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BIOCHEMICAL ASPECTS OF INTERPRETING OXIDATIVE PROCESS INTENSITY IN THE LIVER OF RATS WITH ACETAMINOPHEN-INDUCED INJURY AFTER PARTIAL HEPATECTOMY

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Impaired liver regeneration after partial hepatectomy under conditions of prior toxic injury is a relevant problem in experimental and clinical biochemistry. Previous acetaminophen-induced injury creates an unfavorable redox environment for hepatic parenchymal restoration. In this context, particular importance is attached to the study of metallothioneins as redox-active, thiol-containing proteins, as well as indicators of oxidative protein modification, which reflect the intensity and direction of oxidative processes within the cell. Our study is devoted to the assessment of the content of metallothioneins and the degree of oxidative protein modification in the mitochondrial and cytosolic fractions of rat liver subjected to partial hepatectomy after acetaminophen intoxication. The experiments were performed on white outbred rats divided into two groups: animals that underwent partial hepatectomy by the Mitchell and Willenbring method (C/PH) and animals that underwent two-thirds liver resection after acute paracetamol-induced injury, modeled by intragastric administration of the xenobiotic at a dose of 1250 mg/kg body weight once daily for two days in the form of a 2% starch gel suspension (TI/PH). Tissue sampling was performed at 24, 48, 72, and 168 h after surgical intervention. The content of metallothioneins and the levels of protein carbonylation and free SH groups were assessed using spectrophotometric biochemical methods. The results of the study showed that in animals with partial hepatectomy after toxic injury caused by acetaminophen, the level of metallothioneins in the liver's cytosolic fraction increases throughout the entire regeneration period. At the same time, progressive depletion of the thiol pool and an increase in protein carbonylation levels were recorded in the mitochondrial fraction, indicating the predominance of pro-oxidant processes. The enhancement of oxidative protein modification was accompanied by a decrease in the content of free SH groups, which is consistent with a disturbance of redox balance and depletion of the thiol-disulfide system. Interpretation of the obtained results indicates that the intensity of oxidative processes in the regenerating liver after acetaminophen-induced injury is determined by the compartment-specific interaction between the metallothionein system and the thiol status of proteins. The identified changes have important theoretical significance for understanding the molecular mechanisms of liver regeneration and may be used for the biochemical interpretation of the state of regenerating parenchyma under toxic injury.

Keywords: metallothioneins, protein SH-group, carbonyl derivatives, partial hepatectomy, acetaminophen, toxic injury, liver regeneration, liver

Introduction. The liver has a unique capacity to restore its structural and functional potential after toxic or inflammatory injury and tissue loss. The regenerative reaction is part of liver remodeling that occurs in cirrhosis and transient hepatomegaly in response to increased metabolic demand (van de Laarschot et al., 2016). Radical surgical resection still remains one of the most important methods of treatment of the majority of liver neoplasms (Jia et al., 2018). Immediately after injury, hepatectomy is applied to control sepsis under conditions of liver necrosis and persistent bile leakage from segmental bile ducts that are not amenable to reconstruction (Cohen et al., 2019). The regenerative property of the liver makes it possible to perform transplantation as an effective and primary option for the treatment of terminal liver failure (acute or chronic) (Collin de l'Hortet et al., 2016).

In most literature sources, among the main causes of acute liver failure, injury caused by the over-the-counter analgesic and antipyretic acetaminophen (paracetamol, APAP) is highlighted. Acetaminophen-induced injury is associated with depletion of the glutathione system, impairment of mitochondrial function, activation of oxidative stress, and an imbalance of signaling pathways involved in regulating hepatocyte proliferation (Li et al., 2025; Markose et al., 2018; Luo et al., 2023). Under such conditions, regeneration after partial hepatectomy occurs in an environment of increased prooxidant load and impaired detoxification capacity (Kopylchuk et al., 2025), which may lead to qualitatively deficient liver recovery.

