ISSN: 2309-5288 (Print)
ISSN: 2309-6152 (Online)
CODEN: JCLMC4

Journal of Coastal Life Medicine

Hypoglycemic Activity of Diaglycon in Adrenalin and Alloxan Hyperglycemia

Received: 19 October 2022, **Revised:** 26 November 2022, **Accepted:** 24 December 2022

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Keywords:
diaglycon, alloxan hyperglycemia, adrenaline hyperglycemia, oxyquinoline hyperglycemia, glucair, glypil.

Abstract
Authors studied the hypoglycemic activity of the drug diaglycon in various models of hyperglycemia. In acute alimentary and alloxan hyperglycemia, diaglycon has a pronounced hypoglycemic effect and is not inferior in activity to the comparison drugs - glukeyr and glipil. It has been established that diaglycon and glucair effectively reduce adrenaline-induced hyperglycemia, while glypil shows little effect. Further, the results showed that diaglycon has a positive effect on the course of zinc-deficient forms of hyperglycemia and in this respect is significantly superior to Glucair.

1. Introduction

For the treatment of diabetes and its complications, drugs with various effects on metabolic processes are used. The main spectrum of antidiabetic drugs is represented by endogenous insulin secretion stimulants (sulfonylurea derivatives, meglitinides, glucagon-like growth factor-1 receptor agonists, dipeptidyl peptidase-4 inhibitors) and agents that improve glucose uptake by peripheral tissues (metformin, insulin sensitizers). The therapeutic efficacy of these drugs has been proven in many experimental and clinical studies [1-30].

The bulk of these synthetic drugs are imported, expensive, and they have various side effects [30-36]. Pharmacological properties and mechanisms of action of phytopreparations with hypoglycemic action have not been studied enough. Based on this, the search and pharmacological study of new hypoglycemic agents based on local natural raw materials of the republic is an extremely urgent task.

Material

It is known that for the treatment of diabetes in folk medicine preparations of Jerusalem artichoke is widely used. Jerusalem artichoke herb is a crushed raw material, where there are pieces of stems, leaves, and inflorescences of the aerial part of Jerusalem artichoke, passing through a sieve with a hole diameter of 7 mm. Color - gray-green, grassy smell, taste - bitter-mucous. Jerusalem artichoke tea consists of a mixture of stems, leaves, and inflorescences of Jerusalem artichoke, passing through a sieve with a hole diameter of 3 mm. The color is gray-green, the smell is grassy, and the taste is bitter-mucous. Jerusalem artichoke tea is packaged and dosed at 2.5 g into paper bags for tea packaging (GOST 7933-89 E). Jerusalem artichoke grass and tea contain inulin polysaccharide - not less than 8%, total ash - not more than 9%, organic impurities - not more than 7%, mineral impurities - not more than 0.5%. In the powder of Jerusalem artichoke tubers: inulin content - not less than 18%, total ash - not more than 7.5%. In the ashes of Jerusalem artichoke tubers, the presence of 28 elements, and 12 fatty acids, of which saturated - 33.6% and unsaturated -66.4%.

This paper presents the results of studies of the drug diaglycon based on Jerusalem artichoke. Diaglycon was obtained at the Department of Inorganic, Analytical, and Physical Colloid Chemistry of Tashfarmi. The substance of diaglycon contains inulin 8%, proanthocyanidins (26%), and salidroside (not less than1.5%), as well as: 26 micro and macro elements, including:

Zinc-0.0009%,

Copper-0.0008%,

Manganese-0.03%,

ISSN: 2309-5288 (Print)
ISSN: 2309-6152 (Online)
CODEN: JCLMC4
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Iron-0.2%,

Cobalt-0.002%,

Molybdenum-0.0002%,

Aminoacids-1.6%.

2. Methodology

The model of acute hyperglycemia was called according to the method described in the book by O. V. Remizov and T. L. Kuraev [37]. In order to exclude the effect of food on the absorption of the test substance, feeding of the animals was stopped 4-6 hours before the experiment. Longer fasting is undesirable due to the fact that in this case the severity of the hypoglycemic effect of the drugdecreases.

Experimental hyperglycemia in rats was induced by a single intraperitoneal injection of a hypertonic glucose solution at a dose of 4.5 g/kg. 30 minutes prior to the administration of glucose, the test substances were administered orally using a probe in the form of a 10% aqueous solution. After 30, 60, 90, and 120 minutes, the level of glucose in the blood was determined. On the model of acute hyperglycemia, the activity of diaglycone was compared with the well-known hypoglycemic drug Glucair (Shrey Nutraceuticals Herbals Pvt Ltd India). For this, Diaglycon was used at a dose of 50 and 100 mg/kg, and Glu-Keyr capsules at 100 mg/kg. The experiments were carried out on 24 mature white rats weighing 140-165 g.

In separate series of experiments, the influence of diaglycon on the course of adrenaline hyperglycemia was studied according to the method described in the book by V. G. Baranov et al. The experiments were carried out on 30 rats weighing 170-190 g. For this purpose, the animals of the experimental group were orally administered diaglycon 100 mg/kg. Control animals received saline in the appropriate volume. After 30 minutes, adrenaline was injected at a dose of 50 μg/kg and the sugar level was determined in dynamics by the enzymatic method. Before the experiment according to the method, the rats fasted for 8 hours.

