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# STUDY OF THE HYPOGLYCEMIC EFFECT OF THE EXTRACT FROM THE TUBERS OF *STACHYS SIEBOLDII* MIQ.

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**Abstract**

The prevalence of diabetes mellitus is becoming an epidemic. The variety of etiological factors contributes to the fact that types 2 of diabetes mellitus occur among different age groups and among different segments of the population. Particular attention deserves the different medicinal plants such will have more biologically active substances that will influence all links of the pathogenetic mechanism of development of diabetes mellitus and its complications. Of great interest in this regard is one of the oldest vegetable and medicinal plants *Stachys sieboldii* MIQ. The study of the hypoglycemic effect of the extract from the tubers of *Stachys sieboldii* was conducted on a model of dexamethasone insulin resistance caused in rats weighing 180–230 g by subcutaneous administration of dexamethasone at a dose of 4 mg/kg for 4 days. The most pronounced hypoglycemic effect of the studied extract was found in doses of 25 and 50 mg/kg and with increasing dose, the activity of the test sample decreased. In terms of expressiveness of the hypoglycemic effect, the extract from the tubers of *Stachys sieboldii* at a dose of 25 mg/kg significantly prevailed, and at a dose of 50 mg/kg was not inferior to the reference drug the official herbal mixture "Arfazetin". The results obtained are an experimental rationale for extending the indications of use of the extract from the tubers of *Stachys sieboldii.*

**Keywords**: extract from the tubers of *Stachys sieboldii,* hypoglycemic effect, diabetes mellitus, dexamethasone, insulin

## Introduction

Diabetes mellitus is one of the most problems of the world, which requires instant solutions, as the epidemiological situation is alarming. The number of patients is increasing rapidly each year, leading to increased disability and mortality due to the development of angiopathies [1-3]. Modern pharmacotherapy increasingly takes into account the centuries-old experience of folk medicine with the use of phytopreparations as monotherapy and in combination with synthetic drugs [4, 5]. The advent of synthetic drugs, which mostly simulate the biologically active substances of plants, has not reduced the role of natural drugs [6, 7]. This is quite justified because phytotherapy has a number of advantages over traditional therapy with synthetic drugs, namely, it is low-toxic, has a mild pharmacological effect, and can be used for a long period of time without significant side effects [8, 9].

Medicinal plants are unique sources of healing compounds – biologically active substances that are used both for the prevention and treatment of different diseases of the human body [10-13]. Of great interest in this regard is one of the oldest vegetable and medicinal plants – Japanese artichoke (*Stachys sieboldii* MIQ), also known as stachys or Chinese artichoke. According to traditional oriental medicine, the root tubers of Japanese artichoke help improve digestion and have a healing effect in diabetes and hypertension [14].

Japanese artichoke has long been used in Chinese and Tibetan folk medicine in the treatment of tuberculosis, hypertension, ischemic stroke, senile dementia, and various gastrointestinal diseases. Biologically active substances contained in root tubers have a positive effect on carbohydrate and lipid metabolism, lower blood pressure, cholesterol [15, 16]. Biologically active substances of stachys manifest a wide range of pharmacological properties in the complete absence of toxicity. In folk medicine, its tubers are used as a hypoglycemic, anticoagulant, antihypertensive, antiulcer and sedative agent [17, 18]. It lowers cholesterol, regulates metabolic processes and strengthens the immune system [19, 20]. In the literature there is information about the antimicrobial and antitumor activity of stachys [15].

Hiroaki Nishimura et al. have singled out from the leaves of *Stachys sieboldii* on the basis of chemical and spectral analysis of the structure of three new glycosides, called stachysosides A, B and C, they were identified as 2- (3,4-dihydroxyphenyl) ethyl O-α-l-arabinopyranosyl- (1→2) -α-1-rhamnopyranosyl-(1→3)-4-OE-caffeoyl-β-d-glucopyranoside (stachysosides A); 2-(3,4-dihydroxyphenyl)ethyl O-α-1-arabinopyranosyl-(1→2)-α-1-rhamnopyranosyl-(1→3)-4-OE-feruloyl-β-d-glucopyranoside (stachysosides B)and 2-(3-hydroxy-4-methoxyphenyl)ethyl O-α-1-arabinopyranosyl-(1→2)-α-1-rhamnopyranosyl-(1→3)-4-OE-feruloyl-β-d-glucopyranoside (stachysosides C) [21]. These compounds have been shown to provide *Stachys sieboldii* with antioxidant activity because they inhibit hyaluronidase activity [18].

