**Chikitkina O M, Kononenko N M, Chikitkina V V, Lar'yanovskaya Y B. Antidiabetic action of combined medicine glikverin in terms of experimental Diabetes Mellitus type 2. Journal of Education, Health and Sport. 2015;5(2):11-22. ISSN 2391-8306. DOI: 10.5281/zenodo.14893**
**http://ojs.ukw.edu.pl/index.php/johs/article/view/2015%3B5%282%29%3A11-22**
**https://pbn.nauka.gov.pl/works/534378**
**http://dx.doi.org/10.5281/zenodo.14893**
**Formerly Journal of Health Sciences. ISSN 1429-9623 / 2300-665X. Archives 2011 – 2014**
**http://journal.rsw.edu.pl/index.php/JHS/issue/archive**

**Deklaracja.**
**Specyfika i zawartość merytoryczna czasopisma nie ulega zmianie.**
**Zgodnie z informacją MNiSW z dnia 2 czerwca 2014 r., że w roku 2014 nie będzie przeprowadzana ocena czasopism naukowych; czasopismo o zmienionym tytule otrzymuje tyle samo punktów co na wykazie czasopism naukowych z dnia 31 grudnia 2014 r.**
**The journal has had 5 points in Ministry of Science and Higher Education of Poland parametric evaluation. Part B item 1089. (31.12.2014).**

**The authors declare that there is no conflict of interests regarding the publication of this paper.**
**Received: 20.10.2014. Revised 18.01.2015. Accepted: 25.01.2015.**

**UDC 616.379-008.64: 615.252.349.7**

# ANTIDIABETIC ACTION OF COMBINED MEDICINE GLIKVERIN IN TERMS OF EXPERIMENTAL DIABETES MELLITUS TYPE 2

**O M Chikitkina, N M Kononenko, V V Chikitkina, Y B Lar'yanovskaya**

**National University of Pharmacy, Kharkiv, Ukraine**

**medtrans2@rambler.ru**

## Abstract

Antidiabetic action of a new composition Glikverin was investigated in experimental DM in rats caused by streptozotocin on the background of nicotineamide. It was established that combination of quercetin and voglibose in one remedy determines more significant antidiabetic action than of these components separately. The influence on glicaemia level and lipid peroxidation/anbtioxidative system indexes on this model was of the same significance in Glikverin and standard reference agent tablets metformin. The efficacy of a new composition is confirmed by results of histological study. Positive influence on condition of pancreatic endocrine component in rats was more significant in Glikverin than in reference agents voglibose, quercetin and tablets metformin. Received data justifies and makes reasonable using Glikverin for correction of carbohydrate metabolism and inhibition of lipid peroxidation in terms of relative insulin resistance.

**Key words: experimental diabetes mellitus, oxidative stress, morphological structure of pancreas, glikverin.**

The problem of Diabetes mellitus type 2 (DM2T) is one of the most essential and extensive for the day. This is determined by its widespreadness and development of macro- and microvascular complications, which lead to early loss of work capacity and high mortality. According to WHO data in developed countries incidence of DM account for 5-7 % from the general population [1]. Considering speed of spreading DM experts of WHO forecast the increase in number of diabetic patients to 2025 by half to 380 million people, mainly due to sick people in DM2T. Non-insulin dependent diabetes mellitus is a heterogenous and multifactorial disease that caused mostly by insulin resistance (IR) and relative insulin insufficiency or by breach in insulin secretion in combination with IR. The disease develops with metabolic syndrome in the background and is the basis for development of cardiovascular diseases (CVD), affection of nerves, eyes and kidneys. It is proved that monotherapy of DM2T by one oral hypoglycemic agent is effective only during first 5-6 years of disease. Hereafter occurs a need to prescribe combined therapy by medicines form different groups, which will supplement each other in mechanism of action. But there is another problem occurs – polypragmasy and development of side effects. Aiming to avoid polypragmasy the next combinations of hypoglycemic agents are used: «Glucovans» (metformin+dlibenklamide), «Galvusmet» (metformin+vildagliptin) etc. However along with high efficacy they have numerous

contraindications and side effects. Promising tendency in solution of this problem is development of combined medicines with different mechanisms of antidiabetic action.

