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DISPERSION ANALYSIS OF THE EFFECT OF NETTLE EXTRACT ON SOME BIOCHEMICAL AND HEMATOLOGICAL PARAMETERS IN STRESS-INDUCED RATS

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Background. The effects of 40% ethanolic nettle extract (the first factor) and adrenaline-induced stress (the second factor) were evaluated, both individually and in combination, on some biochemical and hematological parameters in rats using a two-factor analysis of variance.

Materials and Methods. In experiments, we used 4 groups of rats. Animals of groups UD-nettle and UD+A received 40% ethanolic extract of nettle (*Urtica dioica* L.) in a dose of 5 mL/kg of body weight for 4 weeks. Rats of the groups (C-control) and (A-stress) received an appropriate amount of 40% ethanol. On the 29th day of the experiment, the stress was simulated in the animals of groups A and UD + A by an intramuscular injection of 0.1% adrenaline hydrochloride in the dose of 1 mg/kg of the body weight. The rats of the C and UD-nettle groups were injected with the appropriate amount of physiological solution. The animals were decapitated under anesthesia 24 hours after injections. Some hematological and biochemical parameters of the blood, liver, heart, and kidney of rats were studied. All experimental data were processed by ANOVA analysis.

Results. Adrenaline stress has the most intense effect on the elevation of aspartate aminotransferase activity in blood, a decrease of superoxide dismutase activity in erythrocytes and concentration of reduced glutathione in the liver and heart, and increased levels of free radical reaction products in all studied organs of rats.

The ANOVA analysis showed that nettle extract in the body of non-stressed animals has the most intense effect on reducing the content of lipid hydroperoxide in the liver and carbonyl groups of protein in the heart, and activates the glutathione chain of the antioxidant system in all organs. Administration of nettle extract to rats before stress induction inhibits lipid peroxidation in the kidneys and heart, decreases the concentration of carbonyl groups of protein in blood and liver, reduced glutathione concentration and the activity of glutathione peroxidase in erythrocytes.

Our results indicate that the heart is more resistant to stress in terms of free radical formation, but is sensitive to the effect of nettle extract before stress induction in rats which is manifested by the increase in the activity of the enzymatic and non-enzymatic chain of the antioxidant system.

All studied factors significantly affected the TBA-active products in the kidneys accompanied by increasing their concentration. The unaccounted factors affect the accumulation of lipid peroxidation products and catalase activity by more than 50%, while they have the least effect on the content of reduced glutathione in all rat tissues.

Conclusion. The dispersion analysis confirmed the tissue specificity of the investigated factors' individual influence and their combined effect on some biochemical and hematological parameters in the rats, as well as the protective and antioxidant properties of nettle extract.

Keywords: nettle extract, adrenaline stress, rats, dispersion analysis

INTRODUCTION

The redox system in aerobic organisms is essential for maintaining cellular homeostasis. Under physiological conditions, cells maintain redox homeostasis by balancing the production of oxidants, reactive oxygen species (ROS), and their removal by the antioxidant system. All types of ROS (superoxide, hydroxyl radical, and singlet oxygen, as well as non-radical species, such as hydrogen peroxide) at physiological concentrations participate in the processes of growth, differentiation, development, and cell death. They are involved in processes of bioregulation, including the synthesis of natural molecules, signal transmission, and immune response. In addition, they can play a role as intracellular messengers and potential factors in intercellular communication (Bacou *et al.*, 2021). However, under the influence of various stress factors, redox homeostasis can be disturbed by increasing ROS or reducing antioxidants. Oxidative stress causes numerous systemic reactions and damage at the level of cells, tissues, and the whole organism. It is also the source of the development of the main pathological processes in a wide range of diseases (Sedik & Elgohary, 2023; Kim *et al.*, 2020).

Recently, two aspects of oxidative stress have been recognized: (1) the minimum level of oxidant formation necessary for the vital process through the transmission of redox signals, called oxidative eustress, and (2) excessive exposure to oxidants, which leads to nonspecific oxidation of biomolecules (lipid peroxidation, proteins, and DNA) and disruption of redox signaling, called oxidative distress (Sies & Jones, 2020). In animals and humans, oxidative stress is mitigated by endogenous antioxidants that reduce the production of ROS. For these reasons, it is important to better understand the mechanisms of oxidative distress in the body and the effect of exogenous compounds on the normalization of metabolic processes and activation of the endogenous antioxidant system.

Experimental data suggest that most herbs and spices have a wide range of biological and pharmacological activities, including antioxidant properties that can protect tissues from damages caused by oxidative stress (Pérez Gutiérrez *et al.*, 2021). Stinging nettle (*Urtica dioica* L.) has antiproliferative, anti-inflammatory, antioxidant, pain-relieving, anti-infectious, anti-allergic, hypotensive, and anti-ulcer properties. It also has a strong detoxifying effect on the body due to its diuretic and blood-purifying properties (Bhusal *et al.*, 2022). This herb improves biochemical, hematological, and immunological indices due to the presence of a large number of fibers, minerals, vitamins, and antioxidant compounds such as polyphenols and carotenoids, organic and inorganic acids, amino acids, as well as protoporphyrin, tannins, phytosterols, glycokinins in all parts of the plant (Dhouibi *et al.,* 2020).