Liver injury stimulates increased generation of reactive oxygen species (ROS), which is an important factor in modulating the compensatory regenerative response (Tang et al., 2016). According

to the rheostat theory, ROS determine cell fate (survival-death) in a dose-dependent manner (Goltsev et al., 2024). At low and moderate concentrations, ROS serve as mediators of redox signaling (the state of eustress). In contrast, their excessive production leads to biomolecular damage, cellular dysfunction, and cell death. Prevention of ROS-induced harmful effects is ensured by the coordinated action of the components of the antioxidant defense system, which is directed at maintaining intracellular levels of these metabolites within the range of physiological norm (Jomova et al., 2024; Manful et al., 2025).

Under conditions of acetaminophen-induced injury and after partial hepatectomy, the intensity of oxidative processes becomes crucial for the course of liver regeneration, since redox signaling determines the balance between the adaptive proliferative response and cellular damage (Li et al., 2025). In this context, metallothioneins (MTs), as thiol-containing redox-active proteins (Yang et al., 2024), as well as indicators of oxidative protein modification, are considered sensitive biochemical markers that reflect the state of the prooxidant–antioxidant equilibrium in regenerating liver tissue. A comprehensive assessment of these parameters makes it possible to deepen the interpretation of the intensity of oxidative processes and their role in the formation of a functionally competent or maladaptive regenerative response after toxic injury. In this regard, the aim of the work was to assess the content of metallothioneins and the degree of oxidative protein modification in the mitochondrial and cytosolic fractions of rat liver with acetaminophen-induced injury after partial hepatectomy.

Materials and methods. The experiments were performed on white outbred rats aged 140–150 days and weighing 150–180 g, which were kept in the vivarium of the Educational and Scientific Institute of Biology, Chemistry, and Bioresources of Yuriy Fedkovych Chernivtsi National University. During the study, the animals were housed in plastic cages for rodents (one animal per cage). The bedding consisted of sterilized wood shavings. The rats consumed a complete diet and had free access to previously sterilized tap water. The study was conducted in accordance with the current requirements and standards of humane treatment of animals ("European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1986); the Law of Ukraine "On the Protection of Animals from Cruel Treatment" (as amended in accordance with Law No. 5456-VI of 16.10.2012); the provisions set out in the NIH Guide for the Care and Use of Laboratory Animals), in accordance with the decision of the Bioethics Committee on Scientific Research at Yuriy Fedkovych Chernivtsi National University (Protocol No. 1 dated 04.04.2024).

The animals were divided into two groups: Group I – rats subjected to resection of 2/3 of the liver (C/PH); Group II (TI/PH) – rats that underwent partial hepatectomy after modeling of acute toxic injury induced by acetaminophen. Partial hepatectomy was conducted by the method of Mitchell and Willenbring by applying sequential ligatures followed by removal of the left lateral and medial lobes of the liver, which constitutes 2/3 (70%) of its mass (Tsomaia et al., 2020). The surgical procedure in rats was performed in the morning on an empty stomach under thiopental sodium anesthesia with adherence to sterile conditions. The binding of liver tissue was carried out using surgical sterile silk (LLC "Igar", Ukraine). Continuous sutures were applied using surgical sterile material "Kapron B" (LLC RPC "Biopolymer", Ukraine). Acute toxic injury was modeled by intragastric administration of paracetamol via a probe at a dose of 1250 mg/kg of the animal's body weight once per day for 2 days in the form of a suspension of a 2% starch gel solution (Kopylchuk et al., 2025). Removal of the animals from the experiment was carried out in compliance with bioethical principles at 24 (initiation phase), 48 (active cell proliferation phase), 72 (termination phase), and 168 (distant period) hours after partial hepatectomy. The control for comparison was liver tissue resected during partial hepatectomy (preoperative period at 0 h).

The mitochondrial fraction of rat liver was obtained by the method of differential centrifugation (Allen et al., 2023). The liver was homogenized using a Potter–Elvehjem homogenizer in a buffer containing 0.25 M sucrose, 1 mM EDTA, and 10 mM Tris-HCl (pH 7.4). The mitochondrial pellet was suspended in the homogenization medium without EDTA. Isolation of the microsomal fraction was undertaken as described in (Kamath & Narayan, 1972). The principle of the method is based on the fact that microsomes can form aggregates in the presence in the medium of divalent metal ions, particularly Ca^{2+} and Mg^{2+}, as these ions neutralize their negative charge. The supernatant obtained after microsome precipitation was used in further studies as the cytosolic (postmicrosomal) fraction. All stages were carried out at a temperature of 0-4 °C. Protein content was determined by the Bradford method.

