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ANTIOXIDANT DEFENSE SYSTEM OF RAT LIVER UNDER THE INFLUENCE OF THIOSULFONATE ESTERS

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Background. The article presents a study of the antioxidant defense system of the liver of rats under the influence of thiosulfonate esters: *S*-ethyl-4-aminobenzenethiosulfonate (ETS), *S*-allyl-4-aminobenzenethiosulfonate (ATS) and *S*-allyl-4-acetyl-aminobenzenethiosulfonate (AATS) at concentrations of 50 and 100 mg per kg of body weight. Thiosulfonate esters, which are synthetic sulfur-containing analogs of allicin, exhibit antioxidant and anti-inflammatory properties. The liver is the main organ where metabolism of xenobiotics and endogenous molecules occur to maintain metabolic homeostasis of the body, and is constantly exposed to reactive oxygen species (ROS) and subsequently to oxidative stress.

Materials and Methods. The effectiveness of the antioxidant defense system in the rats' liver was evaluated by measuring the level of oxidative stress markers (lipid peroxidation (LPO)) and the activity of the antioxidant enzymes – catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GP), glutathione reductase (GR), and the level of reduced glutathione (GSH).

Results. The potential antioxidant properties of thiosulfonate esters and their dose-dependent effect in the liver were determined. In particular, under the action of thiosulfonate esters at a dose of 100 mg/kg, the content of lipid peroxidation products in the liver did not change significantly. Catalase activity and the content of reduced glutathione increased under the action of ETS dose of 100 mg/kg. Under the action of ATS and AATS doses of 100 mg/kg, the activity of GP decreased. At the same time, the effect of ETS at a dose of 50 mg/kg significantly decreased the level of lipid hydroperoxides. The effect of

ATS and AATS doses of 50 mg/kg decreased TBA-reactive products. Under the action of the studied compounds in a lower dose, the activity of SOD and GP increased, and the content of reduced glutathione increased. At the same time, the decrease in the activity of GR under the action of AATS combined with an increased content of reduced glutathione is probably due to the inhibitory effect of the test substance on energy processes in the body.

Conclusions. The studied thiosulfonate esters demonstrated a dose-dependent effect on the redox balance in the rats' liver, proving to be more effective with lower doses of thiosulfonates.

Keywords: *S*-ethyl-4-aminobenzenethiosulfonate, *S*-allyl-4-aminobenzenethiosulfonate, *S*-allyl-4-acetylaminobenzenethiosulfonate, liver, rats, antioxidant system

INTRODUCTION

Progress in the chemistry of sulfur-containing compounds plays an important role in basic research, contributing to the development of various fields of biology, biotechnology, medicine, and improving our understanding of the nature. Both natural and synthetic derivatives of sulfur-containing compounds, particularly thiosulfoesters, are used in practice as useful sulfonating reagents and compounds with a wide range of aplications and a high biological activity index (Dmitryjuk *et al.*, 2020). The ability of sulfur to exist in different degrees of oxidation allows for the formation of a number of mono- and disulfur-containing substances (Lubenets *et al*., 2018). The synthesis and study of properties of these compounds can contribute to the development of new drugs.

The high reactivity of S-esters of thiosulfonic acids results from the structure of the thiosulfonic group (-SO_2-S-), primarily due to the high polarity of the -S-S- bond. This depends on the nature of the acid and thiol components, which in turn affect biological activity and reactivity of thiosulfonate esters, determining the scope of possible practical applications. The redistribution of electron density and changes in biochemical reactivity allow compounds of this class to be used as highly effective biologically active substances, such as insecticides (Dos Santos *et al.*, 2012), anti-helminthic (Dmitryjuk *et al.*, 2020), plant protection products, and growth regulators (Banya *et al.*, 2015), as well as preservatives for fruit and vegetables, biocides for the protection of materials and products from biodestruction (Martirosyan *et al.*, 2019). Since some of these compounds can affect the ability of platelets to aggregate and form blood clots, they may be useful for the prevention of cardiovascular diseases and treatment of thrombosis (Bolibrukh *et al.,* 2015). Moreover, they can contribute to the development of a new antiplatelet agents with improved efficacy and safety profiles. The competitiveness of S-esters of thiosulfonic acids as highly effective drug substances is illustrated by data on the treatment of fungal skin lesions, particularly the treatment of tinea pedis with ethylthiosulfanylate in the form of a 1% ointment. The therapeutic effect of this ointment exceeds that of the currently used commercial analogs due to its keratolytic properties (Lubenets *et al.,* 2019).