Previously, we conducted a study to identify the antioxidant properties of various extracts (water and water-alcohol solutions with ethanol content of 20%, 40%, 60%, 70%, and 90%) of nettle. It was found that the 40% ethanolic extract exhibits the highest radical scavenging activity and best reduces the formation of free radical products in an *in vitro* system (Buchko *et al.,* 2016). In another study (Havryliak *et al.*, 2019), the antioxidant activity of 40% ethanolic extract was confirmed by three methods, which are based on different abilities to reduce DPPH+ radicals, ABTS+, and Fe^{3+} ions. As a result, we used this extract in our further studies for the correction of stressful conditions in animals, which are accompanied by a violation of the pro-oxidant-antioxidant balance. In experiments on laboratory animals, the administration of the mentioned nettle extract after adrenaline-induced stress showed stimulation of erythropoiesis, activation of protein metabolism, inhibition of free radical processes, and increase in endogenous reserves of antioxidant protection in the blood and tissues of rats (Buchko *et al.,* 2019).

As shown in many studies, the parameters of biological objects depend on a large number of external and internal factors (Lenne & Trivedi, 2022; McCord *et al.,* 2023; Bacou *et al.,* 2021). Scientists have developed special methods to isolate the influence of individual factors and evaluate their relative role (Nieuwenhuijsen & Droz, 2003). One of these methods is dispersion analysis which enables biologists to study and predict the impact of various factors on biological objects. This statistical analysis provides the opportunity not only to estimate the probability of the influence of various factors on the studied indices and their contribution to the overall variability of the indices (within 100%), but also to compare these effects based on the value of the relative (percentage) shares of the influence of the factors.

Therefore, our study aimed to evaluate the effect of two factors (nettle extract and stress) and their combined effect on some hematological parameters and indices of protein metabolism, free radical processes, and antioxidant defence system in rats using a two-factor analysis of variance.

MATERIALS AND METHODS

Phytoextract obtaining method. In our experiment, we used the upper part of stinging nettle (*Urtica dioica* L.) harvested in ecofriendly areas of Lviv region (Ukraine). Nettle extract was prepared by maceration. A detailed description of the extract preparation is presented in the study by O. Buchko *et al.* (2019). It contained chlorophylls *a*, *b*, polyphenols and carotenoids (Dhouibi *et al.*, 2020).

Before the experiment, the dried extract was diluted with a 40% water-ethanol solution to a concentration of 2.5 mg/mL, which corresponds to 12.5 mg of extract/kg body

weight, and administered to rats with water (5 mL of solution/kg body weight). The amount of the extract was selected according to the literature data on the therapeutic dose of phytoextracts in the range of 10–50 mg/kg (Dhouibi *et al.*, 2020; Grauso, *et al.*, 2020; Bhusal *et al.*, 2022; Pérez Gutiérrez *et al.*, 2021). The extract was added to the water in drinking bowls based on the amount of liquid consumed per animal/per day (25–30 mL). In the control group, 40% ethyl alcohol was added to the water in bowls.

Experimental animals. The experiments were performed on Wistar white male rats with a bodyweight of 180–200 g, divided into 4 groups: control (C) та 3 experimental (A-stress, UD-nettle, UD + A), 7 animals in each. The animals were housed in the standard conditions of the vivarium with free access to drinking water and standard feed for laboratory rats. This study was conducted following the ethical principles of the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes (Strasbourg, 2005), Law of Ukraine "On Protection of Animals from Cruel Treatment" (2006)*,* and the Fifth National Congress on Bioethics (Kyiv, 2013). The permission to conduct the experiments was obtained from the Bioethics Committee of the Institute of Animal Biology NAAS of Lviv, Ukraine, protocol No 75/a of 10 April, 2019.

Experimental design. Animals of experimental groups UD-nettle and UD + A received 40% nettle extract in the dose of 5 mL/kg of body weight for 4 weeks. Rats of the control (C) and experimental group (A-stress) received the appropriate amount of ethanol. On the 29th day of the experiment, the stress was simulated in the animals of the A-stress and UD + A groups by a single intramuscular injection of a 0.1% solution of adrenaline hydrochloride in the dose of 1 mg/kg of the body weight. The rats of the C and UD-nettle groups were injected with an appropriate amount of 0.9% NaCl (Yuria-Pharm LLC, Ukraine). The animals were decapitated under light ether anesthesia 24 hours after injections.

Biochemical and hematological analysis. Whole blood, erythrocyte hemolysates, plasma, and homogenates of liver, heart, and kidney of rats were obtained for the study. In whole blood, hematological (the number of erythrocytes and leukocytes) indices and hemoglobin concentration were determined by the hemoglobin-cyanide method using the kits "Simko LTD" (Ukraine).

