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STUDY OF HYPOGLYCEMIC ACTIVITY OF EXTRACT OF YACON (*POLYMNIA SONCHIFOLIA* POEPP. & ENDL.) ROOT TUBERS

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Abstract

Polymnia sonchifolia Poepp. & Endl., commonly known as yacon, belongs to the family *Asteraceae*. It has been introduced into a culture in many countries around the world. For a long time, yacon root tubers have been recommended for use in diseases that are associated with metabolic disorders. Therefore, our study aimed to establish the hypoglycemic activity of yacon extract.

The study of the hypoglycemic effect of the thick extract of yacon root tubers was conducted on a model of dexamethasone insulin resistance caused in rats weighing 250–295 g by subcutaneous administration of dexamethasone at a dose of 0.125 mg/kg during 14 days. A thick extract of yacon (250 mg/kg) showed a pronounced hypoglycemic activity, the degree of which it approached the synthetic hypoglycemic drug metformin, the difference in the relative initial level of which on day 7 of the experiment was +16.57 %, on day 14 +28.20 %. The increase in blood glucose relative to baseline in rats injected with Metformin, on days 7 and 14 was + 14.93 % and +21.13 %, respectively. Therefore, the use of an aqueous solution of a thick extract of yacon root tubers contributed to a significant increase in glucose tolerance in an experiment on rats in a model of chronic dexamethasone hyperglycemia. This substance is promising for the creation of a new herbal drug with a pronounced hypoglycemic effect.

Keywords: yacon, *Polymnia sonchifolia* Poepp. & Endl., *Smallanthus sonchifolius*, root tubers, thick extract, hypoglycemic activity, diabetes mellitus, dexamethasone, Arfazetin, Metformin, inulin

Introduction

Currently, the range of herbal medicines used in official medicine is over 50%. Phytotherapy has a number of edges, such as it is low-toxic, having a mild pharmacological effect, and can be used for a long period without significant side effects [1-4].

Expanding research to find new sources of effective and safe drugs of plant origin is an urgent task of modern pharmaceutical science and medicine [5, 6]. One of the ways to increase the number of herbal medicines is to study new species of medicinal plants that have been introduced and grown in Ukraine.

Given that diabetes mellitus is one of the most important medical and global social problems facing today, it is important to find effective antidiabetic drugs [7]. Today in the world, as well as in Ukraine, there is a rapid increase in the number of patients with diabetes, which leads to disability and high mortality due to the development of diabetic complications [8]. According to the official information of the International Diabetes Federation (2019), the number of patients is projected to increase to 642 million by 2040 [9-12].

There are numerous data on the use of medicinal plants for the treatment of patients with diabetes in scientific and folk medicine. Currently, about 200 plants are known to have an antidiabetic effect.

Phytotherapy in diabetes is based on the following basic principles: partially reproduces or enhances the effects of many oral antidiabetic drugs with a possible reduction in their side effects and dose; promotes insulin synthesis, optimizing its action at the tissue level; stimulates the regeneration of β-cells; improves the work of all parts of the immune system; normalizes secondary metabolic disorders and hormones; provides prevention of complications from the cardiovascular, urinary systems, musculoskeletal system, etc [13, 14].

The range of official herbal medicines recommended in the treatment of diabetes is minor. Therefore, the study and use of cultivated medicinal plants open up certain prospects to create cost-effective, affordable, safe and therapeutically effective domestic drugs, including those with hypoglycemic properties.

Such plants include the yacon (*Polymnia sonchifolia* Poepp. & Endl., synonym *Smallanthus sonchifolius*) of the family *Asteraceae*. The *Asteraceae* family is the largest family of flowering plants [15].

In the wild, yacon grows in Colombia, Ecuador and Peru. Biologically active substances of the yacon have the ability to reduce blood sugar, improve metabolic processes in the body, affect the function of the gastrointestinal tract, have antisclerotic action.

