## THE RESEARCHES OF THE INFLUENCE OF POLYPHENOL CONCENTRATE FROM GRAPE SEEDS WITH STEVIA ON THE DEVELOPMENT OF DIABETES

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Diabetes mellitus (DM ) – is the most common disorder of the endocrine system, which is characterized by disturbance of all types of metabolism and, primarily, the carbohydrate one. Vascular pathologies occupy an important role in this disease, they are as follows: microangiopathy ( retinopathy and nephropathy ), macroangiopathy ( myocardial infarction, stroke , gangrene of the lower limbs), neuropathy. Pathological changes appear in all elements of the vascular wall: endothelium , smooth muscle cells and other cells and structures.

Metabolic disorder of NO is regarded as one of the causes of diabetes mellitus type 2 (DM 2). NO has a pronounced selectivity for pancreas cells, and its negative effect is realized through the toxic forms of nitrogen oxides ( peroxynitrite ).

The purpose of this research has been to investigate the influence of polyphenol concentrate which has been obtained from grape seeds cultural, that contains the extract of stevia, on the work of the insular apparatus and NO-synthase system in the control animals and the animals with experimental DM1 and DM2.

**Materials and methods.** The experiments have been carried out on the rats of the line Wistar with the weight of 140-200 g , which have been contained on a standard diet of a vivarium . The effects of polyphenol concentrate that has had the stevia extract (PCS) for the content of glucose , insulin , nitrite , arginine and citrulline in the blood of the control rats and animals with DM1 and DM2.

DM1 in the animals has been caused by a single intraperitoneal injection of a solution of Streptozotocin (STZ) ("Sigma", USA) in 1 M citrate buffer pH 4.5 at a dose of 55 mg / kg of the body weight. The development of diabetes has been monitored by measuring the level of glucose and insulin in the rats' blood serum. DM2 in the animal has been caused by a high-calorie diet (45 % saturated fat) with

fructose (2 g per 100 g of the body weight per a day ) during 4 weeks. The treatment has been started on 7<sup>th</sup> day after the injection of streptozotocin and on 14<sup>th</sup> day after the initiation of high-calorie diet.

**Results.** Our studies have showed that in the experimental animal with DM1 and DM2 there is the increase of glucose in blood in 4.59 and 2.53 times, respectively, compared to the control animals.

In the experimental animals with DM1, there is also the decrease of insulin levels in the blood in 2.4 times, compared to control animals.

In the experimental conditions DM2, we have observed simultaneous increase of the content of insulin and glucose in the blood of the animals. Furthermore, according to the received data in the present research, the rats that have been kept on a fructose diet, we have observed the reduction of NO and citrulline in the blood and the content of arginine has significantly increased.

Application of the grape seed extract with stevia has reduced glucose and insulin levels in the animals with type 2 diabetes, and positively influenced the indicators of nitric oxide metabolism in the animals with both Experimental Pathology.

**Conclusions.** Thus, these results suggest that PCS, under the conditions of the experimental diabetes, has a normalizing action on both the work of insular apparatus and system for NO generating. Our studies have shown that polyphenolic concentrates that have been obtained from grape seed cultivars "Merlot" and " Rkatsitelli ", during a long administration to the experimental animals have a normalizing effect on the work of insular system, glucose homeostasis, as well as generating system oxide

During Diabetes mellitus the polyphenol concentrate, which has been obtained from grape seeds cultural, containing the stevia extract, has a moderate hypoglycemic effect and shows a pronounced normalizing effect on the the work of insular apparatus according to the models DM1 and DM2.

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