Superoxide dismutase (SOD; EC 1.15.1.1); catalase (CAT; EC 1.11.1.6); glutathione peroxidase (GP; EC 1.11.1.9); glutathione reductase (GR; EC 1.6.4.2) activities and the content of reduced glutathione (GSH) were determined in erythrocyte hemolysates and tissue homogenates (Vlizlo *et al.,* 2012). The concentration of lipid hydroperoxides (LHP); TBA-active products; carbonyl groups of proteins (CP) were measured in blood plasma and tissue homogenates (Vlizlo *et al.,* 2012). Total protein concentration, alanine aminotransferase (ALT, EC 2.6.1.2), and aspartate aminotransferase (AST, EC 2.6.1.1) activity were also investigated in blood plasma. During the study, the clinical condition and health of the animals were monitored.

Statistical analysis. Experimental data are presented as mean values (M), standard error (m), and the degree of difference probability (p). All data were tested for normality by Shapiro–Wilk tests. ANOVA analysis was performed. Statistical processing of all results was carried out using the program "Excel-2010" for Windows.

RESULTS AND DISCUSSION

ANOVA analysis has shown that the administration of nettle extract to rats has a significant effect on the erythrocytes number, the part of which is 50% ($p \geq 0.999$) (**Fig. 1*A***).

According to the absolute values of the studied indices that have already been published (Buchko *et al.,* 2019), we revealed an increase in erythrocytes in the blood of rats after nettle extract administration. It is believed that high chlorophyll content has a positive effect on erythropoiesis (Šic Žlabur *et al.,* 2022). A less effect is fixed on the number of leukocytes. In particular, its part is 20% (p ≥0.95) (**Fig. 1*A***). It is known that nettle contains vitamin C, which causes the proliferation of T- and B-lymphocytes (Tveden-Nyborg, 2021). Thus, the share of the effect of nettle extract on the leukocytes is significan.

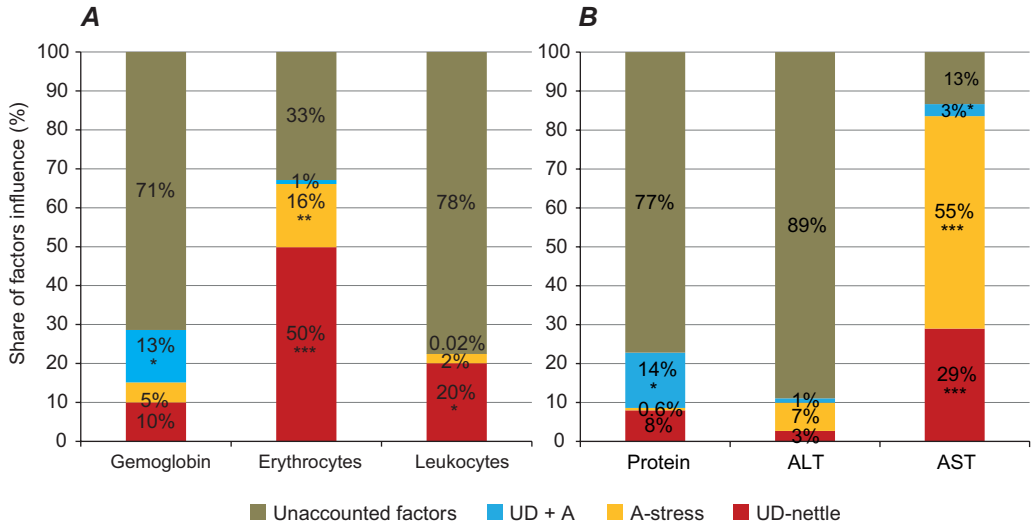

Fig. 1. ANOVA analysis of the effect of nettle extract, stress, and the combined effect of the two factors on the hematological (***A***) (hemoglobin, erythrocytes, leukocytes) and biochemical indices (***B***) (protein, ALT, AST) in the blood of rats (* – p ≥0.95; ** – p ≥0.99; *** – p ≥0.999). Note: here and below: UD + A – animals received 40% extract of nettle for 4 weeks and were exposed to 0.1% solution of adrenaline hydrochloride on the 29th day of the experiment; A-stress – animals were administered 0.1% solution of adrenaline hydrochloride on the 29th day of the experiment; UD-nettle – animals received 40% extract of nettle for 4 weeks

Description analysis revealed a weak, but significant influence of the stress factor on the number of erythrocytes in the blood of rats, their part being 16% (p ≥0.99) (**Fig. 1*A***). These data confirm the information that catecholamines can induce a dramatic increase in the cell volume as a result of an accumulation of sodium and chloride due to the activation of an amiloride-sensitive, cyclic, AMP-dependent Na^+-H^+ exchanger (Brun *et al*., 2022). The absolute values of erythrocyte numbers indicate a slight increase (Buchko *et al.,* 2019).

