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STUDY OF HYPOGLYCEMIC PROPERTIES OF «GLYPHASONORM» TABLETS AND «GLYPHASOLIN» CAPSULES ON THE STREPTOZOTOCIN-INDUCED DIABETIC RAT MODEL

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The risk of developing any complications of diabetes is significantly reduced by monitoring and correcting blood glucose levels and blood pressure, as well as by observing healthy lifestyle rules. Early detection and treatment of type 2 diabetes contribute to the prevention of disease progression and the development of complications.

***The aim** is to study the hypoglycemic effect of «Glyphasonorm» tablets and «Glyphasolin» capsules in a rat model of streptozotocin-induced diabetes.*

***Materials and methods.** The studies were carried out on Wistar rats injected intraperitoneally with nicotinamide at a dose of 230 mg/kg 15 minutes before intravenous injection of streptozotocin at a dose of 65 mg/kg. The dynamics of body weight of rats, glucose and glycosylated haemoglobin levels under the impact of long-term administration of metformin, «Glyphasonorm» tablets and «Glyphasolin» capsules were investigated.*

***Results and discussion.** The studies on a streptozotocin-induced diabetic model have established that under the action of «Glyphasonorm» tablets and «Glyphasolin» capsules, the level of glycosylated haemoglobin, which decreased along with the level of glucose in the blood of animals, was significantly reduced in comparison with diabetic control. After 14 days of research, the «Glyphasolin» capsules showed more pronounced hypoglycemic activity (4.4 % and 8.0 % more) than the «Glyphasonorm» tablets and the reference drug metformin. The «Glyphasolin» capsules on the 12th day of the study showed a marked decrease in glycosylated haemoglobin in the blood of animals (3.1 % and 5.6 % more) than the «Glyphasonorm» tablets and metformin.*

***Conclusions.** In the experimental model of streptozotocin diabetes in rats, "Gliphasolin" capsules showed a more pronounced hypoglycemic effect, which was manifested by a decrease in the content of glycosylated haemoglobin in the blood and prevailed over the effect of the comparative drug metformin and "Gliphasonorm" tablets.*

«Glyphasolin» capsules and «Glyphasonorm» tablets based on bioflavonoid complex from bean show promise in the treatment of type 2 diabetes on the background of obesity and reducing the risk of micro- and macroangiopathy

***Keywords:** streptozotocin-induced diabetes, hypoglycemic activity, glycosylated haemoglobin, metformin, «Glyphasonorm» tablets, «Glyphasolin» capsules*

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1. Introduction

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Chronic hyperglycemia in DM is accompanied by damage, dysfunction, or failure of various organs and systems, including the eyes, kidneys, nervous system, heart, and blood vessels [1, 2]. The results of studies based on the principles of evidence-based medicine indicate that chronic hyperglycemia in DM is accompanied by damage, dysfunction or insufficiency of various organs and systems, including the eyes, kidneys, nervous system, heart and blood vessels – a high risk of developing cardiovascular diseases (CVD) [1, 3].

The risk of developing any complications is significantly reduced by controlling and correspondingly correcting the level of glucose in the blood and blood pressure, as well as following the rules of a healthy diet and performing regular physical exercises. Early detection and treatment of DM type 2 help to prevent the progression of the disease and the development of complications [4, 5].

The updated 2021 American Diabetes Association (ADA) guidelines present glycemic control goals for most patients with type 2 DM. Unfortunately, glycemic control goals are far from glycemic reality: every 8th patient with DM has an HbA_{1c}>10,0 %, every 5th–>9.0 %, and every 2nd–>8.0 %. In general, 64.2 % of patients with DM type 2 in the world are in a state of decompensation.

In connection with the high toxicity and ability to cumulate synthetic hypoglycemic drugs, research on the study of biologically active substances of medicinal plants of the *Fabaceae* family – common bean (*Phaseolus vulgaris L.*) and golden bean (*Phaseolus aureus L.*).

