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Abstract

Nowadays, medical plants are treated as the source of biologically active compounds, which are often extracted on a commercial scale and used in targeted therapies of many diseases. Plant extracts of potential anti-diabetic effect may stabilise blood sugar concentration, increase cell sensitivity to insulin, alleviate inflammations or decrease the number of free radicals generated in diabetes. Taking into consideration the significance of oxidative stress in diabetes pathogenesis, as well as possibly various impact of different plant extracts on pro-oxidant-antioxidant balance, an attempt to find answers to the following questions was made: Does introducing plant extracts into diet modify carbohydrate and lipid metabolism in diabetes? Do the extracts of *Morus alba L., Trigonella foenum graecum L, Pericarpium Phaseolus vulgaris L., Galega officinalis L.*, and *Vaccinium myrtillus L.* activate non-enzymatic antioxidative system of an organism? To what extent do the plant extracts influence the activity of marker antioxidant enzymes? Are there any dose-dependent differences in therapeutic influence of the researched extracts in diabetes? Does the application of plant extracts as dietary supplements have potential preventive significance, as well as, importance for the improvement of a diabetic's quality of life?

The experiments were carried out on 240 male Swiss albino mice *(Mus musculus L.)*, average body weight 25±1 g. Animals were bred in the Institute of Biology of Pedagogical University of Cracow. Throughout the study, the mice were kept in a pathogen-free animal facility with a 12/12-hour light/dark cycle. The study was conducted in two series, differing dose used plant extracts (I series–dose 100 $mg \cdot kg^{-1}$ b.w. per day and II series–dose 500 $mg \cdot kg^{-1}$ b.w. per day). Animals (in each series) were divided into twelve groups (one control and eleven experimental groups) of ten mice each. Mice

of control groups received per os 0.1 ml of 0.9% NaCl solution (Polfa, Poland). Diabetes was induced in the overnight fasted male Swiss albino mice by a single intraperitoneal injection (i.p.) of streptozotocin (75 $mg \cdot kg^{-1}$ b.w.) dissolved in 0.05 M citrate buffer (pH=4.5). The animals confirmed diabetic by the elevated plasma glucose levels (~9 $mM \cdot L^{-1}$) were used for the study. The investigated extracts of: white mulberry leaves (*Morus alba L.*), bilberry (*Vaccinium myrtillus L.*), medical galega (*Galega officinalis L.*) and pericarp of common bean (*Phaseolus vulgaris L. pericarpium*) and fenugreek seeds (*Trigonella foenum graecum L.*) was administered once a day for 4 weeks. Extracts were prepared using commercially available preparations ("Herbapol - Lublin" S. A. ul. Diamentowa 25, 20-471 Lublin, Poland; „Herbapol" w Krakowie SA, ul. Chałupnika 14, 31-464 Kraków, Poland; Zakłady Farmaceutyczne COLFARM S.A. ul. Wojska Polskiego, Mielec, Poland) and were dissolved in water and administered to mice orally. Administrations were carried out at 8.00 am. Two hours after the last administration animals were anaesthetized (Vetbutal Biovet in dose 35 $mg \cdot kg^{-1}$ body wt) and decapitated. The blood samples were collected from the carotid artery. The concentrations of glucose, cholesterol and triglycerides were estimated in the blood serum with STAMAR kits. Reduced glutathione (GSH) in the blood was estimated according to the method of Ellman (1959). The total antioxidant status (TAS) was estimated in the blood serum with RANDOX Laboratories Ltd. apparatus according to the instructions of the producer. The design of superoxide dismutase (SOD) and glutathione peroxidase (GPx) activity assay is based on a sandwich Enzyme-Linked Immunosorbent Assay (ELISA). Catalase (CAT) activity was determined at 25°C according to Aebi (Aebi 1984). After the administration of all extracts (in dose 100 $mg \cdot kg^{-1}$ b.w.) was found a decrease [MA-7.23%; TFG-12.16%; PVP-2.72; GO-0.17%; VM-1.02%] in the concentration of

glucose in comparison to control values. Similarly, after the administration of all extracts (in dose 500 $mg \cdot kg^{-1}$ b.w.) was found a decrease (MA-14.85%; TFG-19.53%; PVP-18.18%) but also increase (GO-22.56%; VM-32.66%) in the concentration of glucose in comparison to control. Moreover, it was observed that combined administration of streptozotocin and all extracts (VII, VIII, IX, X and XI experimental groups) in doses 100 $mg \cdot kg^{-1}$ b.w. and 500 $mg \cdot kg^{-1}$ b.w. caused an decrease in the concentration of glucose in comparison to DM group (I experimental group-after streptozotocin administration). In patients with diabetes, the optimal control of glycaemia is of extreme importance, due to which the improvement of plasma lipid parameters is possible regardless of hypoglycaemic treatment. The studies demonstrated that administration of selectively extracts the effect of changes in the cholesterol and triglyceride concentrations in blood serum of mice. It was found that only a fenugreek extract, significantly ($p<0.001$) decrease of cholesterol, and extract of mulberry ($p<0.001$) and fenugreek ($p<0.05$) decrease in the concentration of triglycerides. Has also been demonstrated that extracts from bilberry and medical galega increase the concentration of cholesterol and triglycerides as compared to the control mice. At the same time, it was found that there is a dose-dependent effect of extracts on lipid profile. Significant increase of antioxidants activities in mice blood serum were observed after administration all extracts and doses in comparison to II experimental group (DM) and control animals ($p<0.001$) except of bilberry and medical galega groups (dose 100 $mg \cdot kg^{-1}$ b.w.). The obtained results suggest that long term application of extracts of *Morus alba L., Galega officinalis L., Vaccinium myrtillus* L. leaves, *Trigonella foenum graecum L.* seeds and *Phaseolus vulgaris L.* pericarp positively influence the alleviation of disturbed, in the course of diabetes, organism homeostasis. The researched extracts display anti-oxidative, hypoglycaemic and hypolipidemic activity.

Hence, they may be used as dietary supplements for diabetics. Moreover, it is worth noticing that various mechanisms of protective effects of extracts may be used in the practice of therapeutic mixtures preparation. The experiment has shown that high dose (500 $mg \cdot kg^{-1}$ b.w.) of plant extracts (of *Vaccinium myrtillus L.* and *Galega officinalis L.*) may be toxic (similarly to streptozotocin). It should, however, be remembered that the disease occurring in a good animal model has to be of the same origin and display the same symptoms as the disease in a human organism. Hence, the conducted research may occur useful not only from the theoretical point of view, but may also provide new cognitive elements in effective and practical support of anti-diabetic chemotherapy.

Key words: *Morus alba L., Trigonella foenum graecum L, Pericarpium Phaseolus vulgaris L., Galega officinalis L., Vaccinium myrtillus L.*, biological active compounds, diabetes, mice