New combined hypoglycemic agent Glikverin was developed in National University of Pharmacy. Composing components of this agent are antioxidant quercetin and α-glucosidase inhibitor voglibose. Pharmacological effects of quercetin are related to its pronounced antioxidant properties [2]. Voglibose competes with polysaccharides for the places of binding on appropriate intestinal enzymes. As a result absorbing of monosaccharides into the blood slows down and the level of postprandial hyperglycemia, which is considered to be one of the main factor for development of complications of DM (particularly CVD) decreases [3]. α-glucosidase inhibitors are safe for long-term use, don't absorb in the blood and have no system toxicity. The only one, but substantial adverse effect of medicines from this group is flatulence and gastrointestinal upsets.

Aim of this work was to investigate antidiabetic action of Glikverin on the model of experimental non-insulin dependent diabetes mellitus in rats.

**Materials and methods.** Experiments were conducted on 55 white male Wistar rats with weight 250-300 g. Experimental diabetes mellitus was designed by single intravenous administration of streptozotocin (STZ, 65 mg/kg) [4, 5]. In order to reduce diabetogenic action of STZ 15minutes before its administration nicotinamide was administered abdominally in dose of 230 mg/kg. Previous nocitinamide administration allows preserve up to 40% pancreatic insulin pool in experimental rats. By this means moderate and stable basal hyperglycemia develops in animals unlike the other streptozotocin models. This model is characterized by development of intolerance towards carbohydrates, relative insufficiency of insulin secretion in response of increased glucose level, maintenance of secretory reaction on non-glucosal secretagogues (which includes reaction on sulphanilamide medicines). Model allows to reconstruct main pathogenic characteristics of DM2T in human, that is disorder in secretion and action of insulin.

Animals were divided in 6 groups: 1 – intact animals; 2 – animals with control pathology; 3 – animals that after modelling of DM2T were administered combined agent Glikverin (50 mg/kg – quercetine and 0,02 mg/kg voglibose); groups 4-6 – animals with pathology which were administered reference agents: substance of quercetine in dose 50 mg/kg, substance of voglibose in dose 0,06 mg/kg or tablets "Metformin" in dose 200 mg/kg. Study agents were administered intragastric once per day during 28 days. First administration of agents was initiated 24 hours after induction of diabetes. Group of animals with control pathology received solvent agent – purified water in similar design.

Condition of glucose homeostasis in animals was determined by dynamics of basal glycaemia. Level of basal glycaemia in blood of animals was identified weekly during 1 month by glucose oxidase test using kits with assay reagents «D-glucose» produced by «Felicit-Diagnostics»

(Ukraine). At the end of experiment (day 30) the speed of glucose utilization by peripheric tissues was evaluated. Evaluation was conducted using intraperitoneal glucose tolerance test (IPGTT, 3 g/kg). Glucose concentration in blood, which was obtained from tail vein of animals, was determined before administration of carbohydrates solution and 30, 60, 90 and 120 minutes after. Additionally the value of integrated index of glicemic area under curve (AUCglu (mmol/L*min) was calculated using statistic programs "MedCalk, v. 9.3.7.0".

Sensitivity of peripheric tissues to insulin action was determined with help of short insulin tolerance test. In this test the percentage of decrease of basal glycaemia was counted 30 minutes after intraperitoneally hormone administration in dose 1 IU/kg in relation to baseline level [6].

At the end of experiment animals were decapitated under ether narcosis. Level of products that react with thiobarbituric acid (TBA) and catalase was measured in blood serum [7, 8]. The red/ox balance index ($K_{lipid\ perox/antioxid}$) was used aiming to evaluate balance of oxidative-reductive processes. The index was counted as a total ratio of prooxidant quantity to total activity of antioxidants [9] and was evaluated in relative units of content of TBA to content of catalase. As a unit were taken values that were determined in intact animals. $K_{lipid\ perox/antioxid} = (TBA_{exp}/TBA_{int})/(Catalasa_{exp}/Catalase_{int})$.

