Innov Biosyst Bioeng, 2026, vol. 10, no. 1,
doi: 10.20535/ibb.2026.10.1.359682

Original article

INDICATORS OF OXIDATIVE STRESS IN RAT BRAIN TISSUE UNDER CONDITIONS OF PROLONGED ARTERIAL HYPERTENSION AND ITS CORRECTION WITH DIFFERENT GENERATIONS OF BETA-BLOCKERS

I.F. Belenichev*, A.O. Svitlytskyi, O.V. Hancheva, T.A. Hrekova, T.M. Matveishyna

Zaporizhzhia State Medical and Pharmaceutical University, Zaporizhzhia, Ukraine

*Corresponding author: i.belenichev1914@gmail.com

Received 13 March 2026; Accepted 27 April 2026

Background. The significant increase in the number of patients with arterial hypertension both worldwide and in our country necessitates a more detailed study of the pathogenetic features of changes that occur in target organs, including the brain, in conditions of prolonged elevated blood pressure and against the background of its correction with beta-blockers of different generations.

Objective. The aim of the study was to examine oxidative stress indicators in brain homogenates of animals with arterial hypertension and to determine the effect of long-term correction with different generations of beta-blockers on the state of pro- and antioxidant components of OS.

Methods. One intact and four groups of experimental animals were studied. Experimental animals with spontaneous arterial hypertension were administered propranolol, carvedilol, and hypertril in therapeutic doses. The oxidative stress indicators (oxidative modification of proteins markers (aldehyde dinitrophenylhydrazones and carboxyphenylhydrazones) and content of reduced glutathione, and the activity of Superoxide dismutase, Glutathione peroxidase) in animal brain homogenates were biochemically studied.

Results. It was established that prolonged arterial hypertension is accompanied by a deterioration in the state of antioxidant systems. Correction of high blood pressure with propranolol does not significantly affect the state of oxidative stress indicators. Carvedilol has a moderate antioxidant effect, while hypertril has a powerful antioxidant effect, which is manifested in a decrease in oxidative modification of proteins markers, and increased of antioxidant system markers content.

Conclusions. Long-term administration of Propranolol stabilizes arterial pressure but does not alleviate oxidative stress in the brain, evidenced by sustained high levels of OMP markers (ADPH and CPH) and suppressed antioxidant defense (SOD, GSH, GPx). Carvedilol exerts a moderate antioxidant effect by lowering CPH levels but fails to significantly restore the activity of key antioxidant enzymes (SOD, GPx) or reduced glutathione levels. Hypertril exhibits a potent dual effect, providing both antihypertensive control and robust antioxidant neuroprotection. Its mechanism involves the significant reduction of OMP markers (ADPH and CPH) and the restoration of the antioxidant defense system (SOD, GSH, GPx).

Keywords: arterial hypertension; beta-blockers; oxidative stress; hippocampus.

Introduction

In daily life, humanity encounters environmental pollution, prolonged sun exposure, smoking, and alcohol consumption. These factors contribute to excessive levels of free radicals; when these exceed the body's antioxidant defense systems, oxidative stress (OS) is initiated. Numerous studies have established that OS is a non-specific factor of cell damage in the pathogenesis of many diseases, including arterial hypertension (AH) [1-3]. It is now clearly proven that AH leads to damage in multiple organs, specifically the brain, through the involvement of small vessels. This results in the development of cognitive dysfunction and, in severe cases, chronic neurodegenerative diseases such as Alzheimer's (AD) or Binswanger's disease [4, 5]. While the role of OS in forming pathological changes in brain vessels and tissues during AH is indisputable, the impact of long-term correction with hypotensive drugs, including various generations of beta-blockers, on the state of the brain's antioxidant system and oxidative processes remains debatable.

For nearly half a century, beta-blockers have proven effective not only in cardiology but also in endocrinology, general therapy, and psychiatry. Notably, for a long time, beta-blockers were considered second-line drugs for AH therapy. However, according to the updated AH treatment recommendations presented at the 2024 ESH (European Society of Hypertension) Congress, beta-blockers have been re-included as first-line antihypertensive therapy. This decision was based on a meta-analysis showing that beta-blockers are not inferior to other major classes in reducing cardiovascular risk and effectively stabilizing blood pressure (BP) [6].

Despite years of studying the influence of beta-blockers on pathophysiological processes, and evidence that metoprolol, carvedilol, and bisoprolol re-

duce OS markers alongside heart failure relief [7], the understanding of their direct influence on oxidative metabolism within brain structures remains insufficiently studied, especially regarding the latest generations of drugs.