Japanese scientists have found that methanolic tuber extract of Japanese artichoke, which contains glycosides, including acteoside and stachysosides C, significantly inhibits induced mortality from potassium cyanide poisoning in mice [22]. This extract inhibits hyaluronidase activity, has anti-inflammatory action, and is effective in kidney disease [17].

The antimicrobial activity of methanolic and ethanolic extracts from the leaves, herb and tubers of Japanese artichoke was studied. It was found that methanol extract from the leaves and tubers and ethanol extract from the tubers of *Stachys sieboldii* show a pronounced antibacterial effect on the culture of *Salmonella typhimurium* [23].

According to literature sources, the tubers of Japanese artichoke contain up to 30.5 % dry matter, of which up to 2.2 % is protein, up to 1.7 % – amides, up to 0.2 % – fats, up to 19 % – carbohydrates. Carbohydrates contain sugars – 1.8 %, fiber – 2.1 %, pectin – 1.9 %. It should be noted that carbohydrates contain a rare tetrasaccharide – stachyose, which is similar in composition and properties to inulin and has an insulin-like effect [24, 25].

Due to the lack of enzymes capable to hydrolyze stachyose, in the human body, this substance is not exposed to digestive enzymes and is not absorbed in the upper gastrointestinal tract. Stachyose

reaches the large intestine in unchanged form, where fermentation occurs with the formation of monosaccharide residues – α-galactose, β-fructose and α-glucose [26].

Stachyose, like insulin (a hormone of the pancreas), provides active absorption of carbohydrates by organs and tissues. Demonstrating such a biological effect, Japanese artichoke becomes an indispensable medicinal plant in diabetes mellitus, which is often complicated by coronary heart disease, arrhythmia, hypertension, pulmonary tuberculosis with the formation of caverns, fatty liver disease, pyelonephritis, neuralgia, severe visual disturbances, ulcers, gangrene of the lower extremities, furunculosis of the skin, etc. [27].

Therefore, the pharmacological study of hypoglycemic action of the studied plant is relevant in order to create domestic new hypoglycemic drugs based on the tubers of *Stachys sieboldii*, which, according to the literature, contains a tetrasaccharide stachyose, which has an insulin-like effect [25].

## Methods

*Plant Materials*

Tubers of Chinese artichoke (*S. sieboldii* Miq.) were collected on research grounds of Educational and Scientific Centre "Institute of Biology and Medicine", Taras Shevchenko National University of Kyiv in November 2017. The tubers was dried using conventional methods and then stored in paper bags in dry place [28-30]. A voucher specimen was deposited in the laboratory herbarium of the Department of Pharmacognosy and Medical Botany (TSMU, Ternopil, Ukraine) [31, 32].

*Preparation of extract*

The dried sample was powdered by a pin crusher and the powders were extracted 3 times with 70% ethanol. 70% ethanolic extract was filtered through filter paper (100 mm; Whatman, Maidstone, UK) and evaporated using a vacuum rotary evaporator [33, 34].

*Animal models*

The experiments were performed on 50 white Wistar rats weighing 180–230 g. All animals were kept on a standard I. Horbachevsky Ternopil National Medical University (TNMU), vivarium diet [35]. The animals were kept in room having temperature 22 ± 2 ° C, and relative humidity of 44-55 % under 12/12 hour light and dark cycle with standard laboratory diet and water given ad libitum [36].

Pharmacological studies have been conducted in accordance with 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 agreed with the provisions of the "European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes" (Council of Europe No 123, Strasbourg 1985), and the Law of Ukraine "On the Protection of Animals from Cruelty" of 26.02.2006 [37-40]. The removal of animals from the experiment was carried out under light inhalation (ether) anesthesia by decapitation.

*Study of the hypoglycemic effect of the extract from the tubers of Stachys sieboldii*

The study of the hypoglycemic effect of the extract from the tubers of Japanese artichoke was conducted on a model of dexamethasone insulin resistance caused in rats weighing 180–230 g by subcutaneous administration of dexamethasone at a dose of 4 mg/kg for 4 days. According to the literature, the administration of glucocorticoids in high doses leads to the development of moderate basal hyperglycemia, increased concentrations of insulin and free fatty acids in the serum of rats. In addition, they show a decrease in the sensitivity of peripheral tissues to insulin and impaired glucose tolerance [41, 42]. On the third day, the level of basal glycemia was determined, which allowed randomization of animals into groups by random sampling using glucose levels as the main sign of distribution.