Comparative histological study of rats pancreas was conducted in order to confirm antidiabetic action of Glikverin. Rear part of pancreas was anchored in 10% solution of formalin, embedded in celloidin-paraffin. Slices were coloured by haematoxylin and eosine [10]. Optical density of pancreatic islets (total quantity of islets in preparation) and percentage of islets with different content of β-cells were estimated on slices of pancreas. According to number of cells in islet they were divided in small (5-20 β-cells), middle (21-60 β-cells) and big (>60 β-cells). Review of microslides was made under light microscope Granum, photographic recording of microscopic images was made with digital video camera Granum DSM 310. Photograhpies were processed on computer Pentium 2,4Ghz using programs Toup View.

Received data was processed using methods of variation statistics [11]. Newman-Keuls and Mann-Whitney tests were used for determination of statistically significant differences between experimental groups. Differences were considered significant at $p<0,05$.

**Results and discussion.** Received data evidence that animals from control group (combined administration of streptozotocin and nicotinamide) leaded to substantial disorder of carbohydrate metabolism (table 1). Animals of this group had an increase of basal glycaemia level almost 3 times and had worsening in glucose tolerance in comparison with intact group (table 1). In terms of carbohydrate loading the glycaemia dynamics characterized by sharp growth of glucose level at 15 minute of test. There also was a disturbance in glycaemia decrease to its baseline level. This reflected on integrated index of glicemic area under curve, which exceeded value of AUCglu of

intact animals in 3 times (table 1). Results of short insulin tolerance test are the evidence of disorder in peripheral glucose disposal and development of insulin resistance in animals of control group. According to these results insulin sensitivity index (ISI) lowered up to 2.8 times in comparison with intact group.

At the moment compelling evidence exist towards the theory that "oxidative stress" participates in development of diabetes mellitus and specific complications [12]. Determination of Lipid peroxidation/antioxidative system indexes in blood serum allows to evaluate condition of oxidative-reductive processes at the level of the whole organism. Estimation of content of different Lipid peroxidation/antioxidative system indexes and estimation of activity of enzymes antioxidative system in blood serum of animals from control group showed significant increase in TBA content and decrease of catalase activity (table 2). It means that in terms of diabetes mellitus significant disorder in oxidative-reductive homeostasis with domination of lipid peroxidation happens. Results of $К_{\text{lipid perox/antioxid}}$ calculation (table 2) are the confirmation of brought conclusions. Due to raise of secondary products in lipid peroxidation and lowering enzyme activity in antioxidative system the increase of $К_{\text{lipid perox/antioxid}}$ up to 3 times took place in control group comparing to intact group index $К_{\text{lipid perox/antioxid}}$ =1. This evidences about significant disorder in red/ox-балансу (table 2).

Gradual lowering of glycaemia happened under the influence of experimantal agents (table 1). At the day 30 in all experimental groups, except animals that were administered quercetin, the level of glucose was the same as in intact animals' group and was statistically significant lower than in control group (table 1). However the highest hypoglycaemic action demonstrated Glikverin. In a week of applying the glucose level in this animals group was statistically significant lower than glucose level in control group and had not statistical differences from basal glycaemia level in intact group. Results of short insulin tolerance test and IPGTT also witnessed of improvement of carbohydrates homeostasis under the influence of Glikverin (table 1). Animals that were administered combined agent had the smallest values of AUKglu, ISI approached to values of intact animals as well.

Determination of separate Lipid peroxidation and antioxidative system indexes with further calculation $К_{\text{lipid perox/antioxid}}$ showed that at the systemic level due to influence of experimental agents the recovery of red/ox balance happened (table 2). In animals' groups that received experimental agents $К_{\text{lipid perox/antioxid}}$ approached to 1.