It was established that the share of nettle extract effect on the hemoglobin concentration under stress conditions is 13% (p ≥0.95) (**Fig. 1*A***). The effect of stress on hemoglobin content is negligible with the share of only 5%. This suggests that stress has a mediated influence on hemoglobin concentration, specifically the pool of iron in the body, vitamin A, B2, B12, and folic acid. Stress accelerates free radical reactions in the body, affecting vitamin, macro-, and microelement levels (Chaparro *et al*., 2019). All of these factors can produce a modest lowering in hemoglobin concentration in the blood under adrenaline stress, despite a slight increase in erythrocyte content.

High percentages of influence of unaccounted factors on hemoglobin (71%) and leukocytes (78%), and a lower percentage of the erythrocytes (33%) were found. Unaccounted factors include all metabolic processes that occur in the body and can directly affect blood parameters. In *in vivo* experiments, the influence of unaccounted factors is always higher compared to *in vitro* studies, since in the latter case the mutual influence of all body systems is excluded.

Nettle extract has an indirect effect on AST activity, the share of influence being 29% ($p \geq 0.999$) (**Fig. 1*B***). AST activity increases 12 hours after damage to the liver and other organs that synthesize this enzyme, their peak levels observed from 24 to 48 hours (Rohani *et al.,* 2020). According to the analysis of absolute values, the activity of this enzyme under the action of nettle extract decreases compared to the rats who received only 40% ethanol (Buchko *et al.*, 2019). Therefore, our data suggest that stress has a direct and powerful influence on the AST activity (the share of influence is 55%; $p \geq 0.999$) (**Fig. 1*B***). It is important to note that the share of the combined effect of stress and nettle extract on AST activity is significant and equals 3% ($p \geq 0.95$). It is known that nettle is characterized by general strengthening properties, which are explained by the presence of a significant amount of chlorophyll (Taheri *et al.,* 2022). A sharp increase in plasma AST activity may indicate necrotic myocardial damage caused by intramuscular injection of adrenaline in the dose we used, and as a result, the release of the enzyme into the blood. It is well known that AST activity is used in clinical trials as a marker of cardiac lesions (Ndrepepa, 2021).

ANOVA analysis revealed a mild effect of nettle extract during stress on the total protein in the blood (the share of influence is 14%; $p \geq 0.95$) (**Fig. 1*B***). This effect is mediated through the introduction of nettle components into the body: urticine glycoside, tannins, carotenoids, chlorophyll, vitamins C, B_2, B_3, organic acids, microelements, which improves metabolic processes (Taheri *et al.,* 2022; Grauso *et al.,* 2020). Literature data report that nettle has a hepatoprotective effect, it does not reduce the content of immune cells, but increases the content of antioxidant enzymes (Jaiswal & Lee, 2022; Golshan *et al.,* 2015). All these factors can lead to a slight increase in the amount of protein in the blood plasma of rats.

A significant share of the influence of unaccounted factors on total protein and ALT activity in the blood of rats was established (77% and 89%, respectively) (**Fig. 1*B***).

Our results have shown that the administration of nettle extract had the most pronounced effect on LHP in the liver of rats (**Fig. 2*A***), the share of which was 36% ($p \geq 0.99$). LHP are the primary products of lipoperoxidation that can further be converted into diene conjugates and malondialdehyde. Stress caused by adrenaline affected LHP in the blood (the share of influence is 36%; $p \geq 0.999$) that may indicate the increase in lipid peroxidation, which include high-density lipoproteins, low-density lipoproteins, total cholesterol, and triglycerides (Agarwal & Khan, 2020).

It was found that the share of nettle effect on the LHP in the kidneys of stress-induced rats is 24% ($p \geq 0.99$) (**Fig. 2*A***). We found that unaccounted factors significantly affect the concentration of LHP in the plasma, liver, kidneys, and heart (**Fig. 2*A***). Their strongest influence is in the heart (81%). The heart is known to have a special gene, NFE2L2, which encodes the transcription factor Nrf2, best known for regulating the expression of antioxidant and detoxification genes. Nrf2 interacts with the Notch signaling pathway to promote wound healing or organ development. These signaling pathways act as a powerful defense against damage (McCord *et al.,* 2023). We hypothesize

that this gene may be one of the unaccounted-for factors influencing the concentration of LHP in the heart.

The results of ANOVA analysis revealed that stress, nettle extract administration, and the effect of nettle extract before stress simulation significantly affected the concentration of TBA-active products in the kidneys. Thus, the share of influence of these factors is 21% (p ≥0.999), 12% (p ≥0.99), and 36% (p ≥0.999), respectively (**Fig. 2*B***).