The study of the properties of functionalized S-esters of thiosulfonic acids is promising in theoretical and practical aspects for establishing the relationship between their structure and reactivity, stability, and biological activity. This allows us to determine

a strategy for the targeted synthesis of compounds of this class with a set of practically valuable properties (Bairamova *et al.,* 2020; Kotyk, 2023). In our previous work, we described the results obtained *in vitro* on the radical scavenging and antiradical activities of *S*-alkyl-4-aminobenzene-, *S*-allyl-4-aminobenzene-, and 4-acetylaminobenzene thiosulfonates to establish the relationship between their structure and activity. Among the studied compounds, the highest rates of these activities were found in *S*-ethyl-4-aminobenzenethiosulfonate (ETS), S-allyl-4-aminobenzenethiosulfonate (ATS), *S*-allyl-4-acetylaminobenzenethiosulfonate (AATS), which were used in experiments *in vivo* (Liubas *et al.,* 2022).

A thorough study of the effects of synthetic sulfur-containing compounds on the body of animals is necessary to determine their potential for use in therapeutic and prophylactic purposes. One of the main criteria for assessing the possible use of new drugs to protect the body from oxidative processes, bacterial and fungal infections is to study their effect on the antioxidant defense system in animal tissues (Mampuys *et al*., 2020). The antioxidant system assessment is a sensitive method for detecting the responce of various organisms to different diseases and changes in the environment (Oliynyk, 2016).

The liver is the main organ that metabolises xenobiotics and endogenous molecules to maintain metabolic homeostasis in the body. Therefore, it is constantly exposed to reactive oxygen species (ROS) among others. The parenchymal cells of the liver are primarily exposed to oxidative stress, which induces further damage to the organ (Cichoż-Lach & Michalak, 2014). Mitochondria, microsomes, and peroxisomes in these cells can produce ROS, which is regulated by peroxisome proliferator-activated receptor alpha (PPAR-α). Peroxisome proliferator-activated receptors (PPARs) are ligand-activated transcription factors of nuclear hormone receptor superfamily comprising the following three subtypes: PPARα, PPARγ, and PPARβ/δ. Activation of PPAR-α reduces triglyceride level and is involved in the regulation of energy metabolism. PPAR-α is primarily found in the liver, heart, muscles, and other tissues, where it controls the expression of genes involved in fat oxidation and the utilization of fatty acids for energy. (Tyagi *et al*., 2011). In addition, Kupffer cells, liver stellate cells, and endothelial cells are also sensitive to oxidative stress. In Kupffer cells, oxidative stress can result in the production of various cytokines, such as TNF-α, which can increase inflammation and apoptosis. Lipid peroxidation caused by oxidative stress can provoke proliferation and collagen synthesis in stellate cells of the liver (Zhang *et al*., 2013).

Oxidative stress not only causes liver damage by inducing irreversible changes in lipids, proteins, and DNA content but also modulates pathways that regulate gene transcription, protein expression, cell apoptosis, and hepatic stellate cell activation. Oxidative stress is considered to be one of the pathological mechanisms that lead to the initiation and progression of various liver diseases. Both enzymatic and non-enzymatic antioxidant systems are required for the cellular response to combat oxidative stress under physiological conditions (Klaassen & Reisman, 2010). Therefore, antioxidant enzymes such as CAT, SOD, and GP, as well as non-enzymatic metabolites such as ROS, are used to assess the level of oxidative stress.

Given the above, the aim of our study was to determine the effect of different concentrations of newly synthesized sulfur-containing compounds, namely ETS, ATS, and AATS, on the state of the antioxidant defense system in the liver of rats.

MATERIALS AND METHODS

The biological effects of *S*-ethyl-4-aminobenzenethiosulfonate (ETS), *S*-allyl-4-aminobenzenethiosulfonate (ATS), and *S*-allyl-4-acetylaminobenzenethiosulfonate (AATS) were the objects of our study. These compounds were synthesized at the department of Technology of biologically active compounds, pharmacy and biotechnology of National University "Lviv Polytechnic" according to the protocol described previously (Lubenets *et al*., 2018). Their chemical and physical properties were described by V. Lubenets and coauthors (Lubenets *et al*., 2019; Mampuys *et al*., 2020). The structural formulas of thiosulfate esters are shown in **Fig. 1**. Replacing the ethyl radical in the structure of thiosulfonate with allyl groups leads to improved antioxidant properties in hepatocytes (Lubenets *et al*., 2019).