The aim of the study was to examine oxidative stress indicators in brain homogenates of animals with arterial hypertension and to determine the effect of long-term correction with different generations of beta-blockers on the state of pro- and antioxidant components of OS.

Materials and methods

The study utilized 50 male rats: 40 spontaneously hypertensive rats (SHR), second generation, aged 8 months, with an initial weight of 280-300 g with systolic/diastolic BP ranged between 178.1 ± 2.61/96.5 ± 2.51 mmHg; 10 normotensive control Wistar-Kyoto rats (WKR), with an initial weight of 200-220 g with BP ranged between 118.1 ± 10.9 / 66.9 ± 2.1 mmHg.

The experimental part of the study was conducted at the Training and Research Medical-Laboratory Center with a Vivarium of Zaporizhzhia State Medical and Pharmaceutical University (ZSMPU) in strict compliance with the national standard "General Ethical Principles of Animal Experiments" (Ukraine, 2001), aligned with Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes. No violations of moral and ethical standards were identified during the research by the Bioethics Committee of Zaporizhzhia State Medical and Pharmaceutical University of the Ministry of Health of Ukraine (Protocol No. 2, dated March 15, 2023).

The study design employed an integrated experimental approach combining parallel instrumental, functional, biochemical, and statistical assessments. The protocol included monitoring body weight and measuring BP using the BP-2000 Series II Blood Pressure Analysis System (Visitech Systems, USA) via a non-invasive tail-cuff method. To ensure data validity and minimize stress-induced artifacts, animals were acclimatized to the restraint holders and the warming platform (maintained at 37°C) prior to data collection. Functional monitoring, including body weight recording and BP measurements, was conducted at three critical timepoints: at baseline (following the acclimatization period), on day 7 and at the study endpoint, day 31, immediately prior to sacrifice. The redox status of the central nervous system was assessed in brain homogenates by quantifying markers of oxidative protein modification (OPM) and evaluating the capacity of the antioxidant defense system (ADS).

The experimental animals were randomly assigned to five experimental groups (n=10 per group). The groups were defined as follows: Group 1 (Control): normotensive WKR; Group 2: SHR (Control); Groups 3-5: SHRs receiving pharmacological treatment daily for 30 days orally (suspended in 1 % starch mucilage). Group 3 animals were treated with "Propranolol" (Pharmaceutical Group "Zdorovje", Ukraine), a non-selective, lipophilic beta1, beta2-adrenoblocker with high neuroavailability, at a dose of 50 mg/kg body weight (b.w.). Group 4 SHRs were treated with "Carvedilol" (Kyiv Vitamin Plant, Ukraine), a hybrid non-selective beta- and alpha1-adrenoblocker with antioxidant activity, at a dose of 50 mg/kg b.w. Group 5 was tested with "Hypertril" (SPA "Pharmatron", Ukraine), a novel derivative of 4-amino-1,2,4-triazole characterized as a super-selective beta-adrenoblocker with NO-modulating effects, at a dose of 20 mg/kg b.w. (Fig. 1).

At the study endpoint (day 31), animals were euthanized by rapid decapitation under sodium thiopental anesthesia (40 mg/kg, intraperitoneally). Brain tissues were rapidly excised and homogenized using a Heidolph Instruments D-91126 homogenizer (ser. 091002770, Germany). The homogenates were subjected to differential centrifugation (Sigma Laborzentrifugen D-37520, Germany) at 15,000 g to isolate the cytosolic fraction for biochemical analysis.

Oxidative stress markers and antioxidant enzyme activities were quantified in brain homogenates. OPM, namely, aldehyde dinitrophenylhydrazones (ADPH) and carboxyphenylhydrazones (CPH) were assayed via reaction with 2,4-dinitrophenylhydrazine by the method of B. Halliwell [8]. Superoxide dismutase (SOD) activity was determined by the inhibition of nitroblue tetrazolium (NBT) reduction (Beauchamp, C. and Fridovich, I.) [9].

Glutathione peroxidase (GPx) activity was measured according to the method of E. Beutler [10].

Reduced glutathione (GSH) was determined by standard spectrophotometric methods (Ellman's assay) [11].

Total protein level was quantified using the Biuret method [12].

All experimental results were processed using the STATISTIKA software package (license No. JPZ804I382130ARCN10-J), Microsoft Excel 10.0 (Microsoft Corporation, USA), and Python 3.0 statistical and visualization libraries.