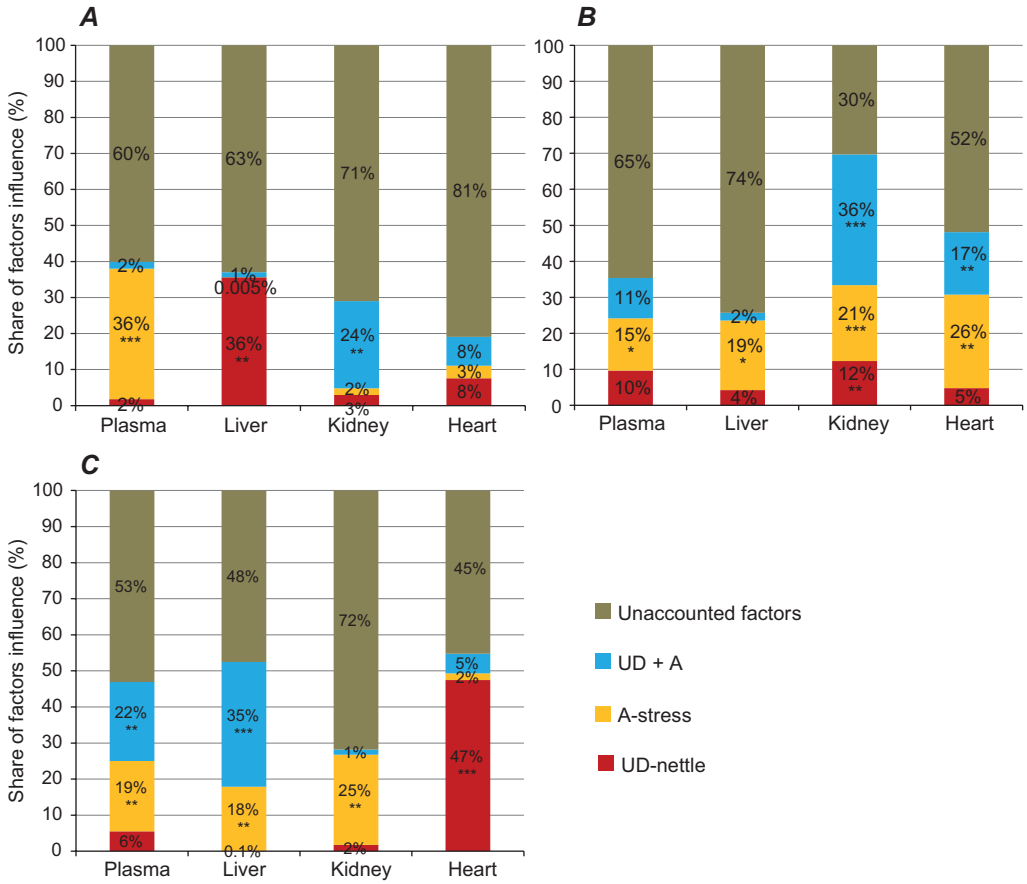

Fig. 2. ANOVA analysis of the effect of nettle extract, stress, and the combined effect of the two factors on the content of LHP (***A***), TBA-active products (***B***) and carbonyl group of proteins (***C***) in the blood, liver, kidney and heart of rats (* – p ≥0.95; ** – p ≥0.99; *** – p ≥0.999)

Variance analysis confirms the weak positive effect of nettle extract on the end products of lipid peroxidation in stress-induced rats. It is important to note that adrenaline, as a stress factor, causes a significant effect on the blood and all the organs. The share of the effect of stress on TBR-active products in plasma is 15% (p ≥0.95), in the liver – 19% (p ≥0.95), in the kidneys – 21% (p ≥0.999), in the heart – 26% (**Fig. 2*B***).

A powerful effect of nettle extract on the formation of oxidative modification of proteins in the heart was established (47%; p ≥0.999) (**Fig. 2*C***). Under these conditions, the content of carbonyl groups of proteins decreases. It is possible to assume that nettle

extract has a protective effect on heart proteins including all carrier proteins, ATPases, and enzymes. The functioning of the cardiovascular system directly depends on these proteins. The effect of nettle extract on the content of CP in the blood plasma and liver of stress-induced rats is significant (22%, p ≥0.99; 35%, p ≥0.999, respectively).

ANOVA analysis testified that the share of nettle extract influence on SOD activity in erythrocytes and the studied organs is within 0.01–1% (**Fig. 3*A***). In rats that were not exposed to stress, nettle extract had no effect on SOD activity. On the other hand, stress factor has a significant effect on the activity of SOD in erythrocytes (the share of influence is 42%; p ≥0.999).