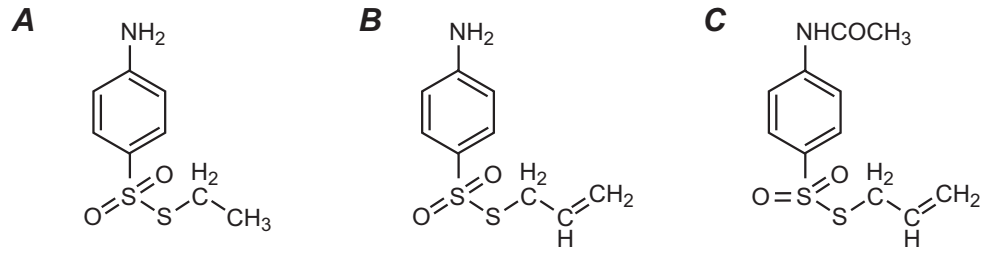

Fig. 1. Structural formulas of thiosulfonate esters: ***A*** – *S*-ethyl-4-aminobenzenethiosulfonate (ETS); ***B*** – *S*-allyl-4- aminobenzenethiosulfonate (ATS); ***C*** – *S*-allyl-4-acetylaminobenzenethiosulfonate (AATS)

The dose and duration of administration were selected based of our previous studies (Kotyk *et al.,* 2019; Liubas *et al*., 2022) and literature data on the use of natural sulfur-containing compounds in *in vivo* experiments (Peinado *et al*., 2012; Batcioglu *et al*., 2012; Cabello-Gómez *et al*., 2020). The selected doses of thiosulfonates were 50 and 100 mg/kg of body weight of rats to be fed per os for 21 days.

The research was conducted at the Laboratory of Biochemistry of Animal Adaptation and Ontogeny of the Institute of Animal Biology of the NAAS on white male *Wistar rats* (190–210 g). The study was carried out in compliance with the general ethical principles of animal experiments adopted by the First National Congress on Bioethics (Kyiv, Ukraine, 2001) and in accordance with the provisions of the "European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes" (Strasbourg, France, 1986). A permission to conduct the study was obtained from the Bioethics Committee of the Institute of Animal Biology NAAS of Lviv (Protocol No. 128 of February 27, 2023). The animals were kept in a vivarium under appropriate lighting and temperature conditions.

Comparison of animal groups. Groups of animals were compared according to the scheme in **Fig. 2.** At the initial stage, the rats were divided into two samples for conducting experiments: Experiment 1 and Experiment 2.

In each experiment, the animals were divided into four groups, of 5 rats in each: group I (control), groups II, III, and IV (experimental) (**Fig. 2**). Group I was a control in relation to experimental groups II, III, IV which received an oil solution of thiosulfonates. The control and experimental groups received standard pelleted food for laboratory rats. All animals of the experimental groups were given 500 μL of oil solution

of thiosulfonates at a rate of 100 mg per kg of body weight (20.0 mg/day for one rat weighing 200 g) once a day with their diet for experiment 1. Rats were given of 50 mg per kg of body weight (10 mg/day for rat weighing 200 g) for experiment 2. Rats in group II received ETS with food, group III received ATS, and group IV received AATS in appropriate doses. Animals in the control group were similarly given 500 μL of oil once a day with their diet. For preparing the oil solutions of synthesized compounds, "Oleina" oil (traditional: refined, deodorized, frozen; Producer of PJSC with II "DOEP"; certified according to State Standard of Ukraine 4492: 2017, complies with ISO 14024) was used. The duration of each experiment was 21 days. Rats from all groups were decapitated under thiopental anesthesia on the 22nd day of the experiment. All procedures were performed at a temperature of +4 °C. Samples of liver tissue were collected for analysis. Within 5–6 minutes of tissue storage on ice, they were exsanguinated by repeated perfusion with a chilled NaCl solution. Liver homogenization, using 1 gram of tissue, was performed in a glass sealed cylinder (beaker) of a homogenizer with a Teflon pestle (MRTOU – 421505-63). Tissue homogenization was carried out for 30–50 seconds, making several up and down movements of the vessel (Dovhan, 1998). The medium used for homogenization was a chilled 0.05 M *Tris*-HCl buffer, pH 7.4, with a ratio of 1:9 (weight/volume: 1 g of tissue and 9 ml of *Tris*-HCl buffer). To obtain the intact fraction and remove incompletely disrupted cells and nuclei, the homogenate was centrifuged for 10 min at 3,000 rpm (t = 0±2 °C) using a refrigerated centrifuge (MLWT23D centrifuge, PK8×90 rotor). The supernatant was used to determine the values of lipid peroxidation products (LPP) and the activity of the antioxidant enzymes.