Statistical significance was calculated by a series of independent pairwise comparisons of groups using Student's t-test / Mann–Whitney U-test. Differences were considered statistically significant at $p < 0.05$.

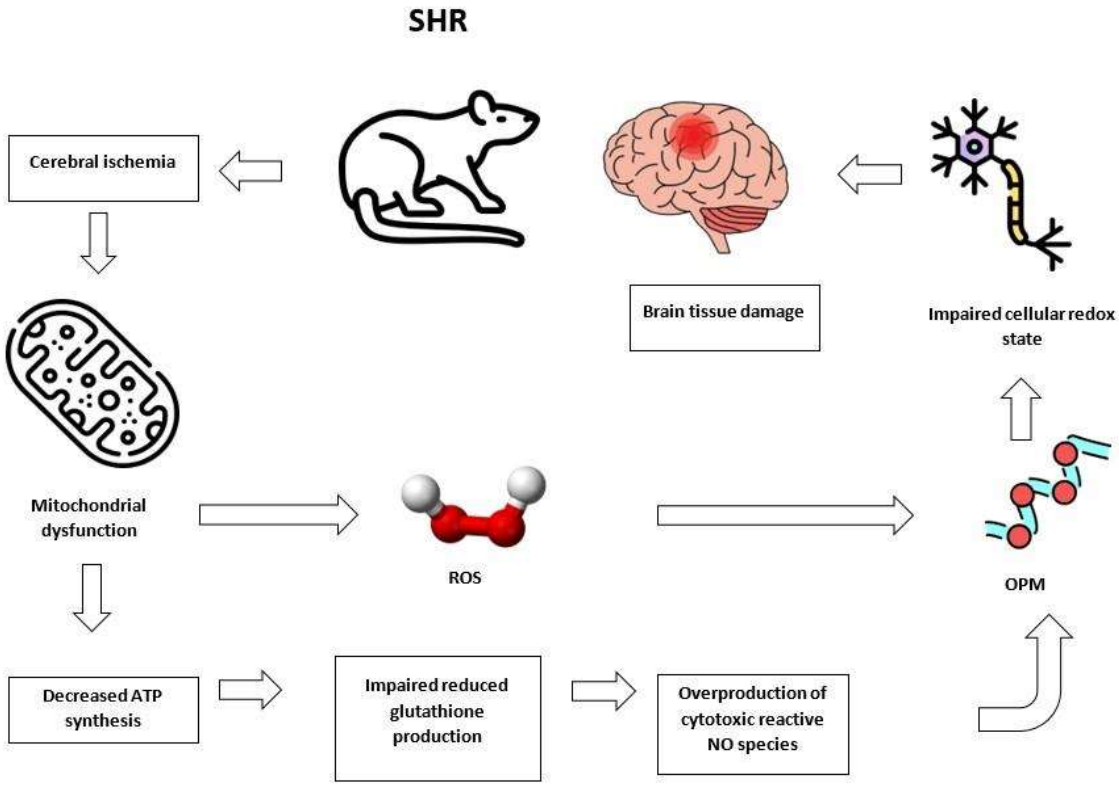

Figure 1. Mechanisms of the influence of mitochondrial dysfunction on the state of the antioxidant system.

Results

Biochemical analysis of OPM parameters in brain tissue of experimental rats has revealed that chronic AH induced significant oxidative damage in the brain. In untreated SHRs (Group 2), there was a marked accumulation of oxidative metabolic products compared to normotensive WKY controls (Group 1). Specifically, levels of ADPH and CPH increased by 72 % and 90.3 %, respectively ($p < 0.05$), indicating severe oxidative modification of neural proteins (Table 1).

The accumulation of oxidized proteins occurred amidst a significant depression of the ADS components, manifested as decreased SOD activity by approximately one-third, GPx activity by 18 %, and more than two-fold dropped reduced GSH levels compared to controls (Table 2).

