

hematuria); Nifedipine is able to cause polyuria, nicturias, hematuria, dysuria; Streptomycin - proteinuria, hematuria; Sevoflurane - glucosuria; Sulfasalazine - proteinuria, hematuria; Thadalafil can cause hematuria; Varenicline causes polakyuria, nectra, glucosuria, polyuria; Olanzapine - glucosuria; Ornidazole - darkening of the color of urine.

Conclusions. Thus, it should be remembered that laboratory indicators are not strictly specific and give a certain percentage of false positive and false negative results. That is why knowledge about the basics of internal diseases and laboratory diagnostics, changes in laboratory parameters in the conditions of the most common diseases and under the influence of medicines are necessary for pharmacies for a qualified consultation of a doctor and a patient on the issues of rational choice of medical therapy. This will significantly improve the quality of treatment and reduce the number of unwanted side effects.

FRIGOPROTECTIVE PROPERTIES OF OLIGOPEPTIDES - HOMOLOGUES OF THE FRAGMENT OF ACTH₁₅₋₁₈

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Introduction. A significant place among the problems of modern medicine and pharmacology is the damage to the body at low temperatures, as residents of most countries and climatic zones experience hypothermia. Particular importance is acquired in the context of military and political conflicts, industrial disasters and environmental incidents. Recently, the number of cases of negative influence of hypothermia is increasing, which leads to the death or disability of the victims. The pathogenic mechanism of low temperature affect on the body includes cardiovascular, endocrine, central nervous, immune, respiratory and other systems. Such multisystemic pathogenic mechanism causes the baffling complexity of treatment. The range of drugs that can increase the body's resistance to hypothermia (frigoprotectors) is rather narrow. In addition, most of them affect only one of the components of the pathogenic mechanism of cold trauma. Therefore, the search for new safe and effective frigoprotectors is relevant. Neuropeptide drugs which are characterized by multi-functionality and the ability to eliminate the disintegration of molecular-biochemical mechanisms, assume importance. Peptide homologous of adrenocorticotropic (ACTH) hormone fragment ₁₅₋₁₈ take particular attention as potential frigoprotectors.

Objective: to conduct an experimental study of frigoprotective properties of oligopeptides - homologues of ACTH fragment ₁₅₋₁₈ on the model of acute total cooling of mice and cold trauma in rats.

Materials and methods. The peptide homologues of the fragment of ACTH₁₅₋₁₈ (Lys-Lys-Arg-Arg) under the code KK-1 and KK-5 were synthesized at the Federal State Unitary Enterprise "State Research Institute of High Pure Biopreparations" of the Federal Medical and Biological Agency of Russia (St. Petersburg, the Russian Federation) supervised by Doctor of Biological Sciences O.O. Kolobova. Peptides were obtained by solid phase synthesis using OSI technology and purified by preparative reversed phase chromatography, with a frequency of at least 98%. In these compounds, one Acetyl-(D-Lys)-Lys-Arg-Arg-amide (KK-1) or two Acetyl-(D-Lys)-Lys-(D-Arg)-Arg-amide (KK-5) natural amino acids is converted to the corresponding D-stereomer. These compounds have increased resistance to human blood serum proteases, and belong to practically non-toxic substances.

The study of frigoprotective effect of peptides was performed on 36 white male mice weighing 17-20 g and 36 white male rats, grown in vivarium of the National University of Pharmacy. The animals were kept in a standard diet without limiting access to water. The study of frigoprotective activity carried out on the models of acute total cooling of mice and cold trauma in rats. The animals were placed in a freezing chamber with a constant temperature of -18°C for the reproduction of acute total cooling of mice. Frigoprotective effect was evaluated for the duration of life of animals in cold conditions. Frigoprotective activity of drugs was calculated as a percentage of increase in life in a freezing chamber compared to control. Oligopeptides were administered by intranasal introduction at a dose of 20 µg/kg for 30 minutes prior to cold exposure. The reference drug "Semax" (CJSC "Innovative Scientific and Production Centre "Peptogen", the Russian Federation) was administered at a dose of 20 µg/kg in the same terms.