The studied drugs were administered in the therapeutic mode, the extract from the tubers of *Stachys sieboldii* in doses of 25, 50 and 100 mg/kg, the reference drug was an aqueous extract of the official herbal mixture "Arfazetin" (Viola, Ukraine) – at a dose of 9 ml/kg. It was started 4 days before the

last dexamethasone injection and continued for 4 consecutive days. Control animals received distilled water in a similar manner.

On the 7th day of the experiment, the level of basal glycemia in animals was determined and the dynamics of hypoglycemic action of the extract from the tubers of *Stachys sieboldii* (STE) was studied. Glucose content was determined before the administration of Japanese artichoke extract (0 h) and 1, 2 and 4 hours after. An Intraperitoneal glucose tolerance test was performed on the 8th day of the experiment (only 5 days of administration of the studied drugs).

Blood glucose was determined by the fasting glucose oxidase method in the morning in blood samples obtained from the tail vein of rats using Phyllis-diagnostics biochemical kits according to the instructions.

Intraperitoneal glucose tolerance test was performed in the morning on an empty stomach loading with glucose solution (3 g/kg) [42]. The studied agents were administered intragastrically 1 hour before intraperitoneal administration of 40 % glucose solution at a dose of 3 g/kg. The blood glucose content of the animals was determined immediately after administration of the studied drugs (0 min) and 15, 45, 60 and 90 min after carbohydrate loading.

The dynamics of hypoglycemic action were assessed within 4 hours: the initial level was determined, 1, 2, 3 and 4 hours after administration of STE in different doses and the official herbal mixture "Arfazetin".

The intensity of lipid peroxidation processes and the state of the antioxidant system were evaluated to characterize the total effectiveness of STE in this model. The content of substances that react with thiobarbituric acid (TBA reactants, TBA-R), which are the end products of degradation of unsaturated fatty acids of membrane phospholipids and catalase activity, an important enzyme of antioxidant system was determined in the serum of experimental animals on the background of diabetes. The content of TBA reactants was determined by I. D. Stalna and T. G. Garishvili methods [43].

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 Newman-Keuls method was used, and the data were presented as mean (M) and mean error (m). In other cases, comparisons of samples using the Mann-Whitney test were used. 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. USA) was used to perform mathematical calculations.

## Results and Discussion

Determination of the dynamics of the hypoglycemic effect of the extract from the tubers of *Stachys sieboldii* (STE) showed that a single injection in rats with diabetes, the studied agent showed a stable moderate hypoglycemic effect, which lasted for 4 h (Table 1). The studied extract showed the greatest hypoglycemic effect at a dose of 25 mg/kg. The activity of the studied agent averaged 19 %. At doses of 50 and 100 mg/kg, the extract almost did not reduce the level of basal glucose, its activity averaged 8–10 %. The official herbal mixture "Arfazetin" showed a similar dynamics of hypoglycemic action, but in terms of expressiveness was inferior to the extract of *Stachys sieboldii* at a dose of 25 mg/kg (Table 1).

According to the data obtained, four-fold administration of dexamethasone to rats at a dose of 4 mg/kg led to the development of moderate hyperglycemia, which lasted for the next 4 days. Basal glucose level in animals after dexamethasone injections increased statistically significantly to 7.89 mmol/l compared with 4.48 mmol/l in intact animals (Fig. 1).

Therapeutic administration of the studied extract in doses of 25 and 50 mg/kg contributed to reduce the level of basal glycemia to the values of intact animals (Fig. 1). Increasing the dose of the extract to 100 mg/kg led to a decrease in efficiency: the level of basal glucose, although statistically significantly lower than in the control pathology group, did not reach the level of intact animals. A similar trend was observed in the group of animals receiving the

reference drug the official herbal mixture "Arfazetin" at a dose of 9 ml/kg (Fig. 1).

At the end of the experiment, an intraperitoneal glucose tolerance test was performed (Table 2), the results of which indicated a violation of glucose utilization processes (Table 2). The glycemic response of rats from the control pathology group to the carbohydrate load was characterized by a slowing of the decrease in glucose level during the whole observation period. The blood glucose level of animals from the control pathology group remained statistically higher than in intact animals at 90 min of the test (Table 2). It was established that the inhibitory effect of glucocorticoids on the secretory activity of pancreatic β-cells is associated with the inactivation of mitochondrial FAD glycerophosphate dehydrogenase, an enzyme that plays a key role in glucose-stimulated insulin secretion.