Assessment of metallothioneins content was conducted by the method described in (Tsudzevich & Kalinin, 2011), which is based on thiols

determination using 5,5′-dithiobis-2-nitrobenzoic acid (DTNB, Ellman's reagent) after extraction in the ethanol/chloroform system. The metallothioneins content in the sample was determined from a calibration curve constructed using reduced glutathione solutions of different concentrations.

The content of protein sulfhydryl groups (SH-) was determined using 5,5′-dithiobis-2-nitrobenzoic acid, which interacts with free SH groups. The reaction products are a mixed disulfide and 5-thio-2-nitrobenzoic acid (TNB). The amount of the formed yellow TNB anion is directly proportional to the concentration of free SH groups in the sample. Sample absorbance was measured at λ=412 nm using a CARY 60 spectrophotometer (USA). The content of thiol groups was calculated taking into account the molar extinction coefficient of 11,400 $M^{-1} \cdot cm^{-1}$ (Murphy & Kehrer, 1989).

The content of carbonyl groups was assessed by the reaction of oxidized amino acid residues with 2,4-dinitrophenylhydrazine (2,4-DNPH), resulting in the formation of protein hydrazones, the optical density of which was measured spectrophotometrically at λ=370 nm. The content of carbonyl groups of oxidatively modified proteins was calculated using the molar extinction coefficient of 21×10^3 $M^{-1} \cdot cm^{-1}$ (Nagasawa et al., 2000).

For statistical processing of the obtained results, the GraphPad Prism 8.0.1 software was used (GraphPad Software, San Diego, California, USA; http://www.graphpad.com). Determination of significant differences between the mean values of samples that corresponded to a normal distribution and had homogeneous variances was performed using two-way analysis of variance with the post hoc Tukey test. Results were considered significant at $p<0.05$. Data are presented as mean value ± SEM.

Results and Discussion. We have established that in the cytosolic and mitochondrial fractions of the liver of rats with partial hepatectomy (C/PH), the content of metallothioneins increases statistically significantly only at the initial stages (24 and 48 h) of recovery of the organ parenchyma, compared with preoperative values at 0 h. If in the cytosol, under the studied conditions, at 24 and 48 h of the experiment the level of metallothioneins increases by 62% and 55.5%, respectively, then in mitochondria at the indicated time points of regeneration, the content of metallothioneins exceeds the preoperative values by 44% and 39%, respectively (Fig. 1). The observed increase in the level of metallothioneins at 24 and 48 h after partial hepatectomy can be considered an early adaptive response of the regenerating liver, aimed at maintaining redox homeostasis during the initiation period and early hepatocyte proliferation. Such induction is likely due to the activation of redox-sensitive signaling pathways that regulate cell entry into the cell cycle. According to the literature, metallothioneins MT1 and MT2 are normally localized predominantly in the cytoplasm; however, they can also be detected in the nucleus and mitochondria, and their subcellular distribution changes depending on the phase of the cell cycle. During liver regeneration after partial hepatectomy, MTs translocate to the nucleus, which is associated with the provision of zinc to transcription factors and enzymes involved in cell proliferation (Mohammed et al., 2025; Smith et al., 2008; Subramanian & Deepe, 2017).