It has been proven that a thick extract from beans, which includes phenolic compounds represented by flavonols, isoflavones, isoflavanones, isoflavans, pterocarpans, oxycinnamic acids, coumarins and amino acids [5] in ED_{50}

40 mg/kg [4] exhibits antihyperglycemic properties, probably reduces glucose intolerance, improves insulin sensitivity and significantly increases glycogen content, exhibits hypolipidemic, antiatherogenic, antihypertensive and antioxidant effects, normalizes the rheological properties of blood in experimental type 2 DM [6, 7].

After the pharmacological studies of the thick bean extract, it was relevant to study the hypoglycemic properties of the thick bean extract in a medicinal form – a tablet or capsule, for use in medical practice for the treatment of type 2 DM.

Based on a thick extract from beans, the tablets *"Glyphasonorm"* and capsules *"Glyphasolin"* were created under the conditional name at the Department Of Industrial Technology of Drugs of the National University of Pharmacy under the leadership of prof. D. I. Dmytryevsky.

The composition of *"Glyphasonorm"* tablets – bean grass thick – 40 mg, basic magnesium carbonate – 38.75 mg, ICD – 51.7 mg, potato starch – 12.80 mg, croscarmellose sodium – 0.75 mg, aerosil – 4.5 mg, magnesium stearate – 1.5 mg. The weight of the tablet is 150.0 mg.

The composition of *"Glyphasolin"* capsules – bean grass extract thick – 0.222 g, basic magnesium carbonate – 0.08255 g, microcrystalline cellulose – 0.1090 g, potato starch – 0.18 g, croscarmellose sodium – 0.0027 g, colloidal silicon dioxide, anhydrous – 0.01125 g, magnesium stearate – 0.0045 g. Weight of the capsule contents – 0.450 g.

The purpose of this study was an experimental study of the hypoglycemic activity of "Glyphasonorm" tablets and "Glyphasolin" capsules on the streptozotocin diabetes model in rats.

2. Research planning (methodology)

Today, the nomenclature of synthetic antidiabetic drugs significantly exceeds the number of phytopreparations. In this regard, herbal preparations with insulin-like action attract special attention. Therefore, the object of the research is the creation of new domestic, highly effective and safe antidiabetic drugs for the treatment of type 2 DM.

To conduct a pharmacological study of new hypoglycemic agents – tablets "Glyphasonorm" and capsules "Glyphasolin" scientifically based: an experimental model of type 2 DM and methods of determining hypoglycemic properties according to generally accepted methods, as well as methods of statistical analysis of research results, were used.

The proposed experimental model of streptozotocin diabetes with simultaneous administration of nicotinamide is due to the partial protection of pancreatic β-cells from the cytotoxic effect of streptozotocin with the help of appropriate doses of nicotinamide. Thus, this model allows you to reproduce the main pathogenetic signs of type 2 DM in humans, namely, impaired insulin secretion and action, and has certain advantages for studying the hypoglycemic effect of new drugs with different mechanisms of action.

During the planning of the experiment, such characteristics of animals as age, sex, and body weight were considered for the formation of experimental groups.

During the modelling of experimental type 2 DM, the possible risk of animal death due to the cytotoxic effect of streptozotocin on pancreatic β-cells was taken into account.

After the reproduction of the experimental model of type 2 DM, starting from the second day of the experiment, the comparison drug and experimental drugs were used in the treatment.

In the dynamics of the experiment, according to methodological recommendations, changes in indicators of the hypoglycemic activity of drugs were studied, such as the level of glucose and glycosylated haemoglobin in the blood of animals and body weight.

The evaluation of the effect of tablets "Glyphasonorm" and capsules "Glyphasolin" was carried out in the middle of the group and between groups, taking into account their characteristics and in comparison with the diabetic control, the comparison drug metformin, using statistical analysis of the study results.

3. Materials and methods

Experimental research is a fragment of the research work of the National University of Pharmacy, approved by the Ministry of Health of Ukraine: "Pharmacological study of biologically active substances and medicinal products" (state registration number 0114U000956).

Experimental studies were conducted in accordance with the requirements of the bioethics commission of the National Academy of Sciences of Ukraine (protocol No. 5 dated 15.01.2019) and the "General ethical principles of animal experiments", which correspond to the provisions of the "European Convention on the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1985) [8].