Therefore, the obtained data indicate the initial disruption of glucose utilization processes due to the administration of excessive doses of dexamethasone.

When using the extract from the STE in doses of 25 and 50 mg/kg, the glycemic curve did not differ from that in intact animals, indicating the restoration of glucose utilization process and carbohydrate metabolism in general (Table 2). The effectiveness of the agent decreased when increasing the dose of the extract to 100 mg/kg.

The dynamics of glycemia during the intraperitoneal glucose tolerance test of the official herbal mixture "Arfazetin" was the same as that under the action of the studied extract, but less pronounced (Table 2).

Determination of the main values of the markers of the state of the lipid peroxidation system/antioxidant system of the body showed that under conditions of dexamethasone diabetes in the blood of rats statistically significantly increases the level of TBA-R. At the same time, the activity of catalase – an enzyme of the antioxidant system, showed a clear tendency to decrease. The absence of a statistically significant difference between the experimental groups is explained by the large variability of intragroup values of this indicator. Thus, the analysis of the obtained data allows stating the imbalance of pro/antioxidant processes in the lipid peroxidation/antioxidant system of the rats' body under the conditions of diabetes mellitus caused by dexamethasone (Table 3).

The administration of the studied extract at doses of 25 and 50 mg/kg led to the normalization of processes in the system of lipid peroxidation/antioxidant system of the body. Increasing the dose of STE to 100 mg/kg contributed to excessive activation of catalase, due to which there was a significant decrease in the level of TBA-R compared with both control pathology and physiological values of intact animals (Table 3). It should be noted that a reference drug the official herbal mixture "Arfazetin" showed the least pronounced antioxidant effect of the studied drugs.

Thus, the model of dexamethasone diabetes has pronounced hypoglycemic and antioxidant properties of the extract from the tubers of *Stachys sieboldii*. The most pronounced hypoglycemic effect of the studied STE was shown in doses of 25 and 50 mg/kg, with increasing dose the activity of the studied agent decreased. In terms of expressiveness of the hypoglycemic effect, the studied extract at a dose of 25 mg/kg significantly prevails, and at a dose of 50 mg/kg is not inferior to the reference drug the official herbal mixture "Arfazetin".

## Conclusions

For the first time, the screening study of the hypoglycemic activity of extract of the *Stachys sieboldii* tubers used in folk medicine for the prevention and treatment of diabetes mellitus type 2 was conducted. The model of dexamethasone diabetes has pronounced hypoglycemic and antioxidant properties of the extract from the tubers of *Stachys sieboldii*. The most pronounced hypoglycemic effect of the studied extract was found in doses of 25 and 50 mg/kg and with increasing dose, the activity of the test sample decreased. In terms of expressiveness of the hypoglycemic effect, the EST at a dose of 25 mg/kg significantly prevailed, and at a dose of 50 mg/kg was not inferior to the reference drug the official herbal mixture "Arfazetin". The antihyperglycemic, hypolipidemic and antioxidant effects make these extract of *Stachys sieboldii* tubers promising tools

for prevention and treatment of diabetes and its complications.