Table 1: OPM markers in brain homogenates of SHRs (M±m)

Animal Groups	ADPH, AU/g protein	CPH, AU/g protein
Group 1, control WKR, n=10	5.11±0.32	9.35±0.21
Group 2, SHRs, n=10	8.79±0.77[1]	17.79±0.37[1]
Group 3, SHRs + propranolol, n=10	9.72±0.43[1,3]	19.21±0.37[1,2,3]
Group 4, SHRs + carvedilol, n=10	8.00±0.11[1,3,4]	14.10±0.28[1,2,3,4]
Group5, SHRs + hypertril, n=10	6.25±0.17[1,2]	12.00±0.23[1,2]

Notes: *([1])* – statistically significant differences between the indicators of Groups 2, 3, 4, and 5 ($p_{st} < 0.05$) compared with the corresponding indicators of the control group.
([2]) – statistically significant differences between the indicators of Groups 3, 4 and 5 ($p_{st}<0,05$) compared with the corresponding indicators of Group 2 SHR.
([3]) – statistically significant differences between the indicators of Groups 3 and 4 ($p_{st}<0,05$) compared with the corresponding indicators of Group 5 SHR.
([4]) – statistically significant differences between the indicators of Groups 3 ($p_{st}<0,05$) compared with the corresponding indicators of Group 4 SHR.

Table 2: ADS parameters in brain homogenates of SHRs

Animal Groups	SOD, U/mg/min	GPx, μg/mg/min	Reduced GSH, μg/g
Group 1, control WKR, n=10	247.6±11.0	67.4±4.3	7.38±0.67
Group 2, SHRs, n=10	177.4±12.7[1]	55.2±3.4[1]	3.57±0.87[1]
Group 3, SHRs + propranolol, n=10	112.1±21.1[1,2,3]	50.1±7.1[1,3]	3.65±0.31[1,3]
Group 4, SHRs + carvedilol, n=10	180.4±17.0[1,3,4]	56.5±3.4[1,3]	4.12±0.35[1,3]
Group5, SHRs + hypertril, n=10	231.0±16.0[2]	68.7±3.2[2]	6.23±0.21[2]

Notes: *([1])* – statistically significant differences between the indicators of Groups 2, 3, 4, and 5 ($p_{st} < 0.05$) compared with the corresponding indicators of the control group.
([2]) – statistically significant differences between the indicators of Groups 3, 4 and 5 ($p_{st}<0,05$) compared with the corresponding indicators of Group 2 SHR.
([3]) – statistically significant differences between the indicators of Groups 3 and 4 ($p_{st}<0,05$) compared with the corresponding indicators of Group 5 SHR.
([4]) – statistically significant differences between the indicators of Groups 3 ($p_{st}<0,05$) compared with the corresponding indicators of Group 4 SHR.

A 30-day therapeutic regimen with beta-blockers resulted in the sustained stabilization of elevated AP [13] in hypertensive animals. However, the response of oxidative metabolism parameters in brain tissue was non-uniform and drug-specific, indicating that hemodynamic control does not automatically translate to neuroprotection.

The analysis of OPM markers has revealed distinct profiles for each pharmacological agent on ADPH and CPH dynamics (see Table 1). Propranolol treatment did not significantly alter ADPH levels but resulted in a statistically significant increase in CPH content by 7.5 % ($p < 0.05$) compared to the untreated hypertensive group. In contrast, carvedilol administration significantly reduced CPH levels by 26 %. Hypertril treatment led to a significant reduction in both ADPH and CPH levels by more than 40 % compared to the hypertensive Group 3. Although these levels remained significantly higher than those of the intact control group ($p < 0.05$, see Table 1), they indicate a substantial mitigation of oxidative stress.

The antioxidant defense system, comprising both enzymatic and non-enzymatic components, has shown divergent responses to the tested drugs (see Table 2). Positive modulation of the ADS was observed exclusively in the hypertril-treated group. This was characterized by a significant upregulation of SOD and GPx activities, as well as an increase in GSH content. Carvedilol did not exert a statistically significant influence on the enzymatic parameters of the ADS in brain homogenates, while propranolol exhibited a negative impact on the antioxidant status, further suppressing SOD activity by more than 50 % compared to the untreated hypertensive rats (Group 3), exacerbating the enzymatic deficit associated with hypertension.

A comparative analysis of different generations of beta-blockers has highlighted significant differences in their impact on brain oxidative metabolism. Propranolol demonstrated high pro-oxidant and low antioxidant activity, characterized by the elevation of ADPH and CPH levels and a drastic reduction in SOD activity. “Carvedilol” at a tested dose of 50 mg/kg b.w. revealed moderate antioxidant activity, primarily limited to the reduction of specific OPM products (CPH). Hypertril displayed a pronounced antioxidant effect, evidenced by a dual mechanism of action, the reduction of oxidative damage markers (ADPH and CPH) and the restoration of antioxidant defense capacity (increased SOD, GPx activity, and reduced GSH content) as compared to Group 2 SHR (see Tables 1 and 2).