Analyses of received data allows to assume that combination of two components - quercetin and voglibose raise antihyperglicaemic and antioxidant action of Glikverin. Under the influence of the experimental agent the meaning of AUKglu was statistically significantly lower than in animals groups that received ubstance quercetin and voglibose. As for the restoring of redox balance - in blood serum was observed accurate tendency in synergism of quercetin and voglibose actions (table

2). The received data is logical and correlates with literature data. It was established that quercetin has pronounced antioxidant properties, moreover there are reports about its inhibition activity on absorption of monosaccharides in intestine [13]. Combination of quercetin and vogliobse in one medicine specify more pronounce antidiabetic action than has its components separately. The efficacy of composition Glikverin at this model wasn't inferior to standard reference agent tablets Metformin in influence on glycaemia level and Lipid peroxidation/antioxidative system indexes.

Confirmation of the effectiveness of Glikverin are the results of histological study of rats' pancreas in terms of experimental diabetes.

Rats from intact group have slices of pancreas of moderate size. Acinar tissue has acinus densely situated, clearly separated from each other. Among acinus in segments of gland there are pancreatic islets (PI) which round or oval, and fill segments evenly. In central parts of PI there are bundles of β-cells. In peripheric parts of islets there is an almost solid limbus of α-cells. Nucleus of β-cells are lighter and bigger than in α-cells (pic. 2, a). Morphometric analysis showed that the optical density of PI was 25 % (Fig. 1). Contentwise of β-cells islets were divided into small (27,2 %), middle (53,2 %) and big (19,2 %).

Despite the fact that in general hystoarchitectonics of exocrine part of pancreas retained, in animals of control group due to streptozotocin administration atrophy of the insular apparatus happened. In comparison with intact group PI bulk density decreased in 1.5 times. Small islets dominated among the total number: their quantity relatively intact group grew bigger in 2,3 times. The part of medium and big islets conversely decreased in 1,6 and 5,2 times. In significant number of islets β-cells are situated chaotic, uneven and nested or even total devastation of these cells was observed (Fig. 2, b-d). The cell boundaries, in β-cells that remained in islets, are often obscure, distorted, nucleus are hypertrophic, cytoplasm is vacuolated, part of cells was at different stages of degradation (Fig. 2, e). In part of PI the nidal proliferation of cells with small hyperchronic nucleus and narrow strip of cytoplasm was observed on the background of exhaustion. Typically, such assemblies contained 10-20 cells. Small assemblies of such cells were observed also near some excretory ducts.

Administration of glikverin to diabetic rats contributed to increase of optical density of PI almost to the level of intact animals (Fig. 1). Part of little islets was smaller in 1,8 times, and of middle – increased in 1,9 times comparative to control group (Fig. 2, f). In many islets β-cells retained morphologically normal structure, with no signs of dystrophy and degeneration. In these islets β-cells evenly filled the islet and the typical location of bundles was preserved. vacuolization of β-cells with exhaustion in their location was visible only in a small number of islets. Part of the pancreatic β-cells contained hypertrophic nucleus. Structural changes in exocrine parenchyma of pancreas were absent.

The increase in optical density of PI in 1,3 times was also observed under influence of quercetin and voglibose substances comparing to control group, but percentage of small islets still was remarkable enough and was equal to 35,5 % in quercetin group and 51 % in voglibose group (Fig. 1). Also appearance of a very small islets was observed. They contained only 2-4 β-cells. However, the number of middle islets raised – in 1,9 times in quercetin group and 1,5 times in voglibose group (Fig. 1). Morphologically, the state of the islands differed significantly (Fig. 2, g-i). On the background of a slight amount of unmodified islets quite a lot of islands with dystrophic β-cells were observed. Distinctivness of vacuolization in such dystrophic β-cells varied within wide limits. At the same time emptiness of islets was expressed slightly. Part of islets had not a typical shape. Macrofocal vacuolization of acinous cells and separate perivascular globocellular infiltration was seen in exocrine part of pancreas.