## References


1. Savych A, Marchyshyn S, Hamyk M. *et al.* Determination of amino acids content in two samples of the plant mixtures by GC-MS. Pharmacia 2020; 68(1): 283–289. https://doi.org/10.3897/pharmacia.68.e634535.
2. American Diabetes Association Standards of Medical Care in Diabetes. Diabetes care 2020; 43(Supplement 1): e1212.
3. Savych A, Marchyshyn S, Basaraba R. et al. Determination of carboxylic acids content in the herbal mixtures by HPLC. ScienceRise: Pharmaceutical Science 2021; 2(30): 33–39. https://doi.org/10.15587/2519-4852.2021.229132.
4. Huzio N, Grytsyk A, Slobodianiuk L. Determination of carbohydrates in *Agrimonia eupatoria* L. herb. ScienceRise: Pharmaceutical Science 2020; 28(6): 35-40. https://doi.org/10.15587/2519-4852.2020.221661.
5. Marchyshyn S, Slobodianiuk L, Budniak L. et al. Analysis of carboxylic acids of Crambe cordifolia Steven. Pharmacia 2021; 68(1): 15-21.https://doi.org/10.3897/pharmacia.68.e56715.
6. Budniak L, Slobodianiuk L, Marchyshyn S. et al. Determination of Arnica foliosa Nutt. fatty acids content by GC/MS method. ScienceRise: Pharmaceutical Science 2020; 6(28): 14-8. https://doi.org/10.15587/2519-4852.2020.216474.
7. Slobodianiuk L, Budniak L, Marchyshyn S. et al. Determination of amino acids and sugars content in Antennaria dioica Gaertn. IJAP 2019; 11(5): 39-43. https://doi.org/10.22159/ijap.2019v11i5.33909.
8. Governa P, Baini G, Borgonetti V. et al. Phytotherapy in the management of diabetes: a review. Molecules (Basel, Switzerland) 2018; 23(1): e105. https://doi.org/10.3390/molecules23010105.
9. Savych A, Basaraba R, Muzyka N. et al. Analysis of fatty acid composition content in the plant components of antidiabetic herbal mixture by GC-MS. Pharmacia 2021; 68(2): 433–439. doi.org/10.3897/pharmacia.68.e66693.
10. Slobodianiuk L, Budniak L, Marchyshyn S. et al. Determination of amino acids of cultivated species of the genus Primula L. Biointerface Res Appl Chem 2021; 11: 8969-77. https://doi.org/10.33263/BRIAC112.89698977.
11. Budniak L, Slobodianiuk L, Marchyshyn S. et al. Determination of composition of fatty acids in Saponaria officinalis L. ScienceRise: Pharmaceutical Science 2021; 1(29): 25-30. doi.org/10.15587/2519-4852.2021.224671
12. Budniak L, Slobodianiuk L, Marchyshyn S. et al. Determination of amino acids of some plants from Gentianaceae family. Pharmacia 2021; 68(2): 441–448.
13. Slobodianiuk L, Budniak L, Marchyshyn S. et al. Analysis of carbohydrates in Saponaria officinalis L. using GC/MS method. Pharmacia 2021; 68(2): 339–345. https://doi.org/10.3897/pharmacia.68.e62691
14. Gins MS, Kononkov PF, Gins VK. Stahys is a promising vegetable crop with medicinal properties. Biochemical and pharmacological properties. Vegetables of Russia 2015; 3: 108-112.
15. Hyeon KC, Chung SK, Kyeong WW. et al. A New Triterpene Saponin from the Tubers of Stachys sieboldii. Bull Korean Chem Soc 2014; 35(5): 1553-1555.
16. Conforti F, Menichini F, Formisano C. et al. Comparative chemical composition, free radical-scavenging and cytotoxic properties of essential oils of six Stachys species from different regions of the Mediterranean Area. Food Chem 2009; 116: 898-905.
17. Takeda Y, Fujita T, Satoh T. et al. On the glycosides constituents of Stachys sieboldii MIQ. and their effects on hyarulonidase activity. Yakugaku Zasshi 1985; 105: 955-959.
18. Yamahara J, Kitani T, Kobayashi H. et al. Studies on Stachys sieboldii MIQ. II Anti-anoxia action and the active constituents. Yakugaku Zasshi 1990; 110: 932-935.
19. Konovalova OY, Mitchenko FA, Shuraeva TK. Biologically active substances of medicinal plants. Kyiv: "Kyiv University" 2008; 280.