Yacon root tubers are low-calorie foods that are very popular among fans of a healthy and balanced diet, given that yacon root tubers contain large amounts of inulin.

Yacon also has an antisclerotic effect, which helps reduce the growth of microorganisms that cause diarrhea. In addition, root tubers stimulate the development of beneficial intestinal bacteria and accelerate the synthesis of B vitamins, reducing constipation [16]. Delgado G.T.C. et all. in their studies showed that the biologically active substances of yacon lower cholesterol and triglycerides [17].

Such biologically active substances of yacon as phytoalexins show antimicrobial activity [18], phenolic compounds (chlorogenic acid) – antioxidant, fructans, fructooligosaccharides – prebiotic [17, 19- 21].

Fatty acids are very important active substances for the treatment and improving the course of diabetes because contribute to the reduction of blood cholesterol, normalize lipid and protein metabolism, and improve microcirculation [22-24]. The fatty acids, present in the plant, were studied by GC/MS analysis [25, 26].

It is known that the main value of yacon root tubers as a source of biologically active substances is that they contain inulin and other fructans. In the early twentieth century, inulin was known as a carbohydrate suitable for diabetics, as it did not give rise to a glycemic response [27, 28]. Therefore, yacon root tubers have long been recommended to use in diseases that are associated with metabolic

disorders: diabetes, obesity, atherosclerosis [29, 30].

It was established that inulin is well absorbed by patients with diabetes, even in large doses. However, it does not affect glucose levels and insulin in the blood. This ability is widely used in the production of dietary foods for diabetics. Due to its low caloric content, inulin is used in the diet of patients with metabolic disorders [31, 32]. Therefore, qualitative and quantitative analysis of inulin in yacon root tubers was performed. The determination was performed by GC/MS method on chromatograph an Agilent 6890N/5973inert (*Agilent Technologies*, USA) [33-38]. It was found that yacon root tubers contain 46.28 mg/g of inulin [39].

The use of inulin increases the number of bifidobacteria in the intestine, reduces the number of enteropathogenic bacteria [40]. Inulin normalizes carbohydrate metabolism, regulates lipid metabolism, thereby normalizing blood glucose levels [41, 42]. It is recommended in the treatment and prevention diet when diabetes [30, 43]. Therefore, our study aimed to establish the hypoglycemic activity of the thick extract of yacon root tubers.

Methods

Plant materials

Root tubers of the *Polymnia sonchifolia* Poepp. & Endl. (*Smallanthus sonchifolius*; yacon) were collected at research plots of Taras Shevchenko National University of Kyiv (Kyiv region, Ukraine). It is collected in autumn after the death of aerial parts. The raw material was authenticated by Prof. L. Mishchenko. [28]. A voucher specimen was deposited in the herbarium at the Department of Pharmacognosy and Medical Botany, TNMU, Ternopil, Ukraine [44-46]. The study plant material was dried using the conventional method and stored in paper bags in a dry place [47-49].

Preparation of extract

About 1000 g of dried root tubers of the *Polymnia sonchifolia* Poepp. & Endl. were powdered with the help of an appropriate grinder [50]. It was taken in an extractor and extracted using water as a solvent. The extract was concentrated under vacuum to half under volume and dried at a temperature of 50±2° C [51].

Animal models

The experiments were performed on 35 nonlinear white rat-females body weight, 250-295 g. All animals were kept on a standard vivarium diet [52-54]. The animals were kept in a room having a temperature 20-22 ° C, and relative humidity of 55-70 % under 12/12 hour light and dark cycle with standard laboratory diet and water was given ad libitum (feeding was stopped 12 hours before blood sampling) [55-57]. Pharmacological studies have been conducted by the rules and requirements of the "General Principles for the Work on Animals" approved by the I National Congress on Bioethics (Kyiv, Ukraine, 2001, and the Law of Ukraine "On the Protection of Animals from Cruelty" of 26.02.2006 and agreed with the provisions of the European Community Guidelines [58-61]. The removal of animals from the experiment was carried out under light inhalation anesthesia by decapitation [62].