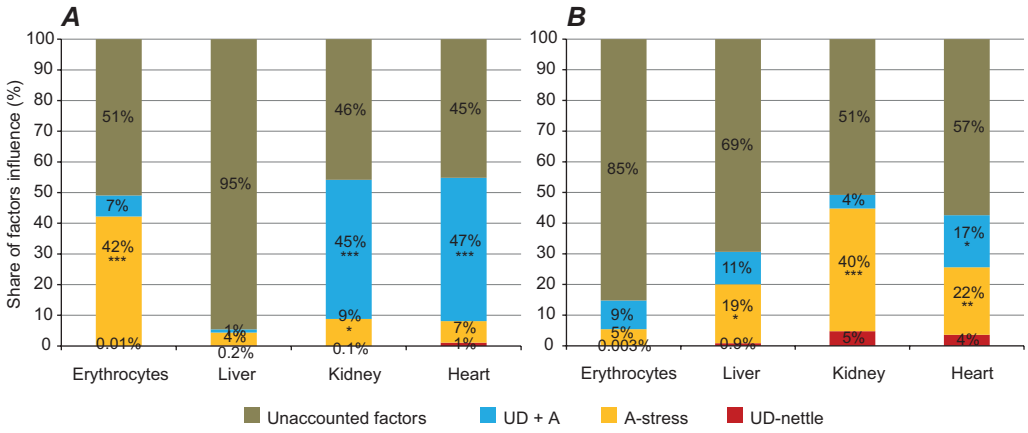

Fig. 3. ANOVA analysis of the effect of nettle extract, stress, and the combined effect of these two factors on the SOD (***A***) and CAT (***B***) activities in the erythrocytes, liver, kidney and heart of rats (* – p ≥0.95; ** – p ≥0.95; *** – p ≥0.999)

The administration of nettle extract before stress induction in rats leads to an increase in the share of this factor's impact on SOD activity in the kidneys and heart to the level of 45% (p ≥0.999) and 47% (p ≥0.999), respectively. However, the combined effect of adrenaline and nettle extract is accompanied by the return of SOD activity in these organs to the norm (Buchko *et al.*, 2019). It is important to note the high share of influence of unaccounted factors on the SOD activity in the liver of rats, which is 95% (**Fig. 3*A***). This may indicate that the hepatocytes have a powerful protective enzyme system against stress and exogenous influences. The monooxygenases constantly interact with active forms of oxygen, so hepatocytes are not very sensitive to oxidative stress (Huang *et al.,* 2021).

Our experimental data have shown a significant share of stress factors' impact on the CAT activity: in the liver – 19% (p ≥0.95), kidneys – 40% (p ≥0.999), heart – 22% (p ≥0.99) (**Fig. 3*B***). Stress led to a decrease in CAT activity. According to ANOVA, the share of the combined effect of nettle extract and adrenaline is significant only in the heart – 17% (p ≥0.95) (**Fig. 3*B***).

Nettle extract significantly affects the activity of GR in erythrocytes and the heart; their influence accounts for 16% (p ≥0.95) and 46% (p ≥0.999) respectively (**Fig. 4*A***). Under adrenalin stress, nettle extract has a positive effect on GR activity in erythrocytes, kidneys, and heart, with corresponding shares of 14% (p ≥0.95), 14% (p ≥0.95) and 13% (p ≥0.99) (**Fig. 4*A***).