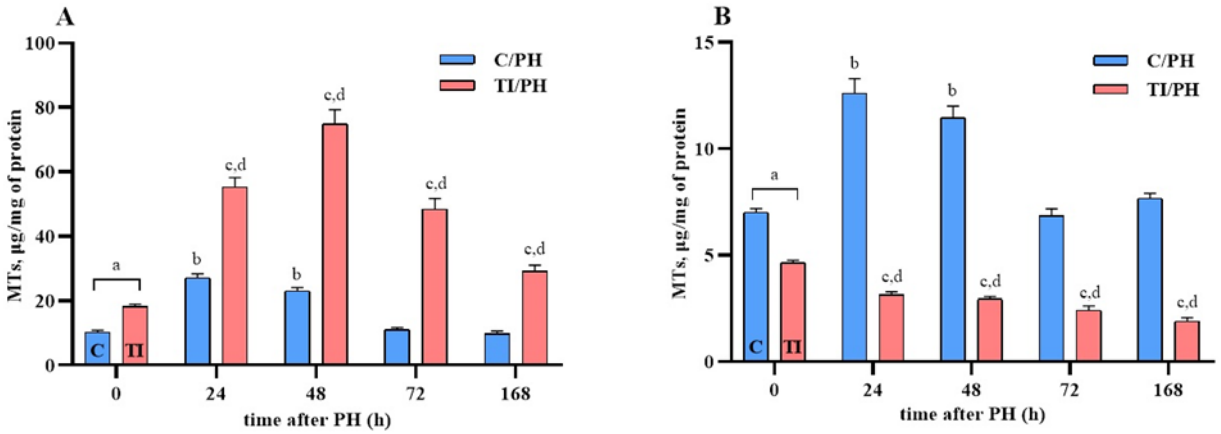

Fig. 1. Metallothioneins content in the cytosolic (A) and mitochondrial (B) fractions of rat liver with partial hepatectomy after toxic injury by acetaminophen.

Note (here and hereinafter): a – statistically significant difference between the TI group and the control group (C) at 0 h; b – statistically significant difference of the C/PH groups at each time point compared to the C group at 0 h; c – statistically significant difference of the TI/PH groups at each time point compared to the TI group at 0 h; d – statistically significant difference between the TI/PH and C/PH groups at the corresponding time point (e.g., 24 h vs 24 h, etc.).

At the same time, in rats with 2/3 hepatic resection after toxic acetaminophen injury (TI/PH), divergent changes in MTs content were recorded depending on intracellular compartmentalization (Fig. 1). Hypothetically, the involvement of metallothioneins in the formation of antioxidant defense may be caused both by their ability to chelate redox-active metals, in particular Cu, which prevents the involvement of the latter in reactions critical for the development of oxidative stress, such as Fenton reactions, and by the direct participation of metallothionein thiol groups in the neutralization of reactive oxygen species and nitrogen oxides (Yang et al., 2024; Ruttkay-Nedecky et al., 2013). In this regard, when interpreting the role of metallothioneins in antioxidant defense, it is advisable to consider two interrelated components: the level of expression, which determines the total cellular pool of metallothioneins, and the functional activity of thiol groups involved in maintaining a reducing intracellular environment. If metallothionein expression can be regulated by the concentrations of reactive oxygen and nitrogen species (ROS/RNS), then the redox state of their thiol groups largely depends on the cell's overall reducing status (Marikar & Zi-Chun, 2023).

In the cytosolic fraction of the liver of animals in the TI/PH group, an increase in levels of metallothioneins was observed throughout the entire experimental period (168 h), with maximal values at 48 h of tissue remodeling (by 76%) compared with the indicators of the TI group at 0 h (Fig. 1A). Such dynamics are consistent with the known role of metallothioneins in maintaining zinc homeostasis and redox equilibrium during active tissue remodeling. Complexation with zinc supports the structural stability of metallothioneins and determines zinc's bioavailability in the cell. In the zinc-bound state, metallothioneins carry out the redistribution of this trace element among cellular pools. This process depends on dietary intake and transporter activity, which can both donate and remove zinc from metalloproteins. The apo-form of metallothioneins is capable of inhibiting the interaction of DNA with zinc-finger type transcription factors (in particular Sp1 and TFIIIA), whereas the Zn-bound form restores their transcriptional activity. By regulating zinc availability, metallothioneins participate in the control of apoptosis, cell proliferation, and gene expression. Under conditions of oxidative stress, metallothioneins effectively neutralize free radicals, accompanying this process with the formation of disulfide forms and additional release of zinc. The disulfide forms of metallothioneins are unstable and are reduced to the thiol state in a more reducing environment, which is maintained by selenium and a high GSH/GSSG ratio (Aziz & Vaithilingam, 2021; Li et al., 2019; Juárez-Rebollar et al., 2017; Domán et al., 2023). Thus, metallothioneins play an important role in preserving the cellular glutathione pool in rats with prior acetaminophen intoxication following partial hepatectomy. Their advantage over glutathione as antioxidants is due not only to the high concentration of thiol groups but also to the specific organization of cysteine clusters, which ensures efficient scavenging of reactive oxygen species and multiple redox cycles. On the other hand, inflammatory processes and oxidative stress activate MTs, which behave similarly to acute-phase proteins. Lipopolysaccharide enhances MT1 induction, particularly in the liver, modulating zinc-dependent proteins such as p53, NF-κB, and Sp1 (Juárez-Rebollar et al., 2017; Mohammed et al., 2025; Yang et al., 2024; Verhoef et al., 2018; Subramanian & Deepe, 2017).