Study of the hypoglycemic effect of Polymnia sonchifolia Poepp. & Endl. root tubers extract

Studies of the hypoglycemic effect of a thick extract of yacon (*Polymnia sonchifolia* Poepp. & Endl.) root tubers were performed on 35 nonlinear white rat-females body weight, 250-295 g. Acute hyperglycemia was caused by intraperitoneal administration of 40 % glucose solution at a dose of 2 g/kg. Animals for the experiment were divided into 5 groups of 7 animals each (n = 7). Group 1 was the control (IC), group 2 (CP) consisted of animals that received dexamethasone at a dose of 0.125 mg/kg, group 3 (CP+TEYRT) received dexamethasone and yacon root tubers thick extract 250 mg/kg, group 4 received dexamethasone and metformin, group 5 received dexamethasone and Arfazetin.

The study of hypoglycemic action of yacon root tubers extract and reference compounds – Arfazetin and Metformin were performed on a model of primary insulin resistance (dexamethasone hyperglycemia), which was caused by subcutaneous administration of Dexamethasone (KRKA, Slovenia), 0.125 mg/kg during 14 days [63, 64].

Yacon root tubers thick extract was studied at a dose of 250 mg/kg intragastrically once daily

beginning from day 1 of glucocorticoid administration.

Metformin in the form of tablets Siofor BERLINCHEMI AG (MENARINI GROUP) (100 mg/kg) and Arfazetin officinal herbal collection (PJSC "Viola", Ukraine) at a dose of 9 ml/kg administered in similar regimens were used as comparison drugs [65-67].

The blood glucose level was measured using BIONIME Rightest GM 550 glucometer [68]. Blood glucose was determined using a glucometer on day 1 (baseline, before the administration of dexamethasone), as well as on days 7 and 14 of the experiment.

Statistical analysis

The obtained experimental data were processed by the methods of variation statistics (arithmetic mean and its standard error were calculated). For multiple comparisons of data with normal distribution, parametric one-way analysis of variance ANOVA was performed and the Newman-Keuls method was used, and the data were presented as mean (M) and mean error (m) [69]. In other cases, comparisons of samples using the nonparametric Mann-Whitney test were used [70, 71]. Differences between experimental groups were considered statistically significant at $p \leq 0.05$. A standard package of statistical programs Statistica, v. 6.0 (StatSoft Inc.) was used to perform mathematical calculations [72].

Results and Discussion

The obtained results indicate that the studied extract when administered intragastrically in a model of acute hyperglycemia has a dose-dependent hypoglycemic effect (Table 1).

Yakon root tuber extract, at the maximum dose (400 mg/kg), 1 h after glucose administration, showed hypoglycemic activity of 18.7 %. Thick extract of yacon root tubers (400 mg/kg) showed hypoglycemic activity of 18.3% 2 h after glucose administration.

The results of determining the glycemia of rats of all groups are shown in Table 2.

The results of the studies showed a reliable control of the increase in basal (after 12 hours of fasting) blood glucose level of rats control pathology (CP), on day 7 (6.04±0.21 mmol/l) and day 14 (6.43±0.17 mmol/l) relative to the normal initial level (4.59 ± 0.13 mmol/l). In animals, the intact control (IC) glycemic level was within normal limits relative to baseline: (5.00±0.1) mmol/l on day 7 and (5.09±0.07) mmol/l on day 14.

In rats treated with an aqueous solution of the thick extract of yacon root tubers at a dose of 250 mg/kg orally, the glycemic level was lower than the CP on both days 7 and 14. Thus, on day 7 of the experiment in animals of this group, the average blood glucose level increased by 16.57 % relative to baseline and was (5.73±0.25) mmol/l, which is 15.21 % lower than the dynamics of blood glucose growth in the group of rats CP, where glucose levels increased by 31.78 % relative to baseline. On day 14 of the experiment, the average value of glycemia in rats treated with the studied extract of yacon on the background of CP was (6.30±0.32) mmol/l, which is 11.99 % lower than the dynamics of blood glucose growth in the group of rats CP, where the glucose level increased by 40.19 % relative to baseline.