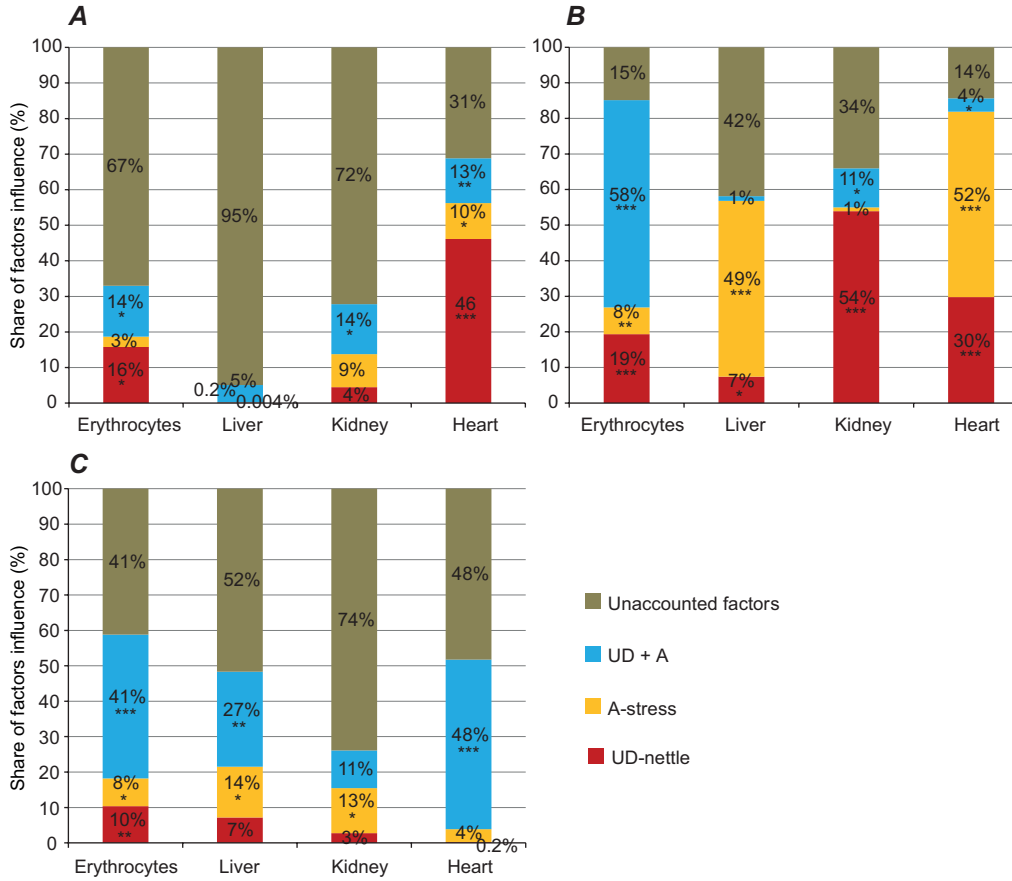

Fig. 4. ANOVA analysis of the effect of nettle extract, stress, and the combined effect of these two factors on the GR (***A***) activity, the content of GSH (***B***) and the GP (***C***) activity in erythrocytes, liver, kidney and heart of rats (* – p ≥0.95; ** – p ≥0.99; *** – p ≥0.999)

It was established that nettle extract has a significant effect on the GSH concentration in erythrocytes and all studied organs. The largest share of influence was detected in kidneys – 54% (p ≥0.999), while it was less pronounced in the heart and erythrocytes – 30% (p ≥0.999) and 19% (p ≥0.999), respectively. The minimum share of nettle extract factor was recorded for the GSH in the liver – 7% (p ≥0.95) (**Fig. 4*B***). These results of ANOVA analysis are very important as they indicate a direct effect of nettle extract (especially in the kidneys) on the glutathione chain of the antioxidant defense system (Zhang *et al.*, 2021).

Stress also has a significant effect on GSH content. Thus, the most pronounced effect is in the heart – 52% (p ≥0.999) and liver – 49% (p ≥0.999), less pronounced in erythrocytes – 8% (p ≥0.99) (**Fig. 4*B***). In stress-induced rats that were administered nettle extract, the share of the combined effect of nettle extract and adrenaline stress reaches 58% (p ≥0.999). This combined effect is significant both in the kidneys (11%; p ≥0.95) and in the heart (4%; p ≥0.95). The powerful effect of nettle extract on the GSH in erythrocytes is related to the fact that the blood reflects the internal state of the body and must, first of all, quickly respond to the increase of free radical processes.

The results of ANOVA analysis have shown that the effect of nettle extract on the activity of GP in erythrocytes is minimal (the share of influence is 10%; p ≥0.99). The share of stress effect on enzyme activity is 8% (p ≥0.95) in erythrocytes, 14% (p ≥0.95) in the liver and 13% (p ≥0.95) in the kidneys (**Fig. 4*C***). The administration of nettle extract before stress induction in rats has the most pronounced effect on GP activity in the heart (48%; p ≥0.999), erythrocytes (41%; p ≥0.999), and liver (27%; p ≥0.99). An independent effect of nettle extract on the activity of GR in erythrocytes and the heart, as well as the content of GSH in all studied organs was revealed.

It should be noted that the study of the share of influence of unaccounted factors, which is based on the calculation of the intragroup dispersion of the general set of data, allows to correctly interpret the results and explain the variability of indices due to the effect of one or another factor. The novelty of this article lies in the fact that this method of statistical analysis made it possible to identify the degree of influence of unaccounted factors on the biochemical and hematological parameters in stress-induced rats.

In our studies, we revealed a significan effect of unaccounted factors on some parameters. This may indicate that, in addition to the studied factors of nettle extract and stress, these parameters are influenced by other factors of both the internal and external environment, influencing the body. However, they were not taken into account in our experiment. Our results have shown that the heart muscle is less sensitive to the influence of unaccounted factors, while the liver is affected the most (possibly due to the intersection of various metabolic processes in this tissue). Unaccounted factors have a significant effect (the share of influence is more than 50%) on the concentration of LHP, ALT and CAT activity, while the least influence of unaccounted factors was detected for GSH in all studied tissues. In our opinion, it is due to the independent action of GSH to intercept free radicals in cells. The functioning of other metabolites and enzymes, such as glutathione peroxidase and glutathione reductase, depend on a glutathione pool. The effect of unaccounted factors on the content of lipoperoxidation products is high because their formation is influenced by various factors, including stress of various origins.