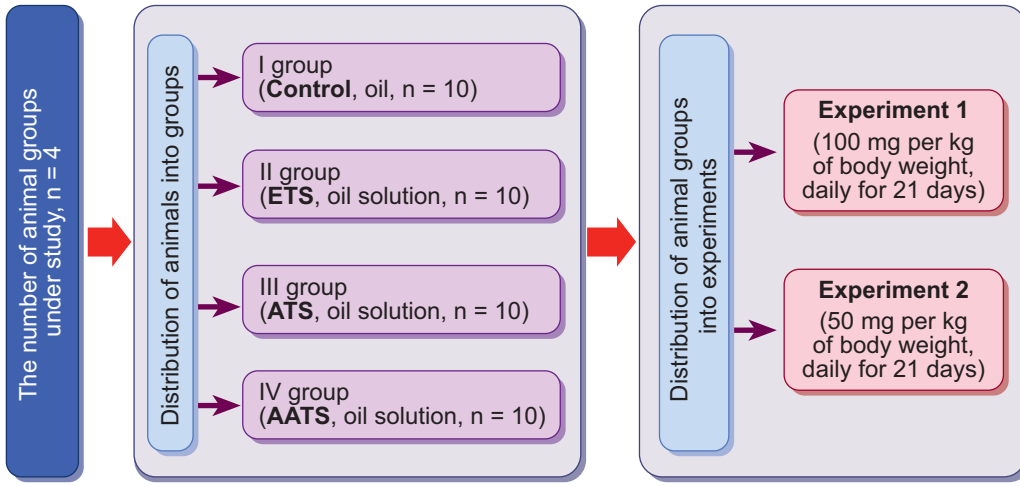

Fig. 2. Comparison of animal groups

The concentration of lipid peroxidation products was determined by the concentration of lipid hydroperoxides (LHP) and TBA-reactive products as described previously (Liubas *et al.,* 2022). The level of LPH was determined by the method based on the precipitation of the protein with trichloroacetic acid, followed by the addition 0.2 mL of 20% ammonium thiocyanate solution. The absorption was measured spectrophotometrically at wave lenght λ 480 nm. The content of LPH was calculated by the difference

between the test sample and the control and expressed in conditional units per 1 gram of tissue. TBA-reactive products were determined using the method based on a color reaction between thiobarbituric acid (TBA) and compounds containing a carbonyl group that interact with thiobarbituric acid. Malondialdehyde (MDA) is the dominant compound among these substances. The level of colored compounds was measured at an optical density of 535 nm and 580 nm to exclude the absorption of non-lipid TBA-complexes; the values were expressed as nmol/g tissue.

The activity of superoxide dismutase (SOD, EC 1.15.1.1.) was determined by the method described previously (Sushko *et al*., 2018) based on the enzyme's ability to compete with nitroblue tetrazolium for superoxide anion radicals, which are formed during the aerobic interaction of NADH and phenazine methosulfate. As a result of this reaction, nitroblue tetrazolium is reduced to formazan. The enzyme activity was determined by the percentage of inhibition of formazan formation and expressed in conventional units per 1 mg of protein.

Catalase (CAT, EC 1.1.6) activity was estimated by the ability of H_2O_2 to form a stable color formation with ammonium molybdate salt. One unit of CAT activity was expressed as nmol of H_2O_2/min·mg of protein (Sushko *et al*., 2018).

The activity of the glutathione peroxidase, glutathione reductase and the content of reduced glutathione were determined by the methods described previously (Iskra, 2013). Glutathione peroxidase (GPx, EC 1.11.1.9) activity was determined by the rate of oxidation of reduced glutathione before and after incubation with tertiary butyl hydroperoxide. GPx activity was expressed in μmol/min·mg of protein. The activity of glutathione reductase (GR, EC 1.6.4.2) was measured by the decrease in NADPH content at 37 °C for 1 min on a spectrophotometer at λ 340 nm. GR activity was expressed in μmole of oxidized NADP/min·mg protein. The GSH content was determined by the level of thionitrophenyl anion formation through the interaction of SH-groups of glutathione with 5,5′-dithiobis-2-nitrobenzoic acid as described previously (Rosalovsky, *et al*., 2015). GSH content was expressed in mmol of GSH per g of tissue. Protein concentration was determined by the Lowry method (Lowry *et al*., 1951) using the "Simko LTD" kit (Ukraine, Lviv). All absorbance values were measured by spectrophotometer "Unico" 1205 (USA).

