ANTIMYCOBACTERIAL ACTIVITY OF SOME 1-R-2-OXO-4-HYDROXY-1,2,5,6,7,8-HEXAHYDROQUINOLINE-3-CARBOXYLAMIDES DERIVATIVES

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Introduction. Tuberculosis (TB) represents one of the leading causes of morbidity and mortality worldwide. Development of new potential drugs is essential because of the existence of latent TB and expansion of drug-resistant TB forms (multidrug-resistant and extensively drug-resistant tuberculosis). Despite the achievements of modern pulmonology, the problem of developing and creating highly effective anti-mycobacterial agents for the treatment of tuberculosis remains essential. Furfuryl-quinoline derivatives deserve special attention. This is a promising class of condensed heterocyclic systems, which are similar to natural and synthetic analogues exhibiting many pharmacological effects.

Aim. The aim were to study the anti-mycobacterial action of 1-furfuryl-2-oxo-4-hydroxy-1,2,5,6,7,8-hexahydroquinoline-3-carboxylic acids derivatives.

Materials and Methods. The furfuryl-quinoline derivatives used in this study were prepared by the reaction of the amidation of ethyl ester 1-furfuryl-2-oxo-4-hydroxy-1,2,5,6,7,8-hexahydroquinoline-3-carboxylic acids. The structural properties of the compounds were confirmed by nuclear magnetic resonance, mass spectrometry, and infrared analyses, and the purity was established by elemental analyses.

Results and discussions. The introduction of a furfuryl substituent in position 1 of hexahydroquinoline nucleus leads to a significant increase the antimycobacterial action. The presence of thiazolyl-2-amide fragments can be assumed to be a positive factor, whereas alkyl or alkoxy-groups as well as para-substituents regardless of their nature, are completely deactivate the molecule.This study extends earlier reports regarding the in vitro efficacies of the furfuryl-quinoline derivatives against *Mycobacterium tuberculosis*. Derivatives of 1-furfuryl-2-oxo-4-hydroxy-1,2,5,6,7,8-hexahydroquinoline-3-carbox-amides were tested in vitro against a broad panel of single-drug-resistant *M. tuberculosis* strains. The susceptibilities of these strains to some compounds were comparable to those of strain $H_{37}Rv$, as indicated by the ratios of MICs for resistant and nonresistant strains, supporting the premise that furfuryl-quinoline derivatives have a novel mode of action unrelated to those of the currently used antitubercular drugs.

Conclusions. Conducted screening creates conditions for further in-depth study of the most active substances among this class of chemical compounds and provides opportunities for the development of a potential antimycobacterial drug.

INFLUENCE OF EXTRACT FROM THE STEVIA LEAVES ON INDICES OF LIPID PEROXYDATION UNDER EXPERIMENTAL DIABETES MELLITUS TYPE II IN RATS

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Introduction. It is proved that diabetes mellitus is a heterogeneous multifactor disease. The concept of diabetes mellitus type II development is based on the presence of two fundamental defects – insulin resistance and dysfunction of β-cells of pancreas, at that both factors aggravating each other.

An important role in pathogenesis of diabetes mellitus also belongs to activation of processes of free radical oxidation (FRO), in particular pro-oxidant and antioxidant imbalance that leads to an excess of free radicals and accumulation of highly toxic products. FRO is an integral part of many vital processes occurring in the body at all the levels. Excessive amounts of oxygen free radicals is released by activated macrophages

and damaged β -cells, the last are extremely sensitive to the toxic effect of free radicals. Thus, the process of lipid peroxidation is most represented in cells of Langerhans islets. Considering the important role of oxidative stress in the development of diabetes mellitus, it is reasonable to search the drugs with high antioxidant activity. The group of such compounds includes the substances of flavonoid row, which are very prospective.

Aim. Purpose of the given work was to study the impact of dry extract from the stevia leaves on metabolic disorders development in rats under experimental insulin resistance induced by high-fructose diet.

Materials and methods. Indices of lipid peroxidation was determined by the content of diene conjugates (DK) and TBK-reactive products (TBK-RAP) by the reaction with thiobarbituric acid using spectrophotometric method, antioxidant system condition was evaluated by determining the concentration of reduced glutathione (GSH) – using spectrophotometer method on the reaction with alloxan.

Results and discussion. As seen from the results, retention of rats on high-fructose diet has led to an increase in the content of TBK-AP and DK (primary products of lipid peroxidation) in the liver of animals, which correlates with the decrease of GSH content, indicating the activation of lipid peroxidation and exhaustion of antioxidant protection means.

Conclusion. Administration of dry stevia leaves extracts in our experimend conditions caused normalization of indicators of antioxidant status of organism of investigated laboratory animals that probably could be explained by antiradical properties of polyphenols of stevia leaves extracts.

THE EFFECT OF LETROZOLE ON THE MORPHOLOGICAL STATE OF VISCERAL ADIPOSE TISSUE AGAINST THE BACKGROUND OF EXPERIMENTAL METABOLIC SYNDROME

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Introduction. Metabolic syndrome is a set of metabolic-modifying factors that include obesity and increase the risk of type 2 diabetes and cardiovascular pathology development. In accordance with WHO data about 11% of adult men and 15% of adult women are afflicted by metabolic syndrome and abdominal obesity. Sex hormones imbalance caused by increased peripheral aromatase activity is also plays an important role in aggressive clinical behavior of metabolic syndrome with overweight and obesity. The most common condition that changes the ratio of sex hormones is the enhancement of peripheral aromatase activity caused by abdominal fat weight gain and increased preadipocyte proliferation.

Aim. Consequently, the testing of letrozole aromatase inhibitor effect on the morphological state of visceral adipose tissue in hamsters with experimental metabolic syndrome became a focal point of our research.

Materials and methods. The study was carried out on 60 Syrian hamsters at the age of 2.5 months, which were divided in 3 groups by 10 animals of each sex. Metabolic syndrome in animals was recreated using classic for hamsters model based on fructose- and fat-enriched diet for 6 weeks. The treatment of animals was carried out by oral administration of letrozole in the dose 0.3 mg/kg for 21 days. After euthanasia, adipose tissue was stained with hematoxylin-eosin and sudan IV.

Results and discussion. Letrozole administration had led to reduced size of the adipocytes in the abdominal-visceral adipose tissue of the both male and female hamsters. It was also decreased lymphocytic-macrophage infiltration in peripheral regions around full-blooded capillaries regardless of the sex. At the same time signs of fibrosis were noticeably diminished. Also it was morphometrically determined that the mean perimeter of adipocytes in animals of the letrozole group decreased in 40.2% and 33.8% in males and females respectively, compared with similar parameters of the negative control. The average cell area decreased in 68.7% (males) and in 65.7% (females).

Conclusions. The results of our study confirm the prospect advisability of letrozole clinical using in the therapy of metabolic syndrome and obesity, especially in adult men with secondary hypogonadism and hyperestrogenemia.