Discussion

Published studies examining the impact of AH and its correction with beta-blockers of various generations on OS markers and the antioxidant system status in brain tissues were identified in MedLine (Ovid), EMBASE (Ovid), Cochrane Library, and PubMed in January 2026. Search terms included "arterial hypertension" (Medical Subject Heading [MeSH]) or “beta-blockers” (MeSH), “oxidative stress” (MeSH), and “hippocampus” (MeSH).

Records were identified through database searches and screened for relevance to AH criteria and symptoms, antioxidant system status, and OMP markers. Articles addressing the antioxidant system status and OS under AH and its correction with beta-blockers were included. Articles published in languages other than English or lacking full-text access

were excluded. Additional articles cited in the reference lists of included studies were also screened for relevance and incorporated into this review. In total, 30 articles were analyzed, of which 21 were included in the study and results discussion.

The study has demonstrated that sustained arterial hypertension in SHR rats (Group 2) was accompanied by the activation of OPM processes parallel to the inhibition of antioxidant enzymes (SOD, GPx) and depletion of the thiol-disulfide system component (reduced GSH) (see Tables 1 and 2). This finding corroborates the hypothesis that hypertension disrupts the thiol-disulfide balance, reducing the pool of reduced thiols [9].

Literature suggests that mitochondrial dysfunction due to chronic ischemia is a primary cause of antioxidant enzyme suppression, particularly glutathione deficiency. Reduced GSH, a potent antioxidant, is not synthesized in mitochondria but requires energy-dependent transport. Mitochondrial impairment compromises energy production and reduced GSH transport, leading to cellular redox deterioration. The resulting imbalance between reduced and oxidized glutathione (GSSG) promotes the generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS), causing oxidation of cysteine-dependent protein domains and mitochondrial pore formation [14] (Fig. 1).

Furthermore, the glutathione system is intrinsically linked to the nitric oxide (NO) system, a key regulator of vascular tone and a potent vasodilator [15]. Glutathione deficiency disrupts NO transport, reduces its bioavailability, and favors the formation of cytotoxic derivatives such as peroxynitrite and nitrosonium ions, culminating in endothelial dysfunction [16].

The depletion of the antioxidant pool, particularly thiol-containing compounds, coupled with the hyperproduction of cytotoxic NO derivatives, creates a pro-oxidant environment conducive to the oxidative modification of macromolecules. This is particularly detrimental to proteins, leading to the excessive accumulation of ADPH and CPH in brain tissue. Analogous findings have been reported in cardiomyocytes of SHRs, where sustained hypertension was associated with a pronounced pro-oxidant shift in mitochondrial fractions and intensified protein oxidation in the cytosol [17].

In the present study, animals with experimental arterial hypertension (Group 2) exhibited a significant activation of OPM processes (see Table 1). The accumulation of chemically modified protein components, potentially affecting receptors, ion channels, and transport proteins, suggests a molecular basis for the disruption of nerve impulse generation, conduction, and signal transduction.

These biochemical alterations correlated with functional impairments. Specifically, SHRs demonstrated a decline in cognitive-mnestic functions, manifesting as a cognitive deficit in the Passive Avoidance Test (PAT) [18]. Biochemically, this was characterized by a surge in OMP markers, ADPH and CPH levels increased by 72 % and 90.3 %, respectively, amidst antioxidant system decompensation. We observed a reduction in SOD activity by nearly one-third, and significant decreases in reduced GSH and GPx levels by 52 % and 18 %, respectively, compared to the normotensive control (see Table 1).

Long-term pharmacological correction for elevated BP using β-adrenergic receptor blockers of various generations resulted in sustained normalization of BP in animal Groups 3-5, despite distinct biochemical profiles of OS markers.

Therapy with propranolol (Group 3) effectively normalized BP but failed to mitigate OS. OMP markers remained critically high, nearly double the values of the control group (Group 1) and not statistically different from the untreated hypertensive Group 2. This accumulation of OMP products occurred alongside a persistent antioxidant deficit: SOD activity remained halved compared to normotensive controls, and a one-third decreased compared with SHRs of Group 2. The glutathione system showed exhaustion, manifested by a 52 % reduction in reduced GSH levels and an 18 % decrease in GPx activity relative to Group 1 animals.