Non-linear white male rats were bred in the vivarium of the Central Scientific Research Laboratory of the National Academy of Sciences and were kept on a standard diet in accordance with sanitary and hygienic requirements.

Nicotinamide was administered intraperitoneally at a dose of 230 mg/kg body weight of rats 15 minutes before intravenous injection of streptozotocin at a dose of 65 mg/kg, which resulted in moderate and stable hyperglycemia and 40 % preservation of pancreatic insulin reserves [9].

When studying hypoglycemic activity, all animals were divided into 5 groups (10 in each). Animals of groups 1 and 2 (intact control and diabetic control) intragastrically received an equivalent amount of drinking water, group 3 – the comparison drug metformin, group 4 – tablets "Glyphasonorm" and group 5 – capsules "Glyphasolin".

The study of the effect of "Glyphasonorm" tablets, "Glyphasolin" capsules and the comparison drug – metformin on the level of glycosylated haemoglobin (HbA1c) was carried out on 4 groups of animals (10 in each). Animals of group 1 (diabetic control) intragastrically received an equivalent amount of drinking water, group 2 – metformin, group 3 – tablets "Glyphasonorm" and group 4 – capsules "Glyphasolin".

Starting from the second day of the study, animals with experimental streptozotocin diabetes were injected orally (twice a day) for two weeks with the comparison drug metformin at a dose of 50 mg/kg, tablets "Glyphasonorm" and capsules "Glyphasolin" at a dose of 40 mg/kg.

Metformin (diaformin, tab. 0.5 g), manufactured by JSC "Farmak", Ukraine, was chosen as a reference drug. The choice of the comparison drug is due to the fact that metformin is a standard hypoglycemic drug, which is included in the treatment standards for DM of both types [10]. The therapeutic dose of metformin for rats was calculated from the daily dose for humans using the species sensitivity coefficients of Y. P. Rybolovlev [11].

The effect of metformin, "Glyphasonorm" tablets and "Glyphasolin" capsules on the body weight dynamics of animals with experimental streptozotocin diabetes was studied after 3 and 14 days of the study and this indicator was evaluated in comparison with the initial body weight of each animal.

The hypoglycemic activity of "Glyphasonorm" tablets and "Glyphasolin" capsules were studied in comparison with metformin in the model of streptozotocin diabetes with long-term administration (after 3, 5, 7, 10, 12 and 14 days).

As indicators of carbohydrate metabolism, the concentration of glucose (glucose oxidase method using a set of reagents from the company "Filisit-Diagnostika", Ukraine) and HbA1c (hemoglobin cyanide method using a set of reagents "Agat-Med", Russia) were determined in the blood serum of animals [12].

The glucose oxidase method (Drabkin method) is based on the reaction of its oxidation in the presence of the enzyme glucose oxidase with the formation of hydrogen peroxide, which in turn oxidizes orthotolidine in the presence of peroxidase to form coloured products. Glucose concentration was judged by the number of coloured products.

The haemoglobin cyanide method consists of the interconnection of Hb with ferric blue potassium, which is oxidized to methemoglobin, forming haemoglobin cyanide. The HbA1c content was estimated by the intensity of haemoglobin cyanide staining [13].

Statistical analysis of the results was performed using the standard package of the STATISTICA 6.0 program. Statistically significant differences between groups in the case of multiple comparisons were determined by Student's test with Bonferroni correction.

4. Research results

The general condition of the animals in the experimental and control groups was assessed by the dynamics of body weight. After 3 days of the study, after simulating streptozotocin diabetes, body weight decreased in all groups of animals. In the group of diabetic control animals, body weight decreased by 10.7 %, in the treatment of which metformin was used – by 7.4 %, "Glyphasonorm" tablets – by 6.6 %, and "Glyphasolin" capsules – by 4.7 % in comparison with initial data (Table 1).

On the 14th day of the study, the greatest loss of body weight was observed in the group of diabetic control animals (by 24.0 %) compared to the initial data. At the same time, a 14.4 % decrease in body weight was recorded in the group of animals receiving metformin and in the groups of animals receiving "Glyphasonorm" tablets – by 11.5 % and "Glyphasolin" capsules – by 7.9 % compared to the initial data, which indicates a more active behaviour of the animals than in the diabetic control group.

