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Fund “Nauka” Project № 16011 Resume – Competition-Based Session 2016:
“Experimental study of the effects of biologically active substances of plant origin in models of metabolic syndrome and liver toxicity in rats with the aim of future development of drugs or dietary supplements”
Project leader: Prof. Stefka Vasileva Valcheva-Kuzmanova, MD, PhD, DSc

The present project aims to study biologically active substances of plant origin in experimental models of metabolic syndrome and liver damage in rats. Metabolic syndrome (MS) is a condition of impaired energy metabolism with visceral obesity, dyslipidemia and insulin resistance. Non-alcoholic fatty liver disease is considered to be the hepatic manifestation of MS. The social significance of MS is determined by the risk of developing diabetes, cardiovascular diseases and neuropsychiatric disorders.

To induce MS, experimental animals are subjected to a diet rich in fructose and saturated animal fats. Liver damage is induced by paracetamol – an established method of organ toxicity by generating free radicals. Experimental animals are treated with three doses of test substances: anethole, fruit juice from Aronia melanocarpa, fruit juice from Chaenomeles maulei, aqueous extract of Kochia scoparia. The effect of Aronia melanocarpa fruit juice is studied in healthy people and patients with metabolic syndrome.

The lipid profile, blood sugar, insulin sensitivity, indicators of oxidative stress, liver enzymes are studied in the MS model. Behavioral tests for anxiety, depression, memory are performed. Pathological changes in the liver, visceral adipose tissue and pancreas are sought with routine histopathological and immunohistochemical methods to prove inflammation and apoptosis. Adult neurogenesis in the hippocampus is studied. In humans (healthy and with MS), lipid profile, blood sugar, oxidative stress indicators, liver enzymes are studied.

In the model of paracetamol-induced liver toxicity, liver enzymes, proinflammatory cytokines, oxidative stress indicators and histopathological changes are investigated.

The tested substances are expected to have a protective effect against organ damage based on their polyphenolic content.

The project contributes to the development of the priority scientific directions in MU-Varna.

Achieved results:

The experimental model of metabolic syndrome (MS) is an innovation in the experimental work of the Department of Pharmacology and Clinical Pharmacology and Therapeutics.

The effects of Aronia melanocarpa fruit juice, Chaenomeles maulei fruit juice, Kochia scoparia infusion and anethole in an experimental model of metabolic syndrome were studied for the first time in the world research practice. In the model of MS in rats, Aronia melanocarpa fruit juice showed a sedative-anxiolytic effect and improved memory functions, an anti-inflammatory effect in carrageenan-induced paw inflammation, prevented obesity and dose-dependently reduced the degenerative changes in the liver, heart and adipose tissue of rats with MS. Chaenomeles maulei fruit juice demonstrated an anxiolytic effect, prevented obesity and dose-dependently reduced the degenerative changes in the liver, heart and adipose tissue. The aqueous infusion of Kochia scoparia seeds showed an anxiolytic and antidepressant effect, improved memory functions, improved lipid profile and dose-dependently reduced the degenerative changes in the liver, heart and adipose tissue of rats with MS. Anethole improved memory functions and dose-dependently reduced the degenerative changes only in the adipose tissue in rats with MS.

The effects of Chaenomeles maulei fruit juice, Kochia scoparia infusion and anethole in an experimental model of paracetamol-induced liver toxicity were studied for the first time in the world research practice. In this model, the fruit juice from Chaenomeles maulei demonstrated a hepatoprotective effect by reducing in the liver necrosis. The aqueous infusion of Kochia scoparia seeds showed a hepatoprotective effect by reducing the liver damage and lowering liver enzymes. Anethole led to some reduction in the area of liver necrosis.

The clinical study in overweight and healthy-weight individuals demonstrated the positive effects of Aronia melanocarpa fruit juice on parameters of the oxidative status. The fruit juice improved the activity of superoxide dismutase and inhibited the process of lipid peroxidation in the overweight participants. It also affected in a favorable manner some of the parameters of energy metabolism and liver function in these individuals.

The investigations in the project contribute to the development of one of the priority scientific fields in MU - Varna: Food and nutrition.

Three doctoral students with supervisor – Prof. Stefka Vasileva Valcheva-Kuzmanova, MD, PhD, DSc, were enrolled as a result of the project activities. They are:

1. Mehmed Reyzov Abtulov with a dissertation topic: “Pharmacological study of the effects of fruit juice from Aronia melanocarpa in an experimental model of metabolic syndrome”,
2. Klementina Moncheva Moneva-Marinova with a dissertation topic: “Pharmacological study of the effects of fruit juice from Chaenomeles maulei in an experimental model of metabolic syndrome”,
3. Elis Rafailova Gasanzadeeva with a dissertation topic: “Pharmacological studies with anethole in an experimental model of metabolic syndrome”.

The results from the project are included in a monograph on the beneficial effects of infusions of seeds of Kochia scoparia. The monograph is used for habilitation of one of the participants in the project – Silvia Gancheva Marinova.