The ability of propranolol to ameliorate neuro-oxidative stress contrasts with some existing literature regarding its antioxidant properties. A recent large-scale literature review by Serreau et al. (2024) highlights the concentration-dependent membrane anti-peroxidative activity concurrently for five β-blockers, including Propranolol, originally described by Mak and Weglicki (1984). The cardioprotective and antioxidant efficacy of propranolol was subsequently corroborated by other research groups, who reported its capacity to significantly attenuate lipid peroxidation products. These studies characterized its antioxidative action across multiple levels, ranging from enzymatic modulation and membrane protection to direct effects on cardiovascular cells. Notably, while its antioxidant activity has been well-established in cardiovascular tissues, no such assertion has been made regarding the central nervous system [19]. Conversely, in a separate 90-day randomized clinical trial involving 18 patients with resistant hypertension, which evaluated the impact of propranolol on oxidative stress markers and total antioxidant capacity, the authors demonstrated a lack of statistically significant effects [20].

The third-generation non-selective β-blocker carvedilol demonstrated a moderate antioxidant effect. While it did not significantly restore SOD activity or the glutathione pool (GSH, GPx), it effectively reduced the levels of CPH, a specific marker of OMP.

This is consistent with reports indicating that carvedilol acts as a free radical scavenger and possesses anti-mitogenic properties, providing protection against oxidative damage in myocardial models [21-23].

Hypertril administration in Group 5 animals exhibited profound therapeutic efficacy, evidenced by the attenuation of ADPH and CPH levels and the restoration of SOD, reduced GSH, and GPx to near-normotensive baseline values. As Hypertril is a novel pharmaceutical agent, the full extent of its antioxidant capacity remains to be comprehensively characterized. Nevertheless, as a 4-amino-1,2,4-triazole derivative, it shares structural similarities with compounds whose antioxidant potential has been well-documented across various conditions, including neurological disorders [24, 25].

The study has certain limitations: only a genetic model of AH was examined, which develops gradually and serves as an analog to essential hypertension in humans, although other pathogenetic models of hypertension (renovascular, pharmacological, salt-induced, neurogenic) could be considered. The study assessed the antioxidant system status and OS markers in brain tissues; future research could determine the relationship between OS markers and cognitive function status. Subsequently, for an integrated assessment of differences between experimental groups and for the identification of key markers contributing most to the differentiation of the studied conditions, principal component analysis (PCA) is planned to be applied.

Conclusions

Long-term administration of Propranolol stabilizes arterial pressure but does not alleviate oxidative stress in the brain, evidenced by sustained high levels of OMP markers (ADPH and CPH) and suppressed antioxidant defense (SOD, GSH, GPx).

Carvedilol exerts a moderate antioxidant effect by lowering CPH levels but fails to significantly restore the activity of key antioxidant enzymes (SOD, GPx) or reduced glutathione levels.

Hypertril exhibits a potent dual effect, providing both antihypertensive control and robust antioxidant neuroprotection. Its mechanism involves the significant reduction of OMP markers (ADPH and CPH) and the restoration of the antioxidant defense system (SOD, GSH, GPx).

Interests disclosure:

The authors declare no conflict of interests.

Funding

The study was conducted under Research Work of Zaporizhzhia State Medical and Pharmaceutical University “Pathogenetic mechanisms of neurodestruction and glial dysfunction in encephalopathies: biomarkers and targeted neuroprotection”, state registration No. 0126U001479 (2026 - 2027), funded by the Ministry of Health of Ukraine.

References

[1] Lysenko V. Oxidative stress as a non-specific factor of organ damage pathogenesis (review of literature and own data). *Emergency Medicine.* 2020;16(1):24–35. DOI: 10.22141/2224-0586.16.1.2020.196926

[2] Egea G, Jiménez-Altayó F, Campuzano V. Reactive oxygen species and oxidative stress in the pathogenesis and progression of genetic diseases of the connective tissue. *Antioxidants (Basel).* 2020;9(10):1013. DOI: 10.3390/antiox9101013

[3] Reddy VP. Oxidative stress in health and disease. *Biomedicines.* 2023;11(11):2925. DOI: 10.3390/biomedicines11112925

[4] Jurcau MC, Jurcau A, Diaconu RG. Oxidative stress in the pathogenesis of neurodegenerative diseases. *Stresses.* 2024;4(4):827–849. DOI: 10.3390/stresses4040055