Influenced by metformin tablets optical density of PI almost didn't change compared with the control group. In that time the percentage of small islets lowered in 1,4 times which was quite indicative (Fig. 1). Part of middle islets enlarged in comparison with control group in 1,6 times. A significant part of PI had typical shape, but there were some islets with nontypical shape and varying degrees of emptiness (Fig. 2, k). State of pancreatic β-cells also varied – from morphologically normal to hypertrophic with vacuolated cytoplasm.

Thus, administration of streptozotocin with the background of nicotinamide leads to pronounced atrophy of insulin producing apparatus of pancreas in rats. simultaneously compensatory growth of characteristics of regenerative processes is observed. This is evidenced by morphometric analysis of changes in pancreatic islets: the decrease in optical density of the islets in 1,5 times, increase in 2.3 times of small and decrease of part of middle (in 1,6 times) and large (5,2 times) islets, and also focal proliferation of small β-cells (cells with small hyperchromic nucleus and narrow strip of cytoplasm). It is known from the literature that there is a subpopulation of pancreatic β-cells of the small size with high mitotic activity [14]. It may be so that proliferating tissue, found in islets, is a manifestation of regenerative processes which are aiming to restore pool of β-cells. Regarding cells assemblies near excretory ducts – one of the theories is that poorly differentiated epithelial cells of small excretory ducts can also be a source while restoring of pancreatic islets [15]. The latter also can be considered an activation of compensatory-regenerative processes in pancreas of diabetic rats.

Preventative administration of Glikverin composition to rats with experimental diabetes mellitus leads to an increase in optical density of PI almost to the level of intact animals, growth of number of middle islets in 1,6 times and decrease in number of small – in 1,5 times comparing to control group. A significant improvement of the morphological status of β-cells occurred under the influence of Glikverin composition. This allows to speak about cytoprotective properties of

Glikverin. Glikverin displays stimulating effect on regenerative processes in insulin producing apparatus of rats' pancreas – the presence of islets with the proliferation of small β-cells is indicating to this fact. It should be noted that affected by Glikverin the most pronounce increase is seen in number of large islets, which is also indicating to significant protective effect of a new composition in terms of pancreas. On the basis of obtained data we can conclude that composition Glikverin is somewhat superior in comparison to reference agents – vogliobse and quercetin substances and tablets metformin in the degree of positive influence on condition of endocrine part of rats' pancreas on this experimental model.

**Conclusion**

1. Combination of two components – quercetin and voglibose increase antihyperglycemic and antioxidantive activity of a new composition Glikverin. Efficacy of Glikverin on the model of diabetes mellitus, caused by streptozotocin with background of nicotinamide, was not less significant in its influence on glicaemia level and lipid peroxidation/anbtioxidative system in comparison with reference agent tablets metformin.

2. Results of histological study of rats' pancreas in terms of experimental diabetes confirm efficacy of a new composition. Influence of Glikverin on condition of pancreatic endocrine component was slightly more significant than in reference agents – voglibose, quercetin and tablets metformin.

3. Received data justifies and makes reasonable using Glikverin for correction of carbohydrate metabolism and inhibition of lipid peroxidation in terms of relative insulin resistance.

Table 1

Influence of Glikverin on carbohydrate metabolism of rats in terms of streptozotocin diabetes mellitus (n=8)

| Animals group | Indexes | | | |
|---|---|---|---|---|
| | Glicaemia, mmol/L | | AUKglu, mmol/l•min (IPGTT) | ISI, % |
| | Baseline data | Day 30 | | |
| Intact group | 4,46±0,28 | 4,02±0,17 | 754,08±11,39 | 54,36±3,71 |
| Control group | 13,13±1,45* | 9,81±2,01* | 2307,7±71,37* | 19,37±3,32* |
| Glikverin | 13,42±1,40* | 5,16±0,70** | 935,97±12,40 */**/$^{vgl}$/$^{kv}$ | 52,22±4,5**/$^{vgl}$ |
| Quercetin substance | 13,09±1,53* | 7,36±1,30 | 1080,48±26,58*/** | 42,54±2,78** |
| Voglibose substance | 13,14±0,95* | 5,81±1,05** | 1121,91±44,16*/** | 32,01±4,61*/** |
| Tablets metformin | 13,29±0,67* | 6,42±1,1** | 984,81±35,57 */**/$^{vgl}$ | 51,12±4,30**/$^{vgl}$ |

