The aim of the study was to establish the impact of 2-benzamido-2-(2-oxoindolin-3-iliden) acetic acid derivative ZNM on the activity of free radical processes in TBI rats.

The research was conducted on 32 white nonlinear mature male rats weighting 180-200 g, divided into 4 groups (n = 8): the first group was injected intraperitoneally the substance ZNM in a dose of 15 mg/kg in the form of an aqueous suspension stabilized by Tween 80 prior the TBI of moderate severity modeling; the second group was administered prior the TBI the reference drug mexidol in a dose of 100 mg/kg; the third (control) group was administered an equivalent amount of solvent; the fourth group – intact control (ether anesthesia without TBI). TBI of moderate severity was modeled under the ether anesthesia with a standardized weight-drop device (0.0495 kg, 0.315 J) inducing a focal blunt injury over the unprotected parietal-occipital head area. Drugs were administered in prophylactic and therapeutic regimen 3 days before (last - 30 minutes prior TBI) and 2 days after it, after which the animals were decapitated under the light ether anesthesia. The animals were kept under the standard vivarium conditions at a constant temperature and humidity with free access to food and water. All manipulations were carried out in accordance with European Union Directive 2010/63/EU on the protection of animals used for scientific purposes.

To study the free radical processes the plasma and homogenates of the animals' brain were used. Activity of lipid peroxidation was evaluated by the content of malonedialdehyde (MDA) and protein peroxidation – by the level of oxidatively modified proteins (OMB). Antioxidant system (AOS) was evaluated by the activity of catalase (CAT), ceruloplasmin level (CP) and SH-groups level. The degree of the cellular energy metabolism disturbances in brain was evaluated by the activity of succinate dehydrogenase (SDH). Statistical analysis of the results was performed using SPSS Statistics 17.0 and Microsoft Excel 2013. Statistical significance was evaluated using parametric Student's t-test (for normal distribution) and non-parametric Mann-Whitney U-test (in case of non-normal distribution). The critical level of significance was accepted with $p \leq 0.05$.

It was experimentally established that TBI is accompanied by a decrease of the antioxidant brain defense, manifested by the deficiency of antioxidant enzymes and non-enzymatic components of AOS. Thus, in the model pathology (TBI) group a decreased activity of CAT by 2.6 times in plasma, and by 1.6 times – in the brain homogenates was registered. It was accompanied by the increased level of lipid peroxidation product MDA in blood plasma by 2.2 times and in brain homogenates – by 1.5 times; and an analogous increase of protein peroxidation products (OMB) level both in blood plasma (by 2.2 times) and in brain homogenates (by 1.6 times). Blood level of SH-groups decreased by 2.6 times. The activity of SDH in brain homogenates was decreased by 8.5 times, indicating the significant disturbance of aerobic metabolism in the central nervous system cells, corresponding to expected changes by the literature data.

However, in the group of rats administered with the substance ZNM, a normalization of free radical oxidation of macromolecules and AOS activity after TBI was observed. Use of ZNM significantly reduced the level of MDA both in plasma and in brain structures (by 40.8% and 17.1% respectively) and OMB level to the control indices. CP content in plasma decreased by 19.6% and fit the control level, the content of SH-groups increased by 1.6 times. CAT activity increased in blood plasma and didn't differ significantly from that of control in brain homogenates. Under the influence of ZNM the SDH activity in brain structures increased by 2.5 times.

Thus, the substance ZNM with antihypoxic activity normalizes the state of prooxidant-antioxidant balance in the brain structures and in the whole organism of animals with TBI and improves energy metabolism in the cells of central nervous system. This suggests that the derivative of 2-benzamido-2-(2-oxoindolin-3-iliden) acetic acid ZNM has antioxidant and cerebroprotective properties.

The action of substance ZNM coincides with the effect of reference drug mexidol. Although the substance ZNM slightly concedes to antioxidant effect of mexidol in reduction of the lipid peroxidation in brain cells, but exceeds the effect of mexidol in normalization of protein peroxidation in the cells of brain and MDA level in blood plasma. Concerning other investigated parameters in blood plasma and brain structures, any of significant difference between the actions of ZNM and mexidol wasn't revealed.

Obtained results confirm the antioxidant and cerebroprotective properties of substance ZNM under the conditions of closed brain injury of moderate severity, contributing to normalization of the prooxidant-antioxidant balance in plasma and brain of rats and improving energy metabolism in cells of the central nervous system. The derivative of 2-benzamido-2-(2-oxoindolin-3-iliden) acetic acid ZNM doesn't concede significantly to the effect of reference drug mexidol under the conditions of a closed traumatic brain injury of moderate severity in the normalization of energy metabolism in nerve cells of rats and prooxidant-antioxidant balance in plasma and brain.

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EFFICACY OF GLUTATHIONE FOR THE PROPHYLACTICS OF GENTAMICIN NEPHROTOXICITY

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Gentamicin is an antibiotic from the aminoglycosides group which is widely used in treatment of infections caused by gram-negative microorganisms.Nephrotoxic effectof gentamicincauses development of nephropathy in 19-25% of cases, significantly restricting its use.Reabsorption of gentamicin in proximal tubules and its interaction with membrane phospholipids causes destabilization of cellular membranes followed by mitochondria damage and development of oxidative stress [JabbariM., 2011]. Taking into account the role of oxidative stress in the development

of gentamicin nephropathy, it's advisable to use medicines with antioxidant properties for the prophylactic and correction of this pathology.Glutathione functionates as a hydrogen donor and a cofactor of principal antioxidant enzymes – glutathione peroxidase and glutathione reductase [AoyamaK.,2015].

