МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ
КАФЕДРА ПАТОЛОГІЧНОЇ ФІЗІОЛОГІЇ
КАФЕДРА БІОЛОГІЧНОЇ ХІМІЇ

І Науково-практична інтернет-конференція
з міжнародною участю

«МЕХАНІЗМИ РОЗВИТКУ ПАТОЛОГІЧНИХ ПРОЦЕСІВ І ХВОРОБ ТА ЇХНЯ ФАРМАКОЛОГІЧНА КОРЕКЦІЯ»

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Механізми розвитку патологічних процесів і хвороб та їхня фармакологічна корекція : тези доповідей І Науково-практичної інтернет-конференції з міжнародною участю (18 жовтня 2018 р.). – Х. : Вид-во НФаУ, 2018. – 276 с.

Збірник містить матеріали І Науково-практичної інтернет-конференції з міжнародною участю: «Механізми розвитку патологічних процесів і хвороб та їхня фармакологічна корекція». В матеріалах Конференції розглянуто сучасні проблеми патофізіології: молекулярна та клітинна патофізіологія; роль генетичних факторів у патогенезі захворювань; механізми розвитку патологічних процесів і хвороб; вікова патофізіологія; клінічна патофізіологія; питання викладання патофізіології; експериментальна терапія найбільш поширених захворювань; фармакологічні дослідження і стандартизація біологічно активних речовин; проблеми та перспективи створення лікарських препаратів різної спрямованості дії (лікувально-косметичних, гомеопатичних, ветеринарних, екстемпоральних); оптимізація технологічних процесів створення лікарських препаратів; інформаційні технології і автоматизація наукових досліджень з розробки лікарських засобів; створення нутрицевтичних засобів та виробів медичного призначення; організаційно-економічні аспекти діяльності фармацевтичних підприємств у сучасних умовах; маркетингові дослідження сучасного фармацевтичного ринку; нанотехнології у фармації; сучасна біотехнологія.

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Book of Abstracts includes materials of I Scientific and practical Internet Conference with international participation: «Mechanisms of development of pathological processes and their pharmacological correction». The materials of the Conference consider modern problems of pathophysiology: molecular and cellular pathophysiology; the role of genetic factors in the pathogenesis of diseases; mechanisms of development of pathological processes and diseases; age pathophysiology; clinical pathophysiology; teaching of pathophysiology; experimental therapy of the most common diseases; pharmacological research and standardization of biologically active substances; problems and perspectives for the development of drugs with different mechanism of action (therapeutic cosmetic, homeopathic, veterinary, extemporal); optimization of technological processes for the creation of drugs; information technologies and automation of scientific research on the development of drugs; creation of nutraceutical and medical products; organizational and economic aspects of the activity of pharmaceutical enterprises in modern conditions; marketing researches of the modern pharmaceutical market; nanotechnology in pharmacy; modern biotechnology.

For a wide audience of scientific and practitioners of medicine and pharmacy.

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INFLUENCE OF CARBOLINE ON REACTIVE OXYGEN AND NITROGEN SPECIES PRODUCTION IN GASTRIC MUCOSA OF RATS UNDER CHRONIC NITRATE-FLUORIDE INTOXICATION

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Certain regions of Ukraine have risk of simultaneous intake of excessive concentrations of nitrates and fluorides with drinking water and food. Fluorides can enter groundwater since they are byproduct of aluminum production. Some regions of Ukraine have high concentration of fluorides in groundwater due to high concentration of fluorine containing salts in ground. Poltava region can serve as good example of such regions. Nitrates are used as cheap and effective fertilizers. Therefore vegetables are the primary source of excessive nitrates intake. Gastro-intestinal system is the first target for adverse effects of both mentioned above environmental pollutants during their alimentary consumption. Combined effect of nitrates and fluorides on gastro-intestinal system is not well researched.

The aim of this study is to determine influence of "Carboline" on production of superoxide anion radical ($O_2^{\cdot -}$) and peroxynitrite ($ONOO^-$) in rats gastric mucosa under chronic nitrate-fluoride intoxication.

Materials and methods. Experiment was performed on 38 Wistar rats weighting 180-230 g. Animals were divided into 3 groups: control group (10), combined intoxication group (15) and "Carboline" group (13). Chronic nitrate-fluoride intoxication (combined intoxication) was induced as described in our previous work [1]. Animals of "Carboline" group were receiving suspension of "Carboline" at a dose 100 mg/kg during combined intoxication induction. Animals were sacrificed under thiopental anesthesia by bloodletting. All biochemical studies were performed in 10% tissue homogenate.

Production of $O_2^{\cdot -}$ was determined as described in [2]. Production of $ONOO^-$ was determined by increase in concentration of peroxynitrites of alkali and alkali-base metals after 40 min incubation in buffer solution (ph=7.4). Concentration of peroxynitrites of alkali and alkali-base metals was determined as described in [1].

Results were analyzed by Mann-Whitney method. Differences between groups were deemed statistically significant if $p<0.05$.

Results and discussion. Combined intoxication increases production of $O_2^{\cdot -}$ by 195% compared to control group. Production of $ONOO^-$ elevates by 17.64%. Suspension of "Carboline" decreases $O_2^{\cdot -}$ production by 21% compared to combined intoxication group. Production of $ONOO^-$ drops by 25%.

Increased $O_2^{\cdot -}$ production during combined intoxication owns to the fact that both nitrates and fluorides can influence mitochondrial electron transport chain. There are evidences in literature that fluoride ions can cause tissue hypoxia by impairing

mitochondrial electron transport. However exact mechanism is not known yet. Cytochromes of mitochondria have ability to reduce nitrates to nitrites sacrificing two electrons in the process. Under physiologic conditions electrons from cytochromes should be used in ATP synthesis. Two electron reduction of nitrates to nitrites in eukariotic cells does not lead to ATP synthesis. This “electron leakage” creates possibility of uncoupling of oxidative phosphorylation and ATP synthesis thus leading to $O_2^{\cdot -}$ production by mitochondria. Judging from almost twofold increase in $O_2^{\cdot -}$ production during combined intoxication we can assume that nitrates and fluorides have synergetic effect on $O_2^{\cdot -}$ production.

$ONOO^-$ is formed in reaction of $O_2^{\cdot -}$ with nitric oxide (NO). Both nitrates and fluorides can lead to increased production of NO [1]. However sources of increased production of NO are different for fluorides and nitrates. Fluorides can increase NO production by activation of inducible NO-synthase, while nitrates can provide excessive amounts of NO by activation of nitrate reductases.

“Carboline” is a sorbent which consists from carbon fibers obtained by extrusion of crushed tissue carbon fiber sorbent of AUT –M brand. “Carboline” has sorption surface of 2500 sq. meters per 1 gram, which allows it efficiently absorb nitrates and fluorides from gastro-intestinal tract.

Conclusion. Suspension of “Carboline” is effective for correction of increased reactive oxygen and nitrogen species production in gastric mucosa of rats under nitrate-fluoride intoxication.

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