[5] Dash UC, Bhol NK, Swain SK, Samal RR, Nayak PK, Raina V, et al. Oxidative stress and inflammation in the pathogenesis of neurological disorders: mechanisms and implications. *Acta Pharm Sin B.* 2025;15(1):15–34. DOI: 10.1016/j.apsb.2024.10.004

[6] Kreutz R, et al. 2024 European Society of Hypertension clinical practice guidelines for the management of arterial hypertension. *Eur J Intern Med.* 2024. DOI: 10.1016/j.ejim.2024.05.033

[7] Toyoda S, Haruyama A, Inami S, Arikawa T, Saito F, Watanabe R, et al. Effects of carvedilol vs bisoprolol on inflammation and oxidative stress in patients with chronic heart failure. *J Cardiol.* 2020;75(2):140–147. DOI: 10.1016/j.jjcc.2019.07.011

[8] Halliwell B, Gutteridge JMC. *Free radicals in biology and medicine.* Oxford: Clarendon Press; 1999. 320 p.

[9] Hemmadi V. Estimation of superoxide dismutase. 2016. DOI: 10.13140/RG.2.1.2204.8407

[10] Sattar AA, Matin AA, Hadwan MH, et al. Rapid and effective protocol to measure glutathione peroxidase activity. *Bull Natl Res Cent.* 2024;48:100. DOI: 10.1186/s42269-024-01250-x

[11] Gok G, Neselioglu S, Ko HL, López-Martínez MJ, Manteca X, Rubio CP. Evaluation of glutathione (GSH) system in porcine saliva: validation and application of colorimetric method. *Antioxidants.* 2024;13(10):1231. DOI: 10.3390/antiox13101231

[12] Mesa SM, Megerssa YC. Comparison of biuret and refractometry method for serum total protein measurements in cattle and goat. *BMC Res Notes.* 2024;17:234. DOI: 10.1186/s13104-024-06906-5

[13] Svitlytskyi AO, Yehorov AA, Melnikova OV, Hrekova TA. Disorders of the central nervous system cognitive and mnestic functions in genetic arterial hypertension and with the use of beta-blockers of different generations. *Modern Medical Technology.* 2024;16(3):220–227. DOI: 10.14739/mmt.2024.3.310996

[14] Erel Ö, Erdoğan S. Thiol-disulfide homeostasis: an integrated approach with biochemical and clinical aspects. *Turk J Med Sci.* 2020;50(SI-2):1728–1738. DOI: 10.3906/sag-2003-64

[15] Belenichev I, Popazova O, Bukhtiyarova N, Ryzhenko V, Pavlov S, Suprun E, et al. Targeting mitochondrial dysfunction in cerebral ischemia: advances in pharmacological interventions. *Antioxidants.* 2025;14(1):108. DOI: 10.3390/antiox14010108

[16] Russell TM, Richardson DR. Glutathione S-transferases as potential targets for modulation of nitric oxide-mediated vasodilation. *Biomolecules.* 2022;12(9):1292. DOI: 10.3390/biom12091292

[17] Chai YC, Mieyal JJ. Glutathione and glutaredoxin: key players in cellular redox homeostasis and signaling. *Antioxidants.* 2023;12(8):1553. DOI: 10.3390/antiox12081553

[18] Belenichev I, Abramov A, Puzyrenko A, Bukhtiyarova N, Gorchakova N, Bak P. Molecular mechanisms of myocardial damage in hypertensive rats and hypertensive rats with metabolic disorders. *Res Results Pharmacol.* 2022;8(4):25–33. DOI: 10.3897/rrpharmacology.8.78534

[19] Serreau R, Amirouche A, Benyamina A, Berteina-Raboin S. Propranolol hydrochloride psychiatric effectiveness and oxidative stress: an update. *Oxygen.* 2024;4(2):139–149. DOI: 10.3390/oxygen4020009

[20] Ranasinghe HN, Fernando N, Handunnetti S, Weeratunga PN, Katulanda P, Rajapakse S, et al. The impact of propranolol on nitric oxide and total antioxidant capacity in patients with resistant hypertension: evidence from the APPROPRIATE trial. *BMC Res Notes.* 2020;13(1):228. DOI: 10.1186/s13104-020-05067-5

[21] Dandona P, Ghanim H, Brooks DP. Antioxidant activity of carvedilol in cardiovascular disease. *J Hypertens.* 2007;25(4):731–741. DOI: 10.1097/HJH.0b013e3280127948