The enzyme activity and the content of non-enzymatic components obtained in the studies were converted into relative values, with the control set as 100%. The control value was chosen as a point of reference. Then, each percentage was calculated as the value of thiosulfonate esters divided by the value of control and multiplied by 100. Such a procedure was done separately for Experiment 1 and Experiment 2.

Statistical Analysis. The results were calculated using Microsoft Excel 2013 and expressed as Mean ± Standard Error of the Mean (M±SEM). The variances between groups were tested for significance using one-way ANOVA, followed by Tukey–Kramer test. For each of the parameters, the significance level was determined using three gradations: * $P \leq 0.05$; ** $P \leq 0.01$; *** $P \leq 0.001$ *. The differences were considered significant at $P \leq 0.05$.

RESULTS AND DISCUSSION

The liver synthesizes antioxidants and enzymes that protect cells from oxidative damage caused by lipid peroxidation products, preventing detoxification of the body, various diseases and pathologies. (Melekh *et al*., 2017). Lipid peroxidation leads to the

formation of lipid hydroperoxides, which are highly reactive and can react with cellular components such as proteins, lipids, and DNA, causing cellular damage. The increased synthesis of reactive oxygen species (ROS) and the free radical processes initiated by them cause oxidative stress and disruption of the pro/antioxidant balance in the body (Li *et al*., 2015). Therefore, maintaining the balance between oxidative stress and antioxidant protection is crucial for preserving the integrity of liver cells and preventing the development of diseases (Casas-Grajales & Muriel, 2015).

The results of our study (Experiment 1) indicate that thiosulfonates at a concentration of 100 mg/kg body weight, did not cause an increase in the content of LHP and TBA-reactive products in liver homogenates. Moreover, the values obtained in the experimental groups did not differ significantly from those obtained in the control group (**Fig. 3**).

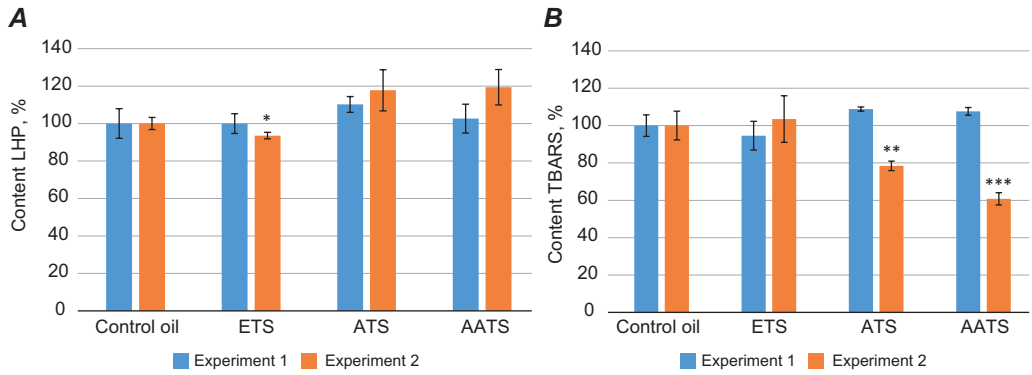

Fig. 3. The effect of thiosulfonates at a concentration of 100 (Experiment 1) and 50 (Experiment 2) mg/kg body weight on the content of indicators of oxidative stress in the liver of rats: ***A*** – LHP, lipid hydroperoxides; ***B*** – TBARS, thiobarbituric acid reactive substances. The results are shown as the Mean ± SEM
Comments: * P ≤0.05; ** P ≤0.01; *** P ≤0.001 – compared to the control group

At the same time, thiosulfonates at a concentration of 50 mg/kg body weight (Experiment 2) caused significant changes in the concentration of LHP and TBK-reactive products. In particular, under the action of ETS, the content of LHP decreased significantly – by 7%, while the content of TBA-reactive products slightly increased (**Fig. 3*B***). Under the action of ATS and AATS, a significant decrease in the concentration of TBA-reactive products – by 22% and 39%, respectively, was observed; at the same time, a tendency to increase the content of LHP was revealed. These results indicate that ETS affects the reduction of the concentration of products of the intermediate stage of lipid peroxidation, while ATS and AATS demonstrate a more profound effect at the final stage. The molecular mechanisms of action of thiosulfonic acid esters involve the reduction of hydroperoxides through the participation of the sulfonate ether group, which is as a structural component of their molecules. Thiosulfonic acid esters exhibit inhibitory effects on the activity of the xanthine-xanthine oxidase system, leading to a reduction in the intensity of reactive oxygen species generation (Mampuys *et al*., 2020).