However, in the liver mitochondria of rats in the TI/PH group, throughout the entire experimental period (168 h), a decrease in MTs content occurs. The lowest indicators of the level of MTs in the TI/PH group are recorded during the final stages of regeneration, at 72 and 168 h after 2/3 liver resection (a decrease of 48% and 59%, respectively) (Fig. 1B). The reasons for this may include both a reduction in the number of metal-depositing molecules at the level of subcellular localization and oxidation of their functional groups, which reduces the deposition potential of the protein.

At the next stage of the study, the content of free SH groups and carbonyl derivatives was determined to assess the degree of protein oxidative modification. In both subcellular fractions of the liver of rats with partial hepatectomy (C/PH), during the 48 h of the regeneration process, accumulation of protein carbonyl derivatives with a simultaneous decrease in the content of free sulfhydryl groups is recorded compared with the preoperative values at 0 h. In particular, in the liver cytosol of animals in the C/PH group at 24 and 48 h after partial hepatectomy, with an increase in the level of carbonyl derivatives by 44% and 34% (Fig. 2A), the content of free protein SH groups decreases by 36% and 26% (Fig. 3A) at the indicated time points of regeneration. Regarding the intensity of changes in the studied indicators in liver mitochondria under these experimental conditions, at 24 and 48 h of tissue recovery the level of protein carbonylation increases by 58% and 50% (Fig. 2B) against the background of a decrease in the content of free thiol groups by 51% and 42% (Fig. 3B), respectively, compared with the preoperative values at 0 h.

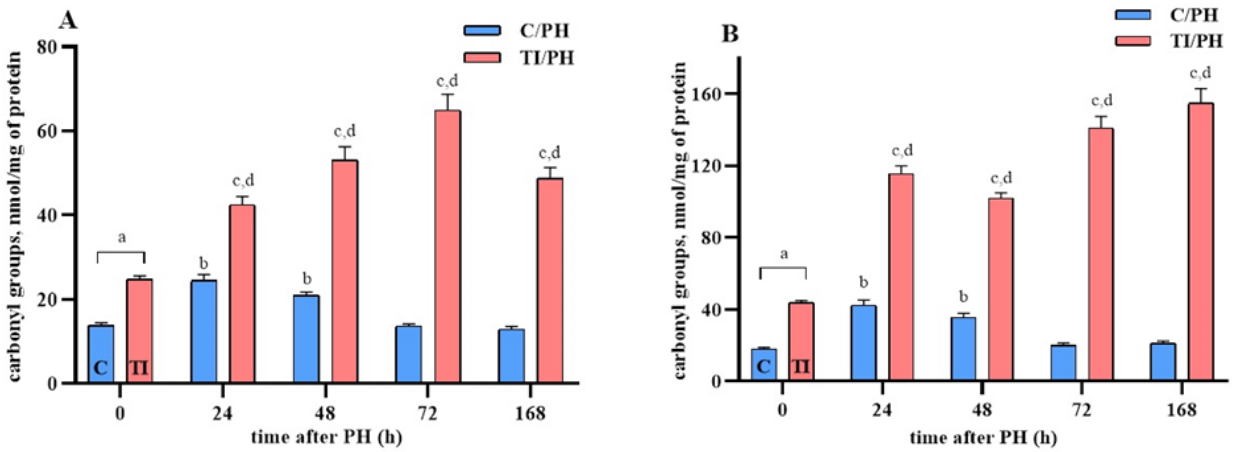

Fig. 2. Carbonyl derivative content in cytosolic (A) and mitochondrial (B) fractions of rat liver with partial hepatectomy after toxic injury by acetaminophen