Notes:

* – differences are statistically significant in reference to values of animals from intact group, p<0,05;

** – differences are statistically significant in reference to values of animals from control group, p<0,05;

$^{vgl}$ – differences are statistically significant in reference to values of animals treated with voglibose substance, p<0,05;

$^{kv}$ – differences are statistically significant in reference to values of animals treated with quercetin, p<0,05.

Table 2

Influence of Glikverin on oxidation-reduction process in blood serum in terms of streptozotocin diabetes in rats (n=7-9)

| Animals group | $K_{lipid\ perox/antioxid}$ (in serum) | TBA, mmol/l | Catalase, mkat/l·sec |
|---|---|---|---|
| Intact group | 1 | 2,08±0,23 | 48,64±5,73 |
| Control group | 3,09±0,42 | 4,45±0,40* | 64,98±6,61 |
| Glikverin | 1,35±0,22* | 2,49±0,19**/ $^{vgl}$ | 63,60±6,98 |
| Quercetin substance | 1,55±0,19* | 3,01±0,28** | 64,54±5,46 |
| Voglibose substance | 2,01±0,25* | 4,07±0,41*/ $^{kv}$ | 78,73±12,63 |
| Tablets metformin | 1,51±0,24* | 3,39±0,18*/** | 64,48±8,97 |

Notes:

* – differences are statistically significant in reference to values of animals from intact group, p<0,05;

** – differences are statistically significant in reference to values of animals from control group, p<0,05;

$^{vgl}$ – differences are statistically significant in reference to values of animals treated with voglibose substance, p<0,05;

$^{kv}$ – – differences are statistically significant in reference to values of animals treated with quercetin, p<0,05