Decoction of Arfazetin collection had little effect on the dynamics of growth of blood glucose in rats and the difference in relative baseline was 7 days + 28.88 %, 14 days – + 39.42 %, which is almost equal to the CP (+31.78 % and + 40.19 % respectively).

A thick extract of yacon (250 mg/kg) showed a pronounced hypoglycemic activity, the degree of which it approached the synthetic hypoglycemic drug metformin. Therefore, the use of an aqueous solution of a thick extract of yacon root tubers contributed to a significant increase in glucose tolerance in an experiment on rats in a model of chronic dexamethasone hyperglycemia.

Conclusions

It was found that a thick extract of yacon (*Polymnia sonchifolia* Poepp. & Endl. synonym *Smallanthus sonchifolius*) root tubers have a hypoglycemic activity and its conditionally effective dose can be considered 250 mg/kg. This dose may

be recommended for further in-depth studies of this extract as a hypoglycemic agent.

Therefore, obtained by the proposed method, a pharmacological substance in the form of a thick extract of yacon is promising for the creation of drugs with a sufficiently pronounced hypoglycemic activity.

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Table 1. Blood glucose content in rats with acute hyperglycemia on the background of the introduction of the thick extract of yacon root tubers (M±m, n=7)

Thick extract of yacon root tubers, dose	The baseline (initial) level of glycemia, mmol/l	In 1 hour	% reduction in glycemia relative to control	In 2 hours	% reduction in glycemia relative to control
Control	3.66±0.19	16.21±0.89	0%	9.17±0.37	0%
50 mg/kg	4.66±0.21	18.87±0.52	-9.91%	11.17±0.65	-6.97%
100 mg/kg	3.59±0.17	14.30±0.50	-12.5%	8.41±0.21	-10.7%
150 mg/kg	3.53±0.22	13.81±0.93	-15.2%	8.31±0.50	-11.1%
200 mg/kg	3.89±0.18	15.06±0.69	-16.2%	8.94±0.37	-14.2%
250 mg/kg	3.64±0.12	13.94±0.40	-17.1%	8.31±0.28	-16.2%
300 mg/kg	3.94±0.11	14.96±0.39	-18.4%	9.00±0.27	-16.2%
400 mg/kg	3.60±0.17	13.63±0.63	-18.7%	8.13±0.33	-18.3%

Table 2. Hypoglycemic activity of a thick extract of yacon root tubers in a model of dexamethasone hyperglycemia in rats (M+m, n=7)

Group of animals	Blood glucose level, mmol/l		
	Day 1 (baseline)	Day 7	Day 14
IC	5.03±0.08	5.0±0.10 (-0.57%)	5.09±0.07 (+1.14%)
CP	4.59±0.13	6.04±0.21 (+31.78%)#	6.43±0.17 (+40.19%)#
CP + TEYRT	4.91±0.25	5.73±0.25 • (+16.57%)*	6.30±0.32 • (+28.20%)*
CP + Arfazetin	4.46±0.20	5.70±0.22 • (+27.88%)#	6.21±0.06 • (+39.42%)#
CP + Metformin	5.07±0.14	5.83±0.18 • (+14.93%)*	6.14±0.28 • (+21.13%)*

Notes: IC – intact control;

CP – control pathology;

TEYRT – thick extract of yacon root tubers;

• - statistically significant differences ($p < 0.05$) relative to baseline in each group;

* statistically significant differences ($p < 0.05$) relative to control pathology (dexamethasone without correction);

- statistically significant differences ($p < 0.05$) relative to metformin.

The number in parentheses indicates the degree of increase in glycemia relative to baseline in each group.