The content of carbonyl derivatives is regarded as a widely used stable marker of oxidative protein damage and, in general, oxidative stress. Primary and secondary protein carbonyl derivatives (aldehydes and ketones) are distinguished. Primary protein carbonylation occurs as a result of oxidative deamination of lysine, arginine, proline, and threonine by means of a radical-mediated mechanism (the main pathway), oxidative deamination of basic amino acids involving dicarbonyls from the Maillard reaction, and oxidative cleavage of the peptide chain through the α-amidation pathway or oxidation of the side chains of glutamyl residues. The formation of secondary carbonyl derivatives is realized through the interaction of amino groups of amino acids, in particular cysteine, lysine, and histidine, with products of lipid peroxidation (malondialdehyde (MDA), 4-hydroxy-2,3-nonenal (HNE), and acrolein) (Estévez et al., 2022; Gonos et al., 2018). Protein carbonylation causes loss of their enzymatic activity and ligand-binding properties, increased sensitivity to proteasomal degradation, aggregation, and modification of transcriptional activity. Severe and prolonged oxidative damage may lead to a decrease in the proteolytic susceptibility of proteins, as is assumed, due to the accumulation of proteolysis-resistant aggregates that bind to the proteasome (Ling et al., 2025; Nyström, 2005; Aryal et al., 2014).

An especially sensitive target for oxidative post-translational modifications by reactive metabolites of oxygen and nitrogen is the sulfhydryl group of the cysteine (Cys) side chain. As is known, SH groups may undergo deprotonation, forming a thiolate anion (RS^-). Thiolated Cys residues exhibit high reactivity. The tendency to donate a proton is determined by the pKα value, local pH, and the electrostatic environment. It is noted that in protein molecules, specific hydrogen bond donors and an electropositive local environment cause a decrease in pKα due to stabilization of the negatively charged thiolate, whereas in a hydrophobic or electronegative local environment the opposite effect is realized (Holendova & Plecita-Hlavata, 2023; Percio et al., 2024).

Oxidation of cysteine residues is classified as reversible or irreversible, depending on the cell's redox state. Reversible oxidative modifications of cysteine (S-sulfenylation, S-nitrosylation, S-glutathionylation, disulfide bond formation, and others) occur under conditions of low oxidative activity and are directed toward the modulation of protein function. Sulfenic acid (SOH) is an intermediate oxoform of cysteine, labile and prone to other modifications. In the presence of excess oxidants, SOH can be gradually converted to sulfinic (SO_2H; less readily reversible modification) and sulfonic acids (SO_3H; irreversible modification) with higher degrees of oxidation (+2 and +4, respectively). Despite available evidence regarding the possibility of enzymatic reduction of SO_2H by ATP-dependent sulfiredoxin, the formation of these oxoforms often indicates oxidative damage and may lead to loss of protein function, making them targets for degradation (Pham et al., 2021; Yang & Silverstein, 2024; Stair & Hicks, 2023; Hayward & Baud, 2025).