No statistically significant differences were found between the comparison drug metformin and the studied drugs (Table 1).

Table 1

The effect of "Glyphasonorm" tablets and "Glyphasolin" capsules on the body weight dynamics of rats in the streptozotocin diabetes model with long-term administration, $(\overline{x} \pm S_{\overline{x}})$, ($n$=10)

Research object, mg/kg	Dynamics of body weight (g)		
	Output data	In 3 days	In 14 days
Diabetic control	220.5±4.14	197.0±3.18 p<0.01	167.5±3.52 p<0.001
Metformin (50 mg/kg)	240.0±1.29	222.3±2.74 p<0.001	205.5±2.52 p<0.001
«Glyphasonorm» tablets (40 mg/kg)	225.3±3.47	210.5±3.11 p<0.05	199.5±1.89 p<0.001
«Glyphasolin» capsules (40 mg/kg)	235.0±1.29	224.0±3.32 p<0.05	216.5±3.58 p<0.001

Note: p – the significance of changes compared to the original data.

It is believed that the primary disorder in type 2 DM and impaired glucose tolerance is a decrease in the sensitivity of peripheral tissues to insulin, and the deterioration of β-cell function occurs secondarily as a mechanism aimed at compensating for insulin resistance [2].

The level of glucose in the blood is an integral indicator of the compensation of carbohydrate metabolism. Therefore, the state of glycemia was evaluated dynamically during the entire experiment.

The research results showed that 3 days after simulating streptozotocin diabetes, a sharp increase in basal hyperglycemia (12.65±0.02) was observed in the rats of the diabetic control group, and after 5 days and before the end of the experiment, a slight decrease in the blood glucose level (8.86±0.04) (Table 2)

At the same time (at the height of the development of non-insulin-dependent diabetes), a high level of glucose was recorded in the blood of animals treated with metformin (10.05±0.06 mmol/l), "Glyphasonorm" tablets (11.75±0.04 mmol/l) and "Glyphasolin" capsules (11.45±0.07 mmol/l) in comparison with the initial data.

After 5 days of using "Glyphasolin" capsules and "Glyphasonorm" tablets in the treatment of diabetic animals, a slight decrease in the level of glucose in the blood was established – by 17.6 % and 15.0 %, compared to when metformin was used in the treatment of animals – by 23.1 % in comparison with the indicators of animals of the diabetic control group.

After 7 and 10 days of research, capsules "Glyphasolin" contributed to a significant reduction in the level of

glucose in the blood of animals (by 30.8 % and by 31.1 %) than metformin (by 28.4 % and by 27.7 %), and tablets "Glyphasonorm" reduced the level of glucose in the blood of animals by 27.2 % and by 28.5 % in comparison with the indicators of animals in the diabetic control group.

The hypoglycemic activity of "Glyphasolin" capsules after 12 and 14 days of the study was 43.5 % and 58.2 %, which is 6.5 % and 8.0 % higher than the hypoglycemic activity of metformin. The more pronounced hypoglycemic activity of tablets and capsules based on thick bean extract than the comparison drug metformin is due to the presence in its composition of various classes of natural compounds represented by flavonols, isoflavones, isoflavanones, isoflavans, pterocarpans, oxycinnamic acids, coumarins and amino acids. Beans contain derivatives of guanidine, which are bases and act according to the type of biguaids, and in the composition of a thick extract, they show a more pronounced, total effect.

"Glyphasonorm" tablets showed less hypoglycemic activity (3.9 % and 4.4 %) than "Glyphasolin" capsules and more (2.6 % and 3.8 %) than metformin.

Thus, "Glyphasolin" capsules, "Glyphasonorm" tablets and metformin contributed to lowering the level of glucose in the blood of animals but did not normalize it to baseline values. "Glyphasolin" capsules showed more pronounced hypoglycemic activity than "Glyphasonorm" tablets and the comparison drug metformin.

It is known that among biochemical indicators, the HbA1c level can be a standard for evaluating the effectiveness of the hypoglycemic effect of the drug, as it represents the average level of glycemia over three months. HbA1c is formed during a non-enzymatic reaction from haemoglobin and blood glucose (Maillard reaction). An increase in the level of blood glucose in DM significantly accelerates this reaction, which leads to an increase in the level of HbA1c in the blood. Since the lifetime of erythrocytes is, on average, 120 days, the level of HbA1c indicates the average level of glycemia during three months [14, 15].