20. Goren A, Akçiçek E, Dirmenci T. et al. Fatty acid composition and chemotaxonomic evaluation of species of Stachys. Nat Prod 2011; 26: 84-90.
21. Hiroaki N, Hiroshi S, Chin M. et al. Nine phenethyl alcohol glycosides from Stachys sieboldii. Phytochemistry 1991; 30 (3): 965-969.
22. Hayashi K, Nagamatsu T, Ito M. et al. Acteoside, a Component of Stachys Sieboldii MIQ, May Be a Promising Antinephritic Agent: Effect of Acteoside on Crescentic-Type Anti-GBM Nephritis in Rats. Jpn J Pharmacol 1994; 65: 143-151.
23. Yang MR, No GR, Kang S-N. et al. Antioxidant and antimicrobial activities of various Stachys Sieboldii Miq extracts for application in meat product. Indian J of Apl Res 2016; 6(9): 70-75.
24. Xianfeng Z, Guidong H, Yan C. et al. Optimization of extracting stachyose from Stachys floridana Schuttl ex. Benth by response surface methodology. J Food Sci Technol 2013; 50: 942-949.
25. Yin J, Wang S, Chen Y. Purification and determination of Stachyose in Chinese artichoke (Stachys sieboldii Miq) by high-performance liquid chromatography with evaporative light scattering detection. Talanta 2006; 70: 208-212.
26. Zaharova LM, Dyatlov AV. Theoretical substantiation of introduction of vegetable crops Stachys sieboldii MIQ to functional products. Vestnik OrelGAU 2013; 4(43): 33-37.
27. Sultanova NA, Sarsenbaev BA, Mursalieva VK. et al. Phytochemical analysis of stevia and stachis for the maintenance of biologically active substances. Bulletin of KazNU. Chemical series: materials of the VII International Beremzhanov Congress on Chemistry and Chemical Technology. Kazakhstan 2012; 1(65): 370-373.
28. Husak L, Dakhym I, Marchyshyn S. et al. Determination of sugars and fructans content in Stachys sieboldii. Int J Green Pharm 2018; 12: 70-4. http://dx.doi.org/10.22377/ijgp.v12i01.1527
29. Marchyshyn S, Budniak L, Slobodianiuk L. et al. Determination of carbohydrates and fructans content in Cyperus esculentus L. Pharmacia 2021; 68(1): 211-6. https://doi.org/10.3897/pharmacia.68.e54762
30. Slobodianiuk L, Budniak L, Marchyshyn S. et al. HPLC analysis of amino acids content in Crambe cordifolia and Crambe koktebelica leaves. IJAP 2021; 13(4): In press. https://doi.org/10.22159/ijap.2021v13i4.41265
31. Budniak L, Slobodianiuk L, Marchyshyn S. et al. Determination of carbohydrates content in Gentiana cruciata L. by GC/MS method. IJAP 2021; 13(1): 124-8. https://doi.org/10.22159/ijap.2021v13i1.39820
32. Marchyshyn S, Polonets O, Savych A. et al. Determination of carbohydrates of Chrysanthemum morifolium L. leaves and flowers by GC-MS. Pharmakeftiki Journal 2020; 32(4): 202-212.
33. Darzuli N, Budniak L, Hroshovyi T. Selected excipients in oral solid dosage form with dry extract of Pyrola rotundifolia L. IJAP 2019; 11: 210-6. https://doi.org/10.22159/ijap.2019v11i6.35282
34. Stoiko L, Kurylo Khr. Development of optimal technology of alcohol extract Centaurium erythraea Rafn. herb. Arch Balkan Med Union 2018; 53: 523-8. https://doi.org/10.31688/ABMU.2018.53.4.06
35. Darzuli N., Budniak L., Slobodianiuk L. Investigation of the antibacterial and antifungal activity of the Pyrola rotundifolia L. leaves dry extract. PharmacologyOnLine 2021; 1: 395-403.
36. Slobodianiuk L, Budniak L, Marchyshyn S. et al. Investigation of the hepatoprotective effect of the common cat's foot herb dry extract. PharmacologyOnLine 2020; 3: 310-8.
37. Gudzenko AV, Kovalchuk AV. Search of markers for standardization of multicomponent phytomedicines with tonic activity. Pharmacology and drug toxicology 2012; 3(28): 66-70.
38. Slobodianiuk L, Budniak L, Marchyshyn S. et al. Experimental studies on expectorant effect of extract from Pimpinella saxifraga L. PharmacologyOnLine 2021; 1: 404-410.