Liver cells are particularly vulnerable to oxidative damage due to their high metabolic activity and exposure to various toxic substances. The most important enzymes that help to protect cells from oxidative damage and maintain cellular function are catalase, superoxide dismutase, and glutathione peroxidase (Ighodaro & Akinloye, 2018).

The results of our research showed a positive effect of the thiosulfonates studied on the activities of superoxide dismutase and catalase in the liver cells of all experimental groups in both experiments (**Fig. 4**).

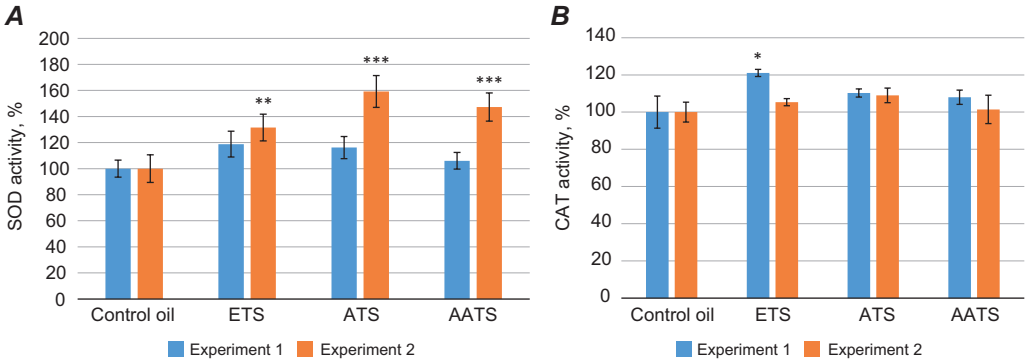

Fig. 4. The effect of thiosulfonates at a concentration of 100 (Experiment 1) and 50 (Experiment 2) mg/kg body weight on the activity of superoxide dismutase (SOD) (***A***) and catalase (CAT) (***B***) in the liver of rats. The results are shown as the Mean ± SEM, n = 5
Comments: * P ≤0.05; ** P ≤0.01; *** P ≤0.001 – compared to the control group

Superoxide dismutase activity in the rat liver increased under the influence of thiosulfonylates at both concentrations. Along with that, under the influence of ETS, ATS, and AATS at a dose of 50 mg/kg body weight, the enzyme activity was significantly higher – by 32%, 60%, and 48%, respectively, compared to the control group (**Fig. 4*A***). Superoxide radicals (O^{2-}) are highly reactive and can cause oxidative damage to cellular macromolecules such as lipids, proteins, and DNA. SOD is an important antioxidant enzyme that catalyzes the breakdown of superoxide radicals to less active ROS such as hydrogen peroxide and molecular oxygen, thus protecting liver cells from oxidative stress. This compensatory increase in SOD activity in response to thiosulfonylates is likely due to the enzyme's ability to scavenge superoxide radicals and reduce their accumulation in the liver, thus preventing oxidative damage.

Hydrogen peroxide (H_2O_2), which accumulates in liver cells as a result of the superoxide dismutase reaction, is further converted into water and oxygen by catalase and glutathione peroxidase. A significant increase in catalase activity (by 21%) was found in the rat liver under the influence of ETS at a concentration of 100 mg/kg body weight (**Fig. 4*B***), indicating the activation of the antioxidant defence under the influence of this compound. The activation of catalase in liver cells can affect their proliferation, regulation of cell signaling pathways, and immune responses. However, catalase activity in all other experimental groups in both experiments did not differ significantly from that of the control group (**Fig. 4***B*). The Se-containing enzyme glutathione peroxidase is responsible for inactivating of hydrogen peroxide and lipid hydroperoxides in cells through the use of reduced glutathione as a co-substrate. This enzyme has high specificity for glutathione. Glutathione peroxidase is an important protective mechanism for liver and other cells against the destructive effects of reactive oxygen species.

Under the action of ATS and AATS at a dose of 100 mg/kg body weight, a decrease in GP activity in rat liver homogenates by 74 and 65%, respectively, was found (**Fig. 5**). However, under the influence of thiosulfonates at a dose of 50 mg/kg body weight, the

enzyme activity increased, in particular, it significantly increased (by 86%) under the action of ETS and trended upward under the action of ATS and AATS. This indicates that thiosulfonates at lower doses can stimulate the activity of GP in the liver, while at higher doses they inhibit it. A similar relationship was observed in other studies of glutathione system activity (Miller & Schmidt, 2019).