An HbA1c level in the range of 5.7 % – 6.4 % is characteristic of prediabetes, and a level of 6.5 % or higher is a manifestation of DM. When the level of HbA1c increases by 1 %, the risk of developing cardiovascular diseases increases by 10 % [16, 17].

Throughout the study, the level of HbA1c in the group of diabetic control animals remained elevated (7.44±0.02 μmol/l – 7.18±0.08 μmol/l) (Table 3), as well as the level of glucose in the blood (12.65±0.02 mmol/l – 8.86±0.04 mmol/l) (Table 2).

In animals treated with metformin, "Glyphasonorm" tablets and "Glyphasolin" capsules, with hyperglycemia at 10.05±0.06 mmol/l; 11.75±0.04 mmol/l and 11.45±0.07 mmol/l (Table 2), after 3 days of the study there was an increase in HbA1c at the level of 6.02±0.03 μmol/l; 6.51±0.03 μmol/l and 6.31±0.08 μmol/l (Table 3), which is a reference to the value of compensated DM [13].

After 5 days of research in the groups of animals treated with metformin, capsules "Glyphasolin" and tablets "Glyphasonorm", there was a significant decrease in the level of HbA1c by 24.2 %, by 23.6 % and by 21.9 % in comparison with the indicators of diabetic control, but its high blood level still persisted.

After 7 days of research and treatment of animals with "Glyphasolin" capsules, the highest reduction of HbA1c by 39.6 % was recorded. Under the influence of metformin, the level of HbA1c decreased by 35.7 %, and under the influence of Glyphasonorm tablets – by 33.6 % compared to the diabetic control.

Since, at the same time, "Glyphasolin" capsules showed a more pronounced hypoglycemic effect and an advantage over metformin and "Glyphasonorm" tablets, this can be seen in the reduction of the HbA1c level, which is directly proportional to the average concentration of glucose in the blood of animals.

It was established that after 14 days of research, "Glyphasolin" capsules reliably reduced the concentration of HbA1c in the blood of animals by 34.1 %, "Glyphasonorm" tablets by 32.2 % and were not inferior to metformin, under the influence of which the level of HbA1c in the blood decreased by 30.9 % ($p<0.05$) in comparison with the indicators of animals with control pathology, which is directly proportional to the average concentration of glucose in the blood of animals. At the same time, an active decrease in the glucose level in the blood of animals under the influence of "Glyphasolin" capsules by 36.8 %, "Glyphasonorm" tablets by 35.0 % and metformin by 33.4 % were determined.

Table 2

Hypoglycemic activity of "Glyphasonorm" tablets and "Glyphasolin" capsules on the streptozotocin diabetes model in rats with long-term administration, ($\overline{x} \pm S_{\overline{x}}$), ($n$=10)

Research object/ mg/kg	Dynamics of glucose content (C, mmol/l)						
	Output data	In 3 days	In 5 days	In 7 days	In 10 days	In 12 days	In 14 days
Intact control	4.49±0.08	4.40±0.02	4.37±0.03	4.43±0.02	4.45±0.02	4.48±0.02	4.41±0.04
Diabetic control	4.32±0.05	12.65±0.02	12.03±0.04	11.75±0.07	10.84±0.05	9.77±0.03	8.86±0.04
Metformin (50 mg/kg)	4.40±0.03	10.05±0.06*	9.77±0.05*	9.15±0.03*	8.49±0.03*	7.13±0.02*	5.90±0.05*
«Glyphasonorm» tablets (40 mg/kg)	4.51±0.02	11.75±0.04*/**	10.46±0.03*/**	9.24±0.02*	8.43±0.02*	7.00±0.04*/***	5.76±0.03*/***
«Glyphasolin» capsules (40 mg/kg)	4.38±0.03	11.45±0.07*/**	10.23±0.03*/**	8.98±0.03*/**	8.27±0.02*/**	6.81±0.06*/**	5.60±0.03*/**