The aim of research was to estimate a nephroprotective potential of glutathione on a model of gentamicin-induced acute kidney injury.

The research was conducted on 21 non-linear white rats weighting 140-180 g, maintained under the standard vivarium conditions with free access to water and food. Animals were divided into three groups (n=7): 1st group – control, 2nd – animals with gentamicin nephropathy, induced by the dailyinjectionof 4% gentamicin solution in dose 80 mg/kg during 6 days, animals of the 3rd group were dailyinjected by glutathione preparation (TAD 600, "BiomedicaFoscama", Italy) in dose 30 mg/kg 40 min after gentamicin administration. Kidney function was assessed 24 h after the last gentamicin injection by the indices of diuresis, creatinine plasma concentration(Pcr), glomerular filtration rate (GFR) and protein concentration in urine(Uprot).

Progression of severe kidney injury after gentamicin administration resulted in the reduction of diuresis by 62% ($p<0.01$), decrease of GFR by 2.4 times ($p<0.01$) with the development of retentional azotemia,confirmed by an increase of Pcr by 72% ($p<0.01$) comparing to control group. Uprot concentration increased by 3.2 times ($p<0.01$),indicating the critical proteinuria caused by tubular damage.

Administration of glutathione significantly improved the excretory kidney function. Diuresis increased by 1.7 times ($p<0.01$),GFR – by 1.8 times ($p<0.01$), what was accompanied by the reduction of Pcr by 52%. Additionally, proteinuria decreased by 2.3 times ($p<0.01$), protein excretion – by 1.5 times($p<0.01$)in comparison to the untreated animals. Obtained results testify the ability of glutathione to mitigate toxic effects of gentamicin, extending the spectrum of its clinical use.

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THE CHANGES OF ENERGY METABOLISM IN THE TISSUE OF KIDNEYS AFTER SUBLIMATE DAMAGE AND MODULATION OF POTASSIUM FLOW WITH FLOCALIN

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A wide range of kidney diseases are caused by toxicants including heavy metals that determine violation of homeostatic kidney function. Nephrotoxicity is caused by the complexes of divalent metals with proteins. These complexes damage epithelium of tubulocytes during reabsorption with selective lesion of cellular membranes, mitochondria, and inhibit energy dependent transport processes in the tubular part of nephron. It is well known that potassium channels are a potent endogenous system of defense of the organism when energy resources of cells (including ATP) decrease. The aim of research was to study the changes of energy metabolism in the tissue of kidneys under the conditions of acute sublimate kidney injury after administration of flocalin which is ATP-dependent potassium channel activator of sarcolemmal and mitochondrial cell membranes.

The experiments were held on nonlinear laboratory white rats of both sexes 150-170 g of weight after a single and multiple (7 days) intraventricular administration of flocalin 5 mg/kg. Sublimate nephropathy was modeled by subcutaneous injection of 0.1% mercury dichloride 5 mg/kg. The activity of alkaline phosphatase (AP) in the cortical layer of kidney was measured on photocolorimeter KFK-2 according to instruction due to the ability of the enzyme to slit phenilphospate with production of phenol. The activity of succinate dehydrogenase (SDH) in cortical and medullary layers of kidney was measured on spectrophotometer according to contents of restored potassium ferricyanide (Prokhorova M.I., 1982). Biochemical research at the day of modeling of renal pathology has shown the decrease of AP activity by 20.3% in comparison to healthy rats. Activity of SDH decreased by 41.9% in the cortical and by 40% in the medullar layers of kidneys. After a single administration of flocalin to the rats with sublimate nephropathy the activity of AP increased by 12.5%. The activity of SDH in the medullary layer of kidney did not reach the level of intact rats. At the same time, the elevation of this enzyme in the cortical layer comprised 29.6%. On the 7^{th} day of acute sublimate nephropathy a decrease of both AP (by 67.7%) and SDH (by 30.8% and 45% in cortical and medullary layers respectively) was observed. After 7 days of flocalin administration AP increased by 41.3% and SDH increased by 19.6% in the cortical layer of kidneys. Therefore under the conditions of toxic kidney injury to prevent excessive accumulation of cytoplasmic calcium ions, pharmacological modulation of K_{ATP} channels is very important. The increase of AP activity which is donator of phosphor for ATP, as well as the increase of SDH activity which is marker of functional state of mitochondria, show the ability of flocalin to improve energy supplement to the nephrocytes.

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STUDY OF THE EFFECT OF DIFFERENT PIRACETAM DOSAGES ON THE CONDITION OF PROOXIDANT-ANTIOXIDANT SYSTEM OF CERTAIN BRAIN STRUCTURES IN CASE OF ACUTE HYPOXIA

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Hypoxia is the basic condition in pathogenesis of numerous neurologic diseases. According to the data of publications, pharmaco-therapeutic issues of cerebral pathology, being the third in the list of general mortality rate in