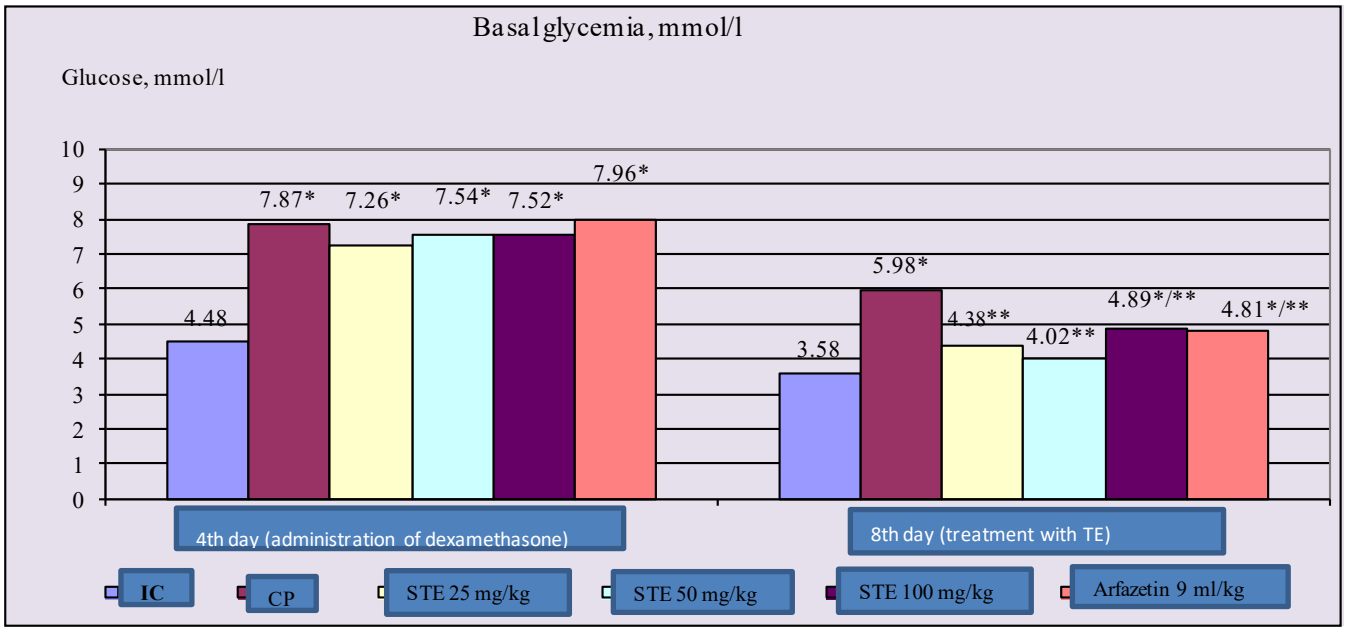
39. Kurylo Kh, Budniak L, Volska A. et al. Influence of phytocompositions on dynamics of change in basic glycemia and glycemia in oral glucose tolerance test in rats with streptozotocin-nicotinamideinduced diabetes mellitus type 2. GMN 2020; 300(3): 112-116.
40. Savych A, Marchyshyn S, Nakonechna S. Influence of some herb-al mixtures on insulin resistance and glucose tolerance in rats. PharmacologyOnLine 2021; 1: 356–364.
41. Horakova O, Kroupova P, Bardova K. et al. Metformin acutely lowers blood glucose levels by inhibition of intestinal glucose transport. Scientific Reports 2019; 9(1). doi: http://doi.org/10.1038/s41598-019-42531-0.
42. Stefanov OV. Preclinical studies of drugs. Kyiv: Avitsena Publishers, 2001; 528.
43. Stalnaya ID, Garishvili TG. Method for the determination of malonic dialdehyde using thiobarbituric acid. Modern methods in biochemistry; ed. V. N. Orekhovich. Moscow: Medicine, 1977; 66–68.

**Table 1.** Dynamics of hypoglycemic action of *Stachys sieboldii* extract on a model of dexamethasone diabetes, n=6 (M±m)

| Group of animals | Term of observation | | | | | | |
|---|---|---|---|---|---|---|---|
| | 0 h | 1 h | | 2 h | | 4 h | |
| | mmol/l | mmol/l | % decrease | mmol/l | % decrease | mmol/l | % decrease |
| Intact control | 4.48± 0.06 | 4.23± 0.16 | 5.70±3.21 | 4.04± 0.10 | 9.84±2.41 | 4.15± 0.16 | 7.32±3.46 |
| Control pathology | 7.87± 0.34* | 7.12± 0.20* | 8.94±3.34 | 7.31± 0.35* | 6.98±2.76 | 7.41± 0.41* | 5.81±3.03 |
| STE, 25 mg/kg | 7.26± 0.47* | 6.04± 0.12** | 15.04± 5.59 | 5.73± 0.21*/** | 20.13± 3.17*/** | 5.59± 0.20** | 22.12± 3.09*/** |
| STE, 50 mg/kg | 7.54± 0.40* | 7.08± 0.22# | 5.52± 2.77 | 6.86± 0.21# | 8.41± 2.69 | 6.65± 0.20# | 11.31± 2.60 |
| STE, 100 mg/kg | 7.52± 0.38* | 6.97± 0.26# | 6.87± 2.27# | 6.84± 0.28# | 8.76± 2.05# | 6.50± 0.27# | 13.36± 2.01# |
| Arfazetin, 9 ml/kg | 7.96± 0.20* | 7.06± 0.29# | 10.82± 4.73# | 7.42± 0.36# | 6.96± 2.77# | 7.20± 0.26# | 8.58± 2.81# |