The model of acute cold trauma in rats was reproduced by placing the rats in a freezer "NordInter-300" at a temperature of -18°C for 2 hours in individual plastic boxes (without limiting air intake). Oligopeptides were administered by intranasal introduction at a dose of $20\ \mu\text{g}/\text{kg}$ for 30 minutes prior to cold exposure. The reference drug "Semax" (CJSC "Innovative Scientific and Production Centre "Peptogen", the Russian Federation) was administered at a dose of $20\ \mu\text{g}/\text{kg}$ in the same terms. The frigoprotective effect was evaluated by changing the rectal temperature in animals, which was measured by a WSD-10 thermometer before cooling and 10 minutes after the acute cold exposure.

Results and discussion. In the course of our investigational studies, it was found that lifetime of mice was 70.57 minutes in the control group affected by acute total cooling. The administration of the investigated substances and reference drug resulted in acceleration of mice's lifetime. Thus, the frigoprotective activity of the KK-1 peptide was 6.5%, the KK-5 peptide was 36.5%, and Semax 8.2%. However, statistically significant acceleration of animals' lifetime against the reference group was observed only under the affect of the KK-5 peptide (by a factor of 1.4). In addition, in regards of frigoprotective activity, the KK-5 peptide of was higher than the reference drug (for 28%) and the KK-1 peptide (for 29.7%).

Analysis of rectal temperature indices in rats 2 hours after acute cold stress testifies to the development of hypothermia (in the control group of animals the rectal temperature was decreased by 8%). KK-1, KK-5 peptides and Semax were contributed to a rise in temperature by 6%, 5.5% and 7% respectively.

Also, the rates of animals receiving study medicines did not statistically differ from the markers of the intact group, indicating the ability of the medicines to prevent the development of hypothermia and further pathophysiological manifestations of hypothermia.

Conclusions. The frigoprotective properties of peptides - homologues of the fragment of $\text{ACTH}_{(15-18)}$ and Semax reference drug were determined on the model of acute total cooling of mice and cold trauma in rats.

The frigoprotective activity of Acetyl (D-Lys) -Lys-Arg-Arg-amide peptide was 6.5%, of Acetyl-(D-Lys) -Lys- (D-Arg) -Arg-amide peptide was 36.5%, Semax reference drug was 8.2%. Acetyl-(D-Lys)-Lys-(D-Arg)-Arg-amide peptide in regards of frigoprotective activity reaches higher heights than Acetyl-(D-Lys)-Lys-Arg-Arg-amide peptide and Semax reference drug.

Peptides - homologues of the fragment AKTG_{15-18} under the names KK-1 and KK-5 under the conditions of acute cold stress prevent the decrease in rectal temperature of rats, not inferior to the Semax.

Today it is important to carry further investigation of mechanisms of frigoprotective effect of peptides - homologues of the fragment of $\text{ACTH}_{(15-18)}$.

DOXEPIN LETHAL POISONING: PROBLEMS OF ANALYTICAL DIAGNOSTICS

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Introduction. Doxepin (3-(dibenz[b,e]oxepin-11(6H)-ylidene)-N,N-dimethylpropylamine) is a tricyclic antidepressant, which is recommended in medical practice for the treatment of depression, which is accompanied by anxiety. According to literature review, the toxic and lethal of Doxepin concentration in the blood is in the range from 0.5 or 0.7 to 29 mg/l.

Aim of the study is analyze of lethal cases of Doxepin poisoning over the past 10 years and identify of factors that contributed to this.

Materials and methods are the search and bibliographic analysis of literature on the causes of antidepressant lethal poisoning, as well as an analysis of factors that increase the likelihood of tricyclic antidepressant Doxepin poisoning.

Results and discussion. Andrea Dettling' study only 9 cases of fatal isolated Doxepin poisoning was found and the concentration of antidepressant was measured in blood samples from peripheral vessels.