[22] Ayashi S, Assareh AR, Jalali MT, Olapour S, Yaghooti H. Role of antioxidant property of carvedilol in mild to moderate hypertensive patients: a prospective open-label study. *Indian J Pharmacol.* 2016;48(4):372–376. DOI: 10.4103/0253-7613.186206

[23] Turco L, Reiberger T, Vitale G, La Mura V. Carvedilol as the new non-selective beta-blocker of choice in patients with cirrhosis and portal hypertension. *Liver Int.* 2023;43:1183–1194. DOI: 10.1111/liv.15559

[24] Rewish NM, Elmorsy MR, Fadda AA, Badawy SA. Design, synthesis, and evaluation of novel triazole-based carbohydrazide derivatives with notable antioxidant activity. *BMC Chem.* 2026;20(1):48. DOI: 10.1186/s13065-026-01736-x

[25] Li Q, Qi S, Liang J, Tian Y, He S, Liao Q, et al. Review of triazole scaffolds for treatment and diagnosis of Alzheimer's disease. *Chem Biol Interact.* 2023;382:110623. DOI: 10.1016/j.cbi.2023.110623

І.Ф. Бєленічев, А.О. Світлицький, О.В Ганчева, Т.А. Грекова, Т.М. Матвєйшина

Запорізький державний медико-фармацевтичний університет, Запоріжжя, Україна

ПОКАЗНИКИ ОКИСЛЮВАЛЬНОГО СТРЕСУ В ТКАНИНАХ ГОЛОВНОГО МОЗКУ ЩУРІВ ЗА УМОВ ТРИВАЛОЇ АРТЕРІАЛЬНОЇ ГІПЕРТЕНЗІЇ ТА ЇЇ КОРЕКЦІЇ БЕТА-БЛОКАТОРАМИ РІЗНИХ ПОКОЛІНЬ

Вступ. Значне збільшення кількості пацієнтів з артеріальною гіпертензією як у світі, так і в нашій країні зумовлює необхідність більш детального вивчення патогенетичних особливостей змін, що відбуваються в органах-мішенях, зокрема в головному мозку, за умов тривалого підвищення артеріального тиску та на тлі його корекції бета-блокаторами різних поколінь.

Мета. Оцінено стан показників оксидативного стресу в тканинах головного мозку за умов артеріальної гіпертензії та тривалого лікування β-блокаторами різних поколінь.

Методи. Досліджено одну інтактну та чотири групи експериментальних тварин. Експериментальним тваринам зі спонтанною артеріальною гіпертензією вводили пропранолол, карведілол та гіпертрил у терапевтичних дозах. Біохімічно досліджені показники оксидативного стресу (маркери оксидативної модифікації білків (альдегіддинітрофенілгідразони та карбоксифенілгідразони) та вміст відновленого глутатіону, а також активність супероксиддисмутази, глутатіонпероксидази) у гомогенатах мозку тварин.

Результати. Встановлено, що тривала артеріальна гіпертензія супроводжується погіршенням стану антиоксидантних систем. Корекція високого артеріального тиску пропранололом суттєво не впливає на стан показників оксидативного стресу. Корекція артеріального тиску карведилол призводить до підвищення рівнів відновленого глутатіону, а також підвищення активності супероксиддисмутази та глутатіонпероксидази на тлі зменшення рівнів показників окисної модифікації білків. Введення тваринам гіпертрилу суттєво зменшує рівні маркерів оксидативної модифікації білків та призводить до збільшення вмісту відновленого глутатіону та активності ензимів антиоксидантної системи.

Висновки. Тривала артеріальна гіпертензія призводить до значного пригнічення антиоксидантної системи мозку, що проявляється зниженням рівнів супероксиддисмутази, глутатіонпероксидази та відновленого глутатіону, а також збільшенням окислювальної модифікації білків, а саме підвищенням рівня альдегіддинітрофенілгідразонів та карбоксифенілгідразонів. Корекція високого артеріального тиску бета-блокаторами різних поколінь призводить до нормалізації артеріального тиску. Корекція високого артеріального тиску неселективними бета-блокаторами (пропранолол) не має особливого впливу на стан антиоксидантної системи в тканинах мозку. Гібридний неселективний бета- та альфа1-адреноблокатор (карведилол) має помірну антиоксидантну активність. «Гіпертрил», нова похідна 4-аміно-1,2,4-тріазолу, що характеризується як суперселективний бета-адреноблокатор з NO-модулюючою дією, має значну антиоксидантну активність.

Ключові слова: артеріальна гіпертензія; бета-блокатори; оксидативний стрес; гіпокамп.