*Note: * – p<0.001 – the significance of changes compared to the "diabetic control" group; ** – p < 0.001 – the significance of changes compared to the "Metformin" group; *** – p<0.05 – the significance of changes compared to the "Metformin" group.*

Table 3

The effect of "Glyphasonorm" tablets and "Glyphasolin" capsules on the level of glycosylated haemoglobin (HbA1c) in the rat model of streptozotocin diabetes with long-term administration, $(\overline{x} \pm S_{\overline{x}})$, ($n$=10)

Research object,mg/kg	Dynamics of HbA1c content (C, μmol/l)					
	In 3 days	In 5 days	In 7 days	In 10 days	In 12 days	In 14 days
Diabetic control	7.44±0.02	7.23±0.05	7.19±0.09	7.15±0.15	7.09±0.09	7.18±0.08
Metformin (50 mg/kg)	6.02±0.03*	5.82±0.12*	5.30±0.04*	5.41±0.03*	5.13±0.04*	0.00±0.00
«Glyphasonorm» tablets (40 mg/kg)	6.51±0.03*	5.93±0.08*	5.38±0.03*	5.33±0.03*	5.04±0.05*	0.00±0.00
«Glyphasolin» capsules (40 mg/kg)	6.31±0.08*	5.83±0.11*	5.15±0.06*	5.25±0.15*	4.93±0.05*/**	0.00±0.00

*Note: * – $p<0,001$ – the significance of changes compared to the "Diabetic control" group; ** – $p<0,05$ – the significance of changes compared to the "Metformin" group.*

After 10 and 12 days of the study, there was an active reduction of HbA1c under the influence of "Glyphasolin" capsules by 36.2 % and 43.8 %, "Glyphasonorm" tablets by 34.1 % and 40.7 %, metformin by 32.2 % and by 38.2 % compared to the diabetic control.

After 14 days of treatment of animals with metformin, "Glyphasolin" capsules and "Glyphasonorm" tablets, HbA1c was not detected in the blood of the animals (Table 3) since, at this time, there was an active decrease in the level of glucose in the blood of the animals of the experimental groups by 50.2 %, by 58.2 % and 53.8 % (Table 2).

The research results showed that the greatest effectiveness in reducing the level of HbA1c in the blood of animals with experimental streptozotocin diabetes was found during the treatment of animals with "Glyphasolin" capsules than with "Glyphasonorm" tablets and metformin.

Thus, it can be assumed that "Glyphasolin" capsules have a longer prolonged effect than "Glyphasonorm" tablets.

5. Discussion of research results

The need for conducting scientific research on the creation of medicinal products of plant origin with multidirectional action lies in the improvement of preventive and curative measures with the help of phytotherapy.

Thus, despite a fairly wide range of drugs that are currently used to correct the hemodynamic and metabolic manifestations of insulin resistance syndrome, they do not fully meet the needs of practical medicine due to the presence of pronounced side effects [18].

In addition, the pharmaceutical market of herbal preparations is very limited and is mainly represented by collections of medicinal plants, which are inconvenient when used in the preparation of infusions (brew, infuse, take warm or chilled).

All this testifies to the relevance of finding, creating and introducing into medical practice effectively and at the same time low-toxic medicinal products based on medicinal plant raw materials for the pharmacotherapy of type 2 DM and its complications.

After 14 days of two-time use in the treatment of animals with streptozotocin diabetes, "Glyphasolin" capsules at a dose of 40 mg/kg produced a reliable, smallest decrease in body weight – by 7.9 % (p<0.001) compared to the initial data. Tablets "Glyphasonorm" at a dose of 40 mg/kg reduced the body weight of animals by 11.5 % (p<0.001), and metformin at a dose of 50 mg/kg – by 14.4 % (p<0.001) compared to the initial data [19].

The hypoglycemic activity of "Glyphasolin" capsules at the end of the study was 36.8 %, which is 3.4 % higher than the hypoglycemic activity of metformin. "Glyphasonorm" tablets showed less hypoglycemic activity (by 1.8 %) than "Glyphasolin" capsules and more (by 1.6 %) than the comparison drug metformin. It should be noted that in animals that received "Glyphasolin" capsules, "Glyphasonorm" tablets, or metformin, the level of glucose in the blood did not normalize [19].