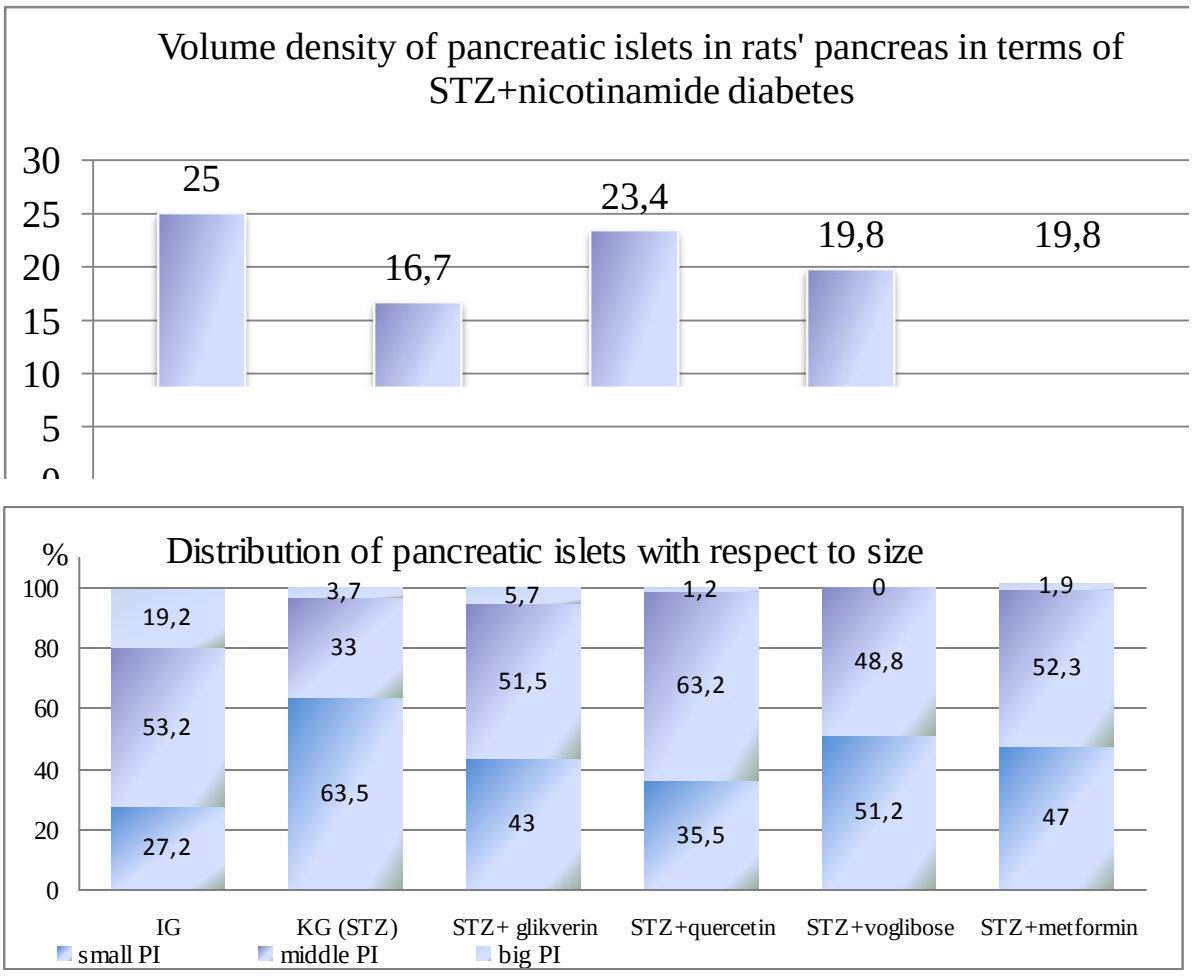


Fig. 1 Morphometric analysis of rats' incretory apparatus in terms of DM (STZ+nicotinamide) and its correction by study agents

**References**


1. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030 / D. R. Whiting, L. Guariguata, C. Weil [et al.] // Diabetes Res. Clin. Pract. – 2011. – Vol. 94, № 3. – P. 311– 321.

2. Quercetin ameliorates hyperglycemia and dyslipidemia and improves antioxidant status in type 2 diabetic db/db mice / S. M. Jeong, M. J. Kang, H. N. Choi [et al.] // Nutr. Res. Pract. – 2012. – Vol. 6, № 3. – P. 201–207.

3. Dabhi A. S., Bhatt N. R., Shah M. J. Voglibose: an alpha glucosidase inhibitor // J. Clin. Diagn. Res. – 2013. – Vol. 12, № 7. – P. 3023–3027.

4. Islam S., Loots D. T. Experimental rodent models of type 2 diabetes: a rewiev // Methods Find. Exp. Clin. Pharmacol. – 2009. – Vol. 31, № 4. – P. 249–261.

5. Masiello P., Broca C, Gross R. et al. Development of a new model in adult rats administrated streptozotocin and nicotinamide // Diab. – 1998. – V Vol. 47. – P. 224–229.

6. Akinmocun A., Selby P., Ramaiya K., Alberti K.G.M.M. The short insulin tolerance test for determination of insulin sensitivity: a comparison with euglycaemic clamp // Diab. Med.– 1992.– Vol. 9.– P. 432–437.

7. Стальная И.Д., Гаришвили Т.Г. Метод определения малонового диальдегида с помощью тиобарбитуровой кислоты // Под ред. В.Н.Ореховича. – М.: Медицина, 1977. – С. 66–68.

8. Aebi H.E. Catalase ed HV In: Bergmeyer H.V. Method of enzymatic analysis. Berlin: Verlag Chemie, 1983. – Vol. 3. – P. 273–286.

9. Коган В. Я. Проблема анализа эндогенных продуктов перекисного окисления липидов / В. Я. Коган, Д. М. Орлов. − М. : Итоги науки и техники, 1986. − Т. 18. − 134 с.