CONCLUSIONS

1. Stress influences the activity of AST and the number of erythrocytes in blood, SOD activity in erythrocytes and kidneys, CAT activity and the TBA-active products in all studied organs, GR activity in the heart, GSH in erythrocytes, liver, and heart, GP activity in erythrocytes, liver, and kidneys, carbonyl groups of proteins concentration in plasma, liver, and kidneys, and LHP in blood plasma.
2. ANOVA analysis showed that in rats that were not exposed to stress, nettle extract influences erythrocytes, leukocytes, and AST activity in blood; LHP in the liver; TBA-active products in kidneys, GR and CP in the heart; and GSH in all studied organs of rats.
3. Administration of nettle extract before stress induction in rats had impact on hemoglobin concentration, protein, and AST activity in blood, LHP in the kidneys and heart, carbonyl groups of proteins in blood and liver; SOD activity in kidneys and heart, CAT activity in the heart, GR activity and GSH content in erythrocytes, kidneys, and heart, GP activity in erythrocytes, liver, and heart.
4. The anti-stress and antioxidant properties of nettle extract in the body of animals were confirmed by ANOVA analysis.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of Interest: The authors received no specific funding for this work and declare no conflict of interest.

Human Rights: The article does not contain any experiments with humans.

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

AUTHOR CONTRIBUTIONS

Conceptualization, [O.B.]; methodology, [O.B.; N.H.]; investigation, [O.B.; O.Y.]; resources, [O.B.; N.H.]; data curation, [O.B., N.H., O.Y.]; writing – original draft preparation, [O.B.; V.H.]; writing – review and editing, [O.B.; V.H.]; visualization, [N.H.; O.Y.] supervision, [O.B.; V.H.]; project administration, [O.B.; V.H.]; funding acquisition, [–].

All authors have read and agreed to the published version of the manuscript.

SUPPLEMENTARY DATA

Detailed information on the principles of sample collection, research methods, and an absolute value of all indices is given in the Supplement via the Mendeley Data repository by the following link: https://doi.org/10.15421/021922

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ДИСПЕРСІЙНИЙ АНАЛІЗ ВПЛИВУ ЕКСТРАКТУ КРОПИВИ НА ДЕЯКІ БІОХІМІЧНІ ТА ГЕМАТОЛОГІЧНІ ПОКАЗНИКИ У СТРЕС-ІНДУКОВАНИХ ЩУРІВ

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Вступ. За допомогою двофакторного дисперсійного аналізу вивчали вплив 40% етанольного екстракту кропиви (перший фактор) й адреналінового стресу (другий фактор) як окремо, так і в поєднанні, на деякі біохімічні та гематологічні показники у щурів.

Матеріали та методи. В експериментах використали 4 групи щурів. Тварини груп UD-nettle та UD + A отримували 40% етанольний екстракт кропиви (*Urtica dioica* L.) у дозі 5 мл/кг маси тіла протягом 4 тижнів. Щури груп (C-контроль) та (A-stress) отримували відповідну кількість 40% етанолу. На 29-ту добу експерименту тваринам груп A-stress та UD+A моделювали стрес внутрішньом'язовим введенням 0,1% адреналіну гідрохлориду в дозі 1 мг/кг маси тіла. Щурам груп C та UD-nettle вводили відповідну кількість фізіологічного розчину. Через 24 години після ін'єкцій тварин декапітували під наркозом. Досліджували деякі гематологічні та біохімічні показники крові, печінки, серця та нирок щурів. Усі експериментальні дані опрацьовували за допомогою ANOVA-аналізу.

Результати. Адреналіновий стрес найінтенсивніше впливає на підвищення активності аспартатамінотрансферази у крові, зниження активності супероксид-дисмутази в еритроцитах і концентрації відновленого глутатіону в печінці та серці, а також на підвищення рівня продуктів вільнорадикальних реакцій у всіх досліджу-

ваних органах щурів. ANOVA-аналіз довів, що екстракт кропиви в організмі тварин, які не зазнавали стресу, найінтенсивніше впливає на зниження вмісту ліпопероксидів у печінці та карбонільних груп протеїнів у серці, а також активує глутатіонову ланку антиоксидантної системи в усіх органах. Введення екстракту кропиви щурам перед індукцією стресу інгібує перекисне окислення ліпідів у нирках і серці, знижує концентрацію карбонільних груп протеїнів у крові та печінці, концентрацію відновленого глутатіону й активність глутатіонпероксидази в еритроцитах.

Отримані результати встановили, що серце є більш стійким до стресу з точки зору утворення вільних радикалів, однак чутливим до дії екстракту кропиви перед індукцією стресу у щурів, що проявляється у підвищенні активності ферментативної та неферментативної ланок антиоксидантної системи. Усі досліджувані чинники суттєво впливали на вміст ТБК-активних продуктів у нирках, що супроводжувалося підвищенням їхньої концентрації. Встановлено, що більше 50% впливу невраховані чинники мають на накопичення продуктів перекисного окиснення ліпідів і активність каталази, тоді як найменше вони впливають на вміст відновленого глутатіону в усіх тканинах щурів

Висновок. Дисперсійний аналіз підтвердив тканинну специфічність індивідуального впливу досліджуваних чинників і їхню комбіновану дію на деякі біохімічні та гематологічні параметри в організмі щурів, а також протекторні й антиоксидантні властивості екстракту кропиви.

Ключові слова: екстракт кропиви, адреналіновий стрес, щури, дисперсійний аналіз

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