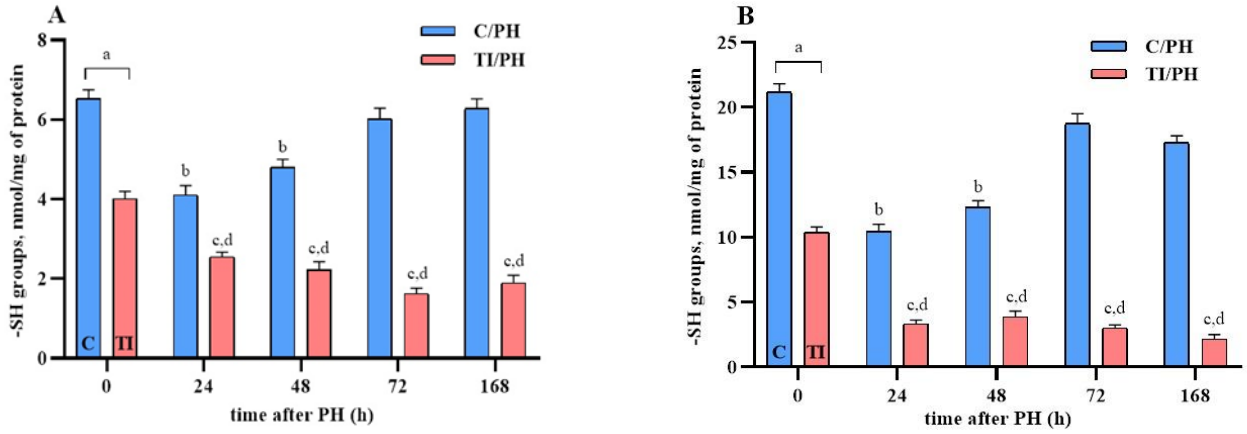

Fig. 3. Free protein SH-group content in cytosolic (A) and mitochondrial (B) fractions of rat liver with partial hepatectomy after toxic injury by acetaminophen

Analysis of the results indicates a slightly higher degree of oxidative damage to proteins in liver mitochondria under conditions of partial hepatectomy (C/PH). The enhancement of oxidative protein damage we established is consistent with the results of parallel studies, in which intensification of ROS formation is recorded at the indicated time points. In particular, in liver mitochondria of animals after partial hepatectomy (C/PH), during the 48 h of the regeneration process, an increase in the rate of superoxide anion radical ($O_2^{\bullet-}$) generation and in the content of hydrogen peroxide (H_2O_2) was observed.

Regarding animals with partial hepatectomy after toxic damage from paracetamol (TI/PH), an increase in protein carbonylation is observed in both the cytosolic and mitochondrial fractions of the liver throughout the entire period of parenchymal recovery (Fig. 2), accompanied by a decrease in the content of free SH groups (Fig. 3). The enhancement of protein carbonylation in the cytosolic and mitochondrial fractions of the liver of animals in the TI/PH group throughout the entire regeneration period reflects the intensification of oxidative processes under the combined action of acetaminophen-induced injury and partial hepatectomy. The simultaneous decrease in the content of free SH groups indicates oxidation of the protein thiol pool and depletion of the redox-buffering capacity of the cell, consistent with a disturbance of the GSH/GSSG ratio. Under these conditions, induction of metallothioneins in the liver cytosol of rats in the TI/PH group may be considered a compensatory adaptive response aimed at maintaining redox homeostasis by scavenging reactive oxygen species and partially substituting the glutathione system in free radical neutralization. However, the persistence of a high level of protein carbonylation, especially in the mitochondrial fraction, indicates that under conditions of excessive oxidative load, the protective potential of metallothioneins is insufficient to fully prevent oxidative damage to biomolecules in the regenerating liver.

Conclusions. It was established that in rats with partial hepatectomy after acetaminophen-induced injury, throughout the entire regeneration process, a compartment-specific rearrangement of the metallothionein system occurs, characterized by an increase in the level of metallothioneins in the cytosolic fraction and a simultaneous decrease in their content in mitochondria. Interpretation of the obtained results indicates that induction of the cytosolic pool of metallothioneins has a compensatory-adaptive character and is aimed at maintaining zinc homeostasis and redox equilibrium under conditions of oxidative load, whereas depletion of mitochondrial metallothioneins reflects the limited protective mechanisms in this compartment.

At the same time, the combination of acetaminophen intoxication with partial hepatectomy intensifies oxidative protein modification, as evidenced by an increase in the level of protein carbonylation and a decrease in the content of free SH groups in the cytosolic and, especially, mitochondrial fractions of the liver. The obtained results indicate depletion of the protein thiol pool and impairment of cellular redox-buffering capacity, consistent with an imbalance in the GSH/GSSG system and reflecting the predominance of prooxidant processes over antioxidant ones during liver regeneration.