Notes: * – the differences are statistically significant for the group of intact control, $p<0.05$;
** – the differences are statistically significant for the group of control pathology, $p<0.05$;
# – the differences are statistically significant for the group of STE (25 mg/kg), $p<0,05$;
n – number of animals in a group;
STE – extract from the tubers of *Stachys sieboldii*.

**Figure 1.** Dynamics of basal glycemia in rats on the background of the administration of extract of the *Stachys sieboldii* tubers in comparison with the official herbal mixture "Arfazetin" in the model of dexamethasone diabetes, n = 6




Notes: IC – intact control;
CP – control pathology (dexamethasone diabetes);
STE – thick extract from the tubers of *Stachys sieboldii* + dexamethasone diabetes;
Arfazetin – the official herbal mixture "Arfazetin" + dexamethasone diabetes;
* – the differences are statistically significant for the group of intact control, $p<0.05$;
** – the differences are statistically significant for the group control pathology, $p<0.05$;
n – number of animals in a group.

**Table 2.** Influence of *Stachys sieboldii* extract on glycemic dynamics in glucose tolerance test in animals with dexamethasone-induced insulin resistance, n = 6 (M ± m)

| Group of animals | Term of observation | | | | |
|---|---|---|---|---|---|
| | 0 min | 15 min | 45 min | 60 min | 90 min |
| Intact control | 3.58± 0.14 | 10.72± 0.43 | 8.50± 0.34 | 6.38± 0.25 | 3.27± 0.13 |
| Control pathology | 5.98± 0.35* | 13.65± 1.05 | 11.63± 1.28 | 8.77± 0.54* | 5.77± 0.39* |
| STE, 25 mg/kg | 4.38± 0.20** | 7.74± 1.03** | 7.79± 0.17** | 5.72± 0.06** | 4.12± 0.21** |
| STE, 50 mg/kg | 4.02± 0.20** | 12.78± 0.49 | 10.39± 1.02 | 7.71± 0.71** | 4.63± 0.32** |
| STE, 100 mg/kg | 4.89± 0.15*/** | 11.86± 1.03 | 6.96± 0.49** | 6.01± 0.52** | 5.97± 0.42* |
| Arfazetin, 9 ml/kg | 4.81± 0,15*/** | 12.11± 1.16 | 9.37± 0.69 | 6.33± 0.41** | 6.06± 0.42* |

Notes: * – the differences are statistically significant for the group of intact control, $p<0.05$;
** – the differences are statistically significant for the group of control pathology, $p<0.05$;
# – the differences are statistically significant for the group of extract from the tubers of *Stachys sieboldii* (dose of 25 mg/kg), $p<0.05$;
n – number of animals in a group;
STE – extract from the tubers of *Stachys sieboldii.*

**Table 3.** Influence of *Stachys sieboldii* extract on the state of pro/antioxidant processes in the LPO/AOS under conditions of dexamethasone diabetes in rats, n = 6 (M ± m)

| Group of animals | Values | |
|---|---|---|
| | TBA-R | Catalase |
| Intact control | 1.20±0.05 | 19.52±2.55 |
| Control pathology | 1.96±0.10* | 13.70±0.67* |
| STE, 25 mg/kg | 1.29±0.08**# α | 17.23±1.18*/** |
| STE, 50 mg/kg | 0.82±0.02**# α | 19.82±1.97**# α |
| STE, 100 mg/kg | 0.78±0.07*/**#α | 23.65±4.46*/**# α |
| Arfazetin, 9 ml/kg | 1.48±0.03**# | 17.27±2.01*/** |

Notes: * – the differences are statistically significant for the group of intact control, p<0.05;
** – the differences are statistically significant for the group of control pathology, p<0.05;
# – the differences are statistically significant for the group of STE (dose of 25 mg/kg), p<0.05;
α – the differences are statistically significant for the group of reference drug the official herbal mixture "Arfazetin", p<0.05;
n – number of animals in a group;
STE – extract from the tubers of *Stachys sieboldii.*