currently in the preclinical development and clinical stages [33]. The decrease in GST activity revealed in our study may be due to both direct interaction of Les-6400 with the enzyme and secondary changes in the redox status of the cells. To clarify the mechanism, additional *in vitro* studies with purified enzyme or analysis of enzyme kinetic are necessary.

Currently, the literature discusses the use of GST inhibitors to affect cellular signaling pathways and intracellular biological processes, as well as investigating the potential of this enzyme for treating diseases. Research on the effects of GST inhibitors on cellular regulatory systems, particularly the glutathione antioxidant system, should lead to a better understanding of the relationship between excessive GST expression and human diseases, which may aid in the future development of drugs targeting GST.

The increase in GPx activity and GR activity indicates activation of the glutathione-dependent antioxidant response aimed at neutralizing peroxides and maintaining cellular redox homeostasis. The simultaneous decrease in GST activity may reflect

a redistribution of the reduced glutathione pool in favor of peroxidase-mediated detoxification, which becomes a higher priority under conditions of oxidative stress. In this context, GSH is preferentially directed toward peroxide neutralization rather than secondary detoxification processes. In this regard, the compound Les-6400, which leads to an inhibition of GST activity, shows promise and requires further study.

Study limitations. In this study, the concentration range of Les-6400 (10^{-6}–10^{-3} M) was chosen based on typical concentrations used for initial evaluation of prooxidant mechanisms of action of small molecules *in vitro*. The extrapolation of the obtained effects to *in vivo* conditions requires further studies of the pharmacokinetics, bioavailability, and distribution of the compound. All experiments in this study were performed at fixed incubation times to standardize conditions and minimize variability in results. Observed effects may be transient or, conversely, become more pronounced with longer exposure to the compound. Further studies are needed with varying incubation time.

In this study, the focus was on analyzing early biochemical markers of compound action, therefore cytotoxicity parameters were not determined. It should be noted that the evaluation of cell viability under exposure to 4-thiazolidinone derivatives was performed in previous studies [34, 35]. These results demonstrated that the concentrations used in the present work were within the sub-cytotoxic range.

Further studies include clarifying the molecular mechanisms of action, in particular the role of redox-dependent signaling processes, and assessing the effect of the compound on various tumor cell lines *in vitro*.

Conclusions. It was shown that the compound Les-6400 significantly affects the regulatory mechanisms of the cell, particularly in blood lymphocytes. Les-6400 activates lipid peroxidation and significantly impacts the activity of enzymes in the glutathione antioxidant system: at high concentrations (10^{-3} M), it activates glutathione peroxidase, and at the same concentrations, it reduces glutathione-S-transferase activity. Thus, the compound Les-6400 significantly affects the pro-/antioxidant status of blood lymphocytes.

Conflict of interest. Authors have completed the Unified Conflicts of Interest form at http:// ukr-biochemjournal.org/wp-content/uploads/2018/12/coi_disclosure.pdf and declare no conflict of interest.

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ПРО/АНТИОКСИДАНТНИЙ СТАТУС ІЗОЛЬОВАНИХ ЛІМФОЦИТІВ КРОВІ ЛЮДИНИ ЗА ДІЇ НОВОСИНТЕЗОВАНОЇ СПОЛУКИ 11-(ФУРАН-2-ІЛ)-9-ГІДРОКСИ-3,11-ДИГІДРО-2Н-БЕНЗО[6,7] ТІОХРОМЕНО[2,3-D]ТІАЗОЛ-2,5,10-ТРІОНУ (LES-6400)

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Відомо, що похідні 1,4-нафтохінону є основою широкого спектра лікарських засобів із різноманітною біологічною активністю. У цьому контексті особливий інтерес викликає новосинтезована сполука цієї групи – (11-(фуран-2-іл)-9-гідрокси-3,11-дигідро-2Н-бензо[6,7]тіохромено[2,3-d] тіазол-2,5,10-тріон), відома під лабораторним шифром Les-6400, з огляду на її потенційні лікоподібні властивості. Метою дослідження було визначення параметрів глутатіонової ланки антиоксидантної системи в ізольованих лімфоцитах периферичної крові за дії Les-6400. У дослідженні використовували сапонін-пермеабілізовані лімфоцити зі зразків крові здорових чоловіків-добровольців віком 20–44 років. Показано достовірне дозозалежне зростання процесів перекисного окислення ліпідів у лімфоцитах крові за дії Les-6400 у концентраціях 10^{-5}–10^{-3} М. За досліджуваних концентрацій впливу Les-6400 на вміст GSH не спостерігалося, тоді як у діапазоні концентрацій 10^{-4}–10^{-3} М активність глутатіонових антиоксидантних ензимів достовірно змінювалась: активність глутатіонпероксидази і глутатіонредуктази була підвищена, тоді як активність глутатіон-S-трансферази була знижена. Таким чином, сполука Les-6400 суттєво впливає на про-/антиоксидантний статус лімфоцитів крові.

Ключові слова: похідне 1,4-нафтохінону, лімфоцити, пероксидне окислення ліпідів, глутатіонпероксидаза, глутатіонредуктаза, глутатіон-S-трансфераза.

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