It was established that after 14 days of research, "Glyphasolin" capsules reliably reduced the concentration of HbA1c in the blood of animals by 34.1 %, "Glyphasonorm" tablets by 32.2 % and were not inferior to metformin, under the influence of which the level of HbA1c in the blood decreased by 30.9 % (p<0.05) in comparison with the indicators of animals with control pathology, which is directly proportional to the average concentration of glucose in the blood of animals. At the same time, an active decrease in the level of glucose in the blood of animals under the influence of «Glyphasolin" capsules by 36.8 %, "Glyphasonorm" tablets by 35.0 % and metformin by 33.4 % were determined [20].

The obtained results are an experimental justification for the use of "Glyphasonorm" tablets and "Glyphasolin" capsules for the complex treatment of DM of mild and moderate severity, as well as with a tendency to obesity. "Glyphasolin" capsules are planned to be introduced at PJSC "Khimpharmzavod "Chervona Zirka"" (Ukraine).

Study limitations. In the conditions of the conducted research, there was a limitation related to the individual non-tolerance (species sensitivity) of specific doses of nicotinamide and streptozotocin by experimental animals during the modelling of type 2 streptozotocin diabetes to study the hypoglycemic properties of "Glyphasonorm" tablets and "Glyphasolin" capsules.

Prospects for further research. The duration and quality of life of patients with DM are currently

determined by the development and progression of late vascular complications of this disease [18], so further research is the search for a possible correction of endothelial dysfunction in metabolic diseases and atherosclerosis [19, 20] using the "Glyphasonorm" tablets and "Glyphasolin" capsules based on a thick bean extract.

6. Conclusions

1. Tablets "Glyphasonorm" and capsules "Glyphasolin" in an experimental model of streptozotocin diabetes probably reduced the level of glycosylated haemoglobin, which decreased together with the level of glucose in the blood of animals compared to diabetic controls.

2. After 14 days of research, "Glyphasolin" capsules showed more pronounced hypoglycemic activity than "Glyphasonorm" tablets and the comparison drug metformin (by 4.4 % and 8.0 %, respectively).

3. Under the influence of "Glyphasolin" capsules, on the 12th day of the study, a more pronounced decrease in glycosylated haemoglobin in the blood of animals was established than in the case of "Glyphasonorm" tablets and metformin (by 3.1 % and 5.6 %, respectively).

4. Capsules "Glyphasolin" and tablets "Glyphasonorm" based on a bioflavonoid complex with beans are promising in the therapy of DM type 2 against the background of obesity and reducing the risk of developing micro- and macroangiopathy.

Conflict of interests

The authors declare that they have no conflict of interest in relation to this research, including financial, personal, authorship or other nature, which could affect the research and its results presented in this article.

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References

1. Nathan, D. M., Buse, J. B., Davidson, M. B. et al. (2009). Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement of the American Diabetes Association and European Association for the Study of Diabetes. Diabetes Care, 32. doi: https://doi.org/10.2337/dc09-0271

2. Rybak, V. A., Maloshtan, L. M. (2014). Vykorystannia bioflavonoidnoho kompleksu z kvasoli dlia likuvannia metabolichnoho syndromu na tli ozhyrinnia. Inform. lyst pro novovvedennia v systemi okhorony zdorov'ia No. 279. Kyiv, 35, 4.

3. Dedov, I. I., Shestakova, M. V. (2003). Sakharnyi diabet. Moscow, 455.

4. Dedov, I. I., Shestakova, M. V. (Eds.) (2009). Algoritm spetcializirovannoi meditcinskoi pomoshchi bolnym sakharnym diabetom. Moscow, 103.

5. Bogachev, V. Yu., Golovanova, O. V., Kuznetsov, A. N., Shekoayan, A. O. (2013). Bioflavonoids and their significance in angiology: focus on diosmi. Angiology and vascular surgery, 19 (1), 73–81.

6. Rybak, V. A. (2014). Determination of the effective dose (ED50) of spissum bean extract with potential hypoglycemic propertie. Problemy ekolohichnoi ta medychnoi henetyky i klinichnoi imunolohii, 1 (121), 225–230.