The model of alloxan hyperglycemia was reproduced according to the method described in the book by O. V. Remizov and T. L. Kuraev. Sexually mature laboratory rats with a weight of 160-175 g were used for the studies. Under the condition of a single intravenous injection, the hyperglycemic dose of alloxan was 150 mg/kg. For complete conviction, the level of sugar in the blood was determined by the enzymatic method. The sensitivity of animals to alloxan can be different in degree, on the basis of which we found alloxan hyperglycemia with the mild and moderate courses. After introduction into the body, alloxan binds to the membranes of pancreatic β-cells and leads to a rapid decrease in insulin secretion. The resulting primary hyperglycemia is associated with the mobilization of glycogen from the liver under the influence of contra insular hormones. Approximately two hours after the injection of alloxan, a significant amount of insulin is released due to the death of β-cells, and hyperglycemia is replaced by severe hypoglycemia. After 1-2 days, persistent hyperglycemia develops. On the model of alloxan hyperglycemia, we studied the effect of diaglycon on the blood glucose level in laboratory animals and compared its effect with the effect of glucair. The studies were carried out on 72 rats of both sexes weighing 180-200 g. Hyperglycemia was reproduced according to the above method. After two days, the blood sugar level was determined.

Further, the animals were divided into 2 groups: animals with a mild course of hyperglycemia and a moderate form. The first group included animals with hyperglycemia 11.5-13.5 mmol/l, and the second group with hyperglycemia 20.0-23.0 mmol/l. Animals were treated by administering diaglycon and glucair at 100 mg/kg. Control animals received the appropriate volume of saline. The studied substances were administered orally for 20 days in the form of a 5% aqueous solution. On the 10th and 20th days, the blood sugar level was determined.

Model of oxyquinoline hyperglycemia. According to the method described in the "Guidelines for the experimental (preclinical) study of new pharmacological substances" [38], oxyquinoline hyperglycemia was reproduced in rabbits by intravenous administration of 5-phenyl azo-8-hydroxyquinoline at a dose of 20-40 mg/kg. To increase sensitivity to oxyquinoline derivatives, the animals were not fed for 2 days before the experiment.

Downstream, hyperglycemia caused by oxyquinoline derivatives coincides with insulin-dependent hyperglycemia and proceeds in 3 phases:

ISSN: 2309-5288 (Print)
ISSN: 2309-6152 (Online)
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hyperglycemia, hypoglycemia, and persistent hyperglycemia.The ease of obtaining hyperglycemia, the high selectivity of action on pancreatic islets, absence of side effects on other organs, and long life expectancy of experimental animals without insulin administration allows us to consider the oxyquinoline test as a convenient experimental model.

The hypoglycemic effect of diaglycone and preparations from Chicory was studied on the model of oxyquinoline hyperglycemia. Hyperglycemia was reproduced according to the method [38] on 24 rabbits of both sexes, weighing 2.3-2.9 kg. To confirm hyperglycemia after 2 days, blood was taken from the ear vein and the glucose level was determined. Animals were treated by oral administration of diaglycon at 50 and 100 mg/kg, glucair at 100 mg/kg in the form of a 10% aqueous solution. The experiment was continued for 30 days; on the 15th and 30th days, the level of glycemia was observed in dynamics. In the following experiments, some mechanisms of the hypoglycemic action of diaglycone were studied. The effect of diaglycon on the level of C-peptide in the blood was studied on 24 rats weighing 170-190 g under conditions of alloxan hyperglycemia. Experimental animals were treated with oral administration of diaglycon 50 mg/kg, glucair 100 mg/kg for 2 weeks. Control animals received saline in the appropriate volume. On the 7th and 14th days of the experiment, the level of C-peptide in the blood was determined.

The effect of diaglycon on the content of glycogen in the liver was studied on 42 rats weighing 170-180 g in the above model of alloxan hyperglycemia. Animals of the experimental group were administered diaglycon orally at 50 and 100 mg/kg for 3 days. The control group received physiological saline in the appropriate volume.

At the end of the experiment, the content of glycogen in the liver and muscles was determined using the anthrone reagent. According to the method [39], the liver tissue is subjected to desmolysis with 30% KOH, glycogen is precipitated from the desmolysate by adding alcohol, which is treated with the anthrone reagent in concentrated sulfuric acid. Glucose formed as a result of hydrolysis of glycogen, dehydrated in the presence of concentrated sulfuric acid and condensed with anthrone, stains the solution blue, which is measured with a red filter on FEC.

The following experiments were devoted to studying the effect of diaglycon on the activity of hexokinase and phosphorylase enzymes. Experiments were carried out on 24 rats weighing 170-190 g under conditions of alloxan hyperglycemia. Animals of the experimental group received diaglycon at 50 mg/kg and 100 mg/kg for two weeks. The control group of animals received physiological saline in the appropriate volume. Before the introduction of alloxan and at the end of the experiment, the activity of enzymes in the biomaterial was determined.

Hexokinase activity was determined by a method based on the decrease in glucose consumed for the formation of glucose-6-phosphate during the hexokinase reaction:

Glucose + ATP + hexokinase Glucose-6-phosphate + ADP The methodology consists of two stages: Own hexokinase reaction. Quantitative determination of glucose in experimental and control samples.

Hexokinase activity is expressed in conventional international units (IU), 1 IU is equal to 1 micromole of glucose converted in 1 minute per 1 liter of blood serum at a temperature of 370 C, pH - 7.8.

Hexokinase activity in IU = initial amount of glucose in 1 liter of blood serum in µmol / amount of glucose in 1 liter of blood serum after hexokinase reaction, in µmol.

Thus, to determine the activity of hexokinase, the initial amount of glucose (control samples) and the amount of glucose remaining in the samples after the hexokinase reaction (experimental samples) are measured, and the hexokinase activity is calculated from the difference between the control and experimental samples.

3. Results

We have studied the activity of diaglycon in the model of acute alimentary hyperglycemia, comparing it with other hypoglycemic drugs, glucair and glypil.

The results of comparative experiments showed that after the administration of glipil at a dose of 50 mg/kg, diaglycon 50 mg/kg, and Glukeyr at a dose of 100 mg/kg against the