2. Streszczenie w języku angielskim

INTRODUCTION

In the search for compounds with anti-cancer effects, research on genistein has received considerable attention. It has been shown that genistein can exhibit anticancer effects by, among other things, inducing apoptosis, affecting the cell cycle, inhibiting angiogenesis, and antiproliferative activity. On the other hand, there are data supporting the pro-cancerous effect of genistein, especially in hormone-dependent cancer types. In view of the above, we still do not know to whom, in what doses genistein should be administered to achieve the desired health effect, the mechanism of its action at the stage of initiation and progression of the cancer process is still unknown to the end. It is also important to answer the question of whether it is safe for women to use supplements containing genistein in the context of cancer risk. Another important aspect is the answer to the question of how genistein in micro and nano forms will work? Nanoparticles exhibit different physical, chemical and biological activity than macro compounds. It should be noted that there is still a lack of research in the literature in the field presented.

AIM

The aim of this study was to evaluate the effect of genistein in nano, micro and macro forms on the intensity of 7,12-dimethylbenzo[a]anthracene-induced tumorigenesis in rats and to understand the mechanisms of this effect. The effect of genistein on the kinetics of changes in the content of 3-methyladenine, 7-methylguanine, 1-methylguanine, 1-methyladenosine, 7-methylguanosine, O-methylguanosine, N6-methyl-2'-deoxyguanosine in the urine of rats under the conditions of the tumor process was evaluated. The content of fatty acids in the blood serum of rats was determined. The effect of genistein on the activity of Δ6-desaturase and Δ5-desaturase and the degree of atherogenicity and thrombogenicity of fatty acids in rat serum was evaluated. The effects of nano-, micro- and macro-genistein on the content of 5-, 12- and 15-hydroxyyeicosatetraenoic acids, hydroxyoctadecadienoic acids and 12-hydroxyyeicosapentaenoic acid, as well as the content of interleukin 6 (IL-6), interleukin 1 (IL-1) and metalloproteinase 9 (MMP-9) in rat serum were investigated.

MATERIAL AND METHODOLOGY

The biological material for the study was urine, blood serum and tumors obtained from female rats of the Sprague-Dawley strain (n=32). After a 10-day period of adaptation to the conditions of the experiment, the animals were randomly divided into 4 groups: unsupplemented animals, animals supplemented at a dose of 0.2 mg/kg b.w. with macro, micro (587±83 nm), or nano (92±41 nm) genistein. The genistein, suspended in 0.4 ml of water, was administered to the animals via an intragastric probe from the 40th day of life to the 20th week of life of the rats. To maintain experimental conditions, animals in the control group received 0.4 ml of water via an intragastric probe. To induce mammary neoplasia (adenocarcinoma), the rats were administered with an intragastric probe (DMBA). The following analytical techniques were used to conduct the study: liquid chromatography with mass spectrometry detection, gas chromatography with mass spectrometry detection, immunoenzymatic methods, liquid chromatography with UV detection, and spectrophotometric method.

RESULTS

Based on the study, it was shown that supplementation of animals with genistein in macro, micro and nano forms increased the intensity of the tumor process in rats. Nanogenistein stimulated the initiation of the tumor process, caused stimulation of tumor growth. Macro and micro genistein caused an increase in the intensity of tumor cell proliferation. The effect of supplementation of animals with genistein was an increase in the content of 3-methyladenine, 7-methylguanine, 1-methylguanosine, 1-methyladenosine, 7-methylguanosine, O-methylguanosine, N6-methyl-2'-deoxyguanosine in the urine of rats under tumor process conditions. Supplementation of animals with nano, micro and macrogenistein affects both the content of individual fatty acids and the fatty acid profile in the blood serum of DMBA-treated rats. Animals supplemented with micro- and nanogenistein were characterized by a statistically significantly higher content of pentadecanoic, heptadecanoic, palmitoleic, hexadecenoic, vaccenic acids, as well as linoleic, gamma-linolenic and arachidonic acids, with respect to animals receiving a standard diet only (without supplementation). There was a statistically significantly higher content of both monounsaturated and polyunsaturated fatty acids (total value) in the blood serum of micro- and nanogenistein-supplemented animals, with respect to animals receiving only a standard diet (without supplementation). There was a statistically significantly lower content of 12-HEPE, HODE and 12-HETE in the blood serum of genistein-

supplemented rats, with respect to the content of the aforementioned markers in the blood serum of rats receiving only a standard diet, devoid of supplementation.

CONCLUSIONS

Based on the study, it was shown that supplementation of animals with nano, micro and macro genistein had an effect on both the development of the tumor process, as well as on the concentrations of selected markers in the biological fluids of rats treated with 7,12-dimethylbenzanthracene. Learning about the mechanisms of action of genistein based on the analysis of selected biomarkers seems to be of great importance in assessing the safety of its use. There is a need for further research in this direction.