7. Rybak, V. A., Maloshtan, L. M., Poltorak, V. V., Krasova, N. S. (2015). Vplyv tryvaloho zastosuvannia hustoho ekstraktu kvasoli na dynamiku masy tila, masy fraktsii abdominalnoi zhyrovoi tkanyny u shchuriv z tsukrovym diabetom 2-ho typu na tli ozhyrinnia. Svit medytsyny ta biolohii, 2 (50), 172–175.

8. Rieznykov, O. H. (2003). Zahalni etychni pryntsypy eksperymentiv na tvarynakh. Endokrynolohiia, 8 (1), 142–145.

9. Stefanov, O. V. (Ed.) Doklinichni doslidzhennia likarskykh zasobiv. Kyiv: Avitsena, 528.

10. Baynes, J. W. (1991). Role of oxidative stress in development of complications in diabetes. Diabetes, 40 (4), 405–412. https://doi.org/10.2337/diabetes.40.4.405

11. Rybolovlev, Iu. R. (1979). Dozirovanie veshchestv dlia mlekopitaiushchikh po konstante biologicheskoi aktivnosti. Zhurnal AN SSSR, 247 (6), 1513–1516.

12. Nazarenko, G. I., Kishkun, A. A. (2002). Klinicheskaia otcenka rezultatov laboratornykh analizov. Moscow: Meditcina, 544.

13. Rybak, V. A., Maloshtan, L. M., Poltorak, V. V., Krasova, N. S. (2015). Vyvchennia antyoksydantnykh vlastyvostei hustoho ekstraktu kvasoli na modeli tsukrovoho diabetu 2-ho typu na tli ozhyrinnia v shchuriv. Farmakolohiia ta likarska toksykolohiia, 1 (42), 76–81.

14. Patel A., MacMahon S., Chalmers J. et al. (2008). Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. New England Journal of Medicine, 358, 2560–2572. doi: https://doi.org/10.1056/nejmoa0802987

15. Skyler, J. S., Bergenstal, R., Bonow, R. O., Buse, J., Deedwania, P., Gale, E. A. M. et al. (2009). Intensive Glycemic Control and the Prevention of Cardiovascular Events: Implications of the ACCORD, ADVANCE, and VA Diabetes Trials. Diabetes Care, 32 (1), 187–192. doi: https://doi.org/10.2337/dc08-9026

16. Gerstein, H. C., Miller, M. E., Byington, R. P. et al. (2008). Effects of Intensive Glucose Lowering in Type 2 Diabetes. New England Journal of Medicine, 358 (24), 2545–2559. doi: https://doi.org/10.1056/nejmoa0802743

17. Risk of hypoglycaemia in types 1 and 2 diabetes: effects of treatment modalities and their duration (2007). Diabetologia, 50 (6), 1140–1147. doi: https://doi.org/10.1007/s00125-007-0599-y

18. Voloshin, O. I., Glubochenko, O. V., Pankiv, I. V., Glubochenko, V. G., Malkovich, N. M. (2021). Peculiarities of phytotherapy of diabetes mellitus through the prism of comorbidity and prevention of complications (review of literature). International Journal of Endocrinology (Ukraine), 15 (3), 258–267. doi: https://doi.org/10.22141/2224-0721.15.3.2019.172113

19. Kurylo, Kh. I., Klishch, I. M., Volska, A. S., Barchuk, O. Z. (2016). Research of hypoglycemic properties of dry extract of vaccinium myrtillus L. Medical and Clinical Chemistry, 18 (2), 38–41. doi: https://doi.org/10.11603/mcch.2410-681x.2016.v0.i2.6669

20. Kurylo, Kh. I., Klishch, I. M., Volska, A. S., Rozhkovskyi, Ya. V. (2020). Investigation of the influence of phytocompositions on the process of non-permanent glycosylation, activity of cytolytic processes, indicators of lipid exchange and lipid peroxidation balance in animal's body in experimental diabetes. Medical and Clinical Chemistry, 4, 162–168. doi: https://doi.org/10.11603/mcch.2410-681x.2019.v.i4.10854

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