Overall, the interpretation of the obtained results allows the conclusion that the intensity of oxidative processes in the regenerating liver after acetaminophen-induced injury is determined by the consistency between the metallothionein system, the thiol status of proteins, and the glutathione

component of antioxidant defense. The identified compartment-specific redox dysregulation is of fundamental importance for understanding the molecular mechanisms underlying qualitatively deficient liver regeneration and may be used to develop biochemical criteria for evaluating the effectiveness of recovery processes and potential approaches to their therapeutic correction.

Conflict of interest. *The authors declare that the study was conducted in the absence of any commercial or financial relationships that could be interpreted as a potential conflict of interest.*

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БІОХІМІЧНІ АСПЕКТИ ІНТЕРПРЕТАЦІЇ ІНТЕНСИВНОСТІ ОКИСЛЮВАЛЬНИХ ПРОЦЕСІВ У ПЕЧІНЦІ ЩУРІВ ІЗ АЦЕТАМІНОФЕН-ІНДУКОВАНИМ УРАЖЕННЯМ ПІСЛЯ ЧАСТКОВОЇ ГЕПАТЕКТОМІЇ

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Порушення регенерації печінки після часткової гепатектомії за умов попереднього токсичного ураження є актуальною проблемою експериментальної та клінічної біохімії. Попереднє ацетамінофен-індуковане ушкодження формує несприятливе редокс-середовище для відновлення печінкової паренхіми. У цьому контексті особливого значення набуває вивчення металотіонеїнів як редокс-активних тіоловмісних білків, а також показників окислювальної модифікації протеїнів, які відображають інтенсивність та спрямованість окислювальних процесів у клітині. Наше дослідження присвячене оцінці вмісту металотіонеїнів та ступеня окислювальної модифікації протеїнів у мітохондріальній та цитозольній фракціях печінки щурів із частковою гепатектомією після ацетамінофенової інтоксикації. Експерименти проводили на білих нелінійних щурах двох груп: тварини, яким виконували часткову гепатектомію методом Mitchell and Willenbring (C/PH) та тварини з резекцією 2/3 печінки після гострого парацетамол-індукованого ураження, що моделювали шляхом внутрішньошлункового введення ксенобіотика в дозі 1250 мг/кг маси тіла тварини один раз на добу протягом двох діб у вигляді суспензії 2% розчину крохмального гелю (TI/PH). Забір матеріалу здійснювали через 24, 48, 72 та 168 год після оперативного втручання. Уміст металотіонеїнів, рівень карбонілювання протеїнів та вільних SH-груп оцінювали із застосуванням спектрофотометричних біохімічних методів. Результати досліджень показали, що у тварин із частковою гепатектомією після токсичного ураження ацетамінофеном відбувається підвищення рівня металотіонеїнів у цитозольній фракції печінки впродовж усього регенераційного періоду. Водночас у мітохондріальній фракції реєстрували прогресивне виснаження тіолового пулу та зростання рівня карбонілювання протеїнів, що свідчить про домінування прооксидантних процесів. Підвищення окислювальної модифікації білків супроводжувалося зниженням вмісту вільних SH-груп, що узгоджується з порушенням редокс-балансу та виснаженням тіол-дисульфідної системи. Інтерпретація отриманих результатів свідчить, що інтенсивність окислювальних процесів у регенеруючій печінці після ацетамінофен-індукованого ураження визначається компартмент-специфічною взаємодією металотіонеїнової системи та тіолового статусу протеїнів. Виявлені зміни мають важливе теоретичне значення для розуміння молекулярних механізмів регенерації печінки та можуть бути використані для біохімічної інтерпретації стану регенеруючої паренхіми за умов токсичного ушкодження.

Ключові слова: металотіонеїни, протеїнові SH-групи, карбонільні похідні, часткова гепатектомія, ацетамінофен, токсичне ураження, регенерація печінки, печінка

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