10. Меркулов Г. А. Курс патологогистологической техники. – М.: Медицина, Ленингр. отд-ние, 1969. – 424с.

11. Лапач С.Н., Чубенко А.В., Бабич П.Н. Статистические методы в медико-биологических исследованиях с использованием Excel. – 2001. – 320 с.

12. Maeda Y. Oxidative stress [Text] / Y. Maeda, T. Inoguchi // Nippon Rinsho. – 2010. – Vol. 68, № 5. – P. 814–818.

13. Quercetin attenuates fasting and postprandial hyperglycemia in animal models of diabetes mellitus / J. H. Kim, M. J. Kang, H. N. Choi [et al.] // Nutr. Res. Pract. – 2011. – Vol. 5. - № 2. – P. 107–111.

14. Bonner-Weir S., Trent D., Honey R. Responses of neonatal rat islets to strepto-zotocin // Diabetes. – 1981. – Vol. 30, № 1. – P. 64–69.

15. Хэм А., Кормак Д. Гистология: Пер. с англ. – М.: Мир, 1983. – Т.5. – 296 с.

УДК 616.379-008.64: 615.252.349.7

## АНТИДІАБЕТИЧНА ДІЯ НОВОЇ КОМПОЗИЦІЇ «ГЛІКВЕРИН» ЗА УМОВИ ЦУКРОВОГО ДІАБЕТУ 2 ТИПУ

**Національний фармацевтичний університет, м. Харків, Україна**

Досліджена антидіабетична дія нової композиції Гліквери на моделі експериментального цукрового діабету у щурів, викликаного стрептозотоцином на тлі нікотинаміду. Встановлено, що поєднання кверцетину та воглібозу в одному засобі обумовлює більш виразну антидіабетичну дію, ніж окремих його складових. Гліквери на даній моделі за впливом на рівень глікемії та показники ПОЛ/АОС не поступався за виразністю стандартному препарату порівняння таблеткам метформіну. Результати гістологічного дослідження підшлункової залози підтверджують ефективність нової композиції. За виразністю позитивного впливу на стан ендокринної складової підшлункової залози щурів Гліквери дещо переважає препарати порівняння воглібоз, кверцетин і таблетки метформіну. Отримані дані обґрунтовують доцільність застосування Гліквери з метою корекції вуглеводного обміну та гальмування вільно-радикального окиснення ліпідів в умовах відносної інсулінової недостатності.

**Ключові слова: експериментальний цукровий діабет, оксидативний стрес, морфоструктура підшлункової залози, гліквери.**

УДК 616.379-008.64: 615.252.349.7

## АНТИДИАБЕТИЧЕСКОЕ ДЕЙСТВИЕ НОВОЙ КОМПОЗИЦИИ «ГЛИКВЕРИН» В УСЛОВИЯХ САХАРНОГО ДИАБЕТА 2 ТИПА

**Национальный фармацевтический университет, г. Харьков, Украина**

Исследовано антидиабетическое действие новой композиции Гликверин на модели экспериментального сахарного диабета у крыс, вызванного стрептозотоцином на фоне никотинамида. Установлено, что сочетание кверцетина и воглибоза в одном средстве обусловливает более выраженное антидиабетическое действие, чем его отдельные составляющие компоненты. Гликверин на данной модели не уступал стандартному препарату сравнения таблеткам метформина по выраженности влияния на уровень гликемии

и показатели ПОЛ/АОС. Результаты гистологического исследования поджелудочной железы подтверждают эффективность новой композиции. По выраженности положительного влияния на состояние эндокринной составляющей поджелудочной железы крыс Гликверин несколько превосходит препараты сравнения воглибоз, кверцетин и таблетки метформина. Полученные данные обусловливают целесообразность использования Гликверина в условиях относительной инсулиновой недостаточности с целью коррекции углеводного обмена и торможения свободно-радикального окисления липидов.

**Ключевые слова: экспериментальный сахарный диабет, оксидативный стресс, морфоструктура поджелудочной железы, гликверин.**