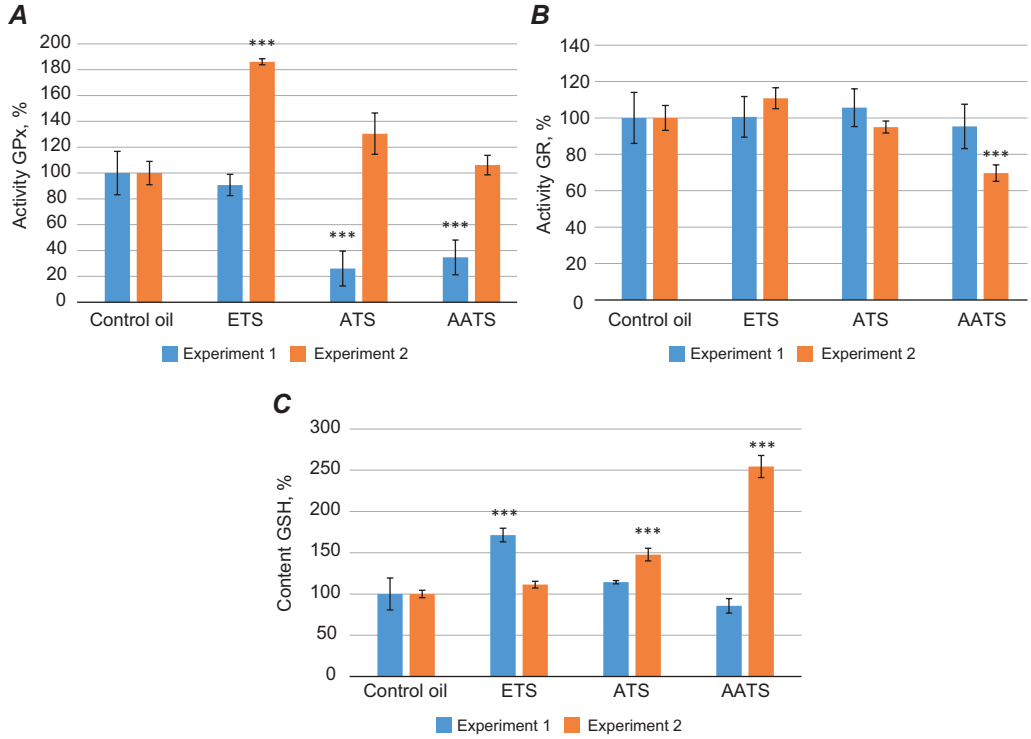

Fig. 5. The effect of thiosulfonates at a concentration of 100 (Experiment 1) and 50 (Experiment 2) mg/kg body weight on the content of indicators of glutathione system in the liver of rats: ***A*** – glutathione peroxidase (GP); ***B*** – glutathione reductase (GR); ***C*** – reduced glutathione (GSH). The results are shown as the Mean ± SEM
Comments: * P ≤0.05; ** P ≤0.01; *** P ≤0.001 – compared to the control group

The activation of GP under the influence of thiosulfonates at a dose of 50 mg/kg may possibly occur if a sufficiently high level of intracellular GSH is maintained. GP not only acts as a substrate for reactions, but also plays a role in the constant reduction of selenol groups located in the enzyme's catalytic center which are oxidized during the glutathione peroxidase reaction. In the catalytic center of GP, the selenocysteine residue forms a covalent intermediate with the peroxide substrate. This center is crucial for the efficient detoxification of peroxides and protection against oxidative stress in the liver (Ighodaro & Akinloye, 2018). This is supported by a significant increase in the concentration of GSH – by 48% and 155% – under the influence of ATS and AATS, respectively, and a tendency to increase under the influence of ETS (by 11%). This indicates that at lower doses thiosulfonate esters can enhance the liver's antioxidant capacity by increasing the GSH content. The increase in hepatic GSH content by 70% in rats under the action of ETS at a concentration of 100 mg/kg, against the unchanged activity of

GP and GR, may indicate that ETS can enhance the de novo synthesis of GSH involving gamma-glutamylcysteine synthetase. Thiosulfonates can be transformed into other sulfur compounds during biotransformation processes, which can serve as a source for the synthesis of GSH molecules.

The decrease in GR activity (by 30%) under the influence of AATS can be explained by the inhibitory effect of the substance on energy processes in the body, which result in the formation of reduced nicotinamide coenzymes (NADH and NADPH), causing inhibition of enzyme activity, despite the high level of GSH in the liver in this group of rats. This confirms the idea that the appropriate level of GSH in hepatocytes under the influence of AATS is not ensured by the functioning of GR, which catalyzes the reduction of the disulfide bond of oxidized glutathione (GSSG) to its sulfhydryl form (GSH). The obtained results suggest that the thiosulfonates ETS, ATS, and AATS may have a differential effect on the formation of reducing equivalents in the liver, which may affect the activity of the glutathione link of the SOS in liver cells (Sánchez-Valle *et al*., 2012). Obviously, thiosulfonates can affect the transcription factor Nrf2 (Nuclear Factor Erythroid Related Factor 2), which is the main regulator of redox balance in cells. It regulates the basal and induced gene expression of many antioxidant enzymes. It has been shown that enhanced activation of Nrf2 by various compounds protects the liver in various models of oxidative stress (Tang *et al*., 2014).

CONCLUSION

The studied thiosulfonates demonstrated a dose-dependent effect on the redox balance in the rat liver, with lower doses of thiosulfonylates proving to be more effective in maintaining it. However, further studies are needed to confirm these results, fully understand the mechanisms underlying these effects, and determine the optimal doses and duration of thiosulfonate administration to achieve the desired therapeutic effect while minimizing potential side effects.

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COMPLIANCE WITH ETHICAL STANDARDS

Conflict of Interest: The authors did not receive any funding for this research and delare no conflicting interests.

Human Rights: This article does not contain any experiments with human objects.

Animal Rights: All international, national and institutional guidelines for the care and use of laboratory animals were followed.

AUTHOR CONTRIBUTIONS

Conceptualization, [I.R.; L.V.]; methodology, [I.R.; L.N.]; investigation, [L.N.]; resources, [L.N.; I.R.]; data curation, [I.R.; L.V.]; writing – original draft preparation, [L.N.; I.R.; L.V.]; writing – review and editing, [L.N.; I.R.; L.V.] visualization, [L.N.] supervision, [I.R.; L.N.]; project administration, [I.R.; L.V.]; funding acquisition, [–].

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СИСТЕМА АНТИОКСИДАНТНОГО ЗАХИСТУ ПЕЧІНКИ У ЩУРІВ ЗА ДІЇ ЕСТЕРІВ ТІОСУЛЬФОНАТІВ

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Вступ. У статті представлено дослідження системи антиоксидантного захисту печінки щурів за дії естерів тіосульфонатів: *S*-етил-4-амінобензентіосульфонату (ЕТС), *S*-аліл-4-амінобензентіосульфонату (АТС) та *S*-аліл-4-ацетил-амінобензентіосульфонату (ААТС) у концентраціях 50 та 100 мг/кг маси тіла. Естери тіосульфонатів як синтетичні сульфуровмісні аналоги аліцину проявляють антиоксидантні та протизапальні властивості. Печінка є основним органом, який метаболізує ксенобіотики й ендогенні молекули для підтримання метаболічного гомеостазу в організмі і зазнає постійного впливу активних форм оксигену, а згодом і оксидативного стресу.

Матеріали та методи. Ефективність функціонування системи антиоксидантного захисту в печінці щурів аналізували за допомогою вимірювання рівня маркерів оксидативного стресу (продуктів перекисного окиснення ліпідів (ПОЛ) і активності ензимів антиоксидантної системи – каталази (КАТ), супероксиддисмутази (СОД), глутатіонпероксидази (ГП), глутатіонредуктази (ГР) та рівня відновленого глутатіону (ВГ).

Результати. Встановлено потенційні антиоксидантні властивості естерів тіосульфонатів і їхній дозозалежний вплив на печінку. Зокрема, за дії естерів тіосульфонатів у дозі 100 мг/кг вміст продуктів ПОЛ у печінці вірогідно не змінювався. За дії ЕТС підвищувалися каталазна активність та вміст ВГ, а за дії АТС і ААТС активність ГП знижувалася. Водночас за дії ЕТС у дозі 50 мг/кг вірогідно знижувався вміст ГПЛ, а за дії АТС і ААТС – ТБК-активних продуктів. За дії досліджуваних сполук у меншій дозі підвищувалася активність СОД, ГП та збільшувався вміст ВГ за дії АТС і ААТС. Однак зниження активності ГР за дії ААТС на тлі підвищеного вмісту ВГ, очевидно, зумовлено інгібуючим впливом досліджуваної речовини на енергетичні процеси в організмі.

Висновки. Досліджувані тіосульфонати продемонстрували дозозалежний вплив на окисно-відновний баланс у печінці щурів, причому нижчі дози тіосульфонатів проявили себе ефективніше для його підтримки.

Ключові слова: *S*-етил-4-амінобензентіосульфонат, *S*-аліл-4-амінобензентіосульфонат, *S*-аліл-4-ацетиламінобензентіосульфонат, печінка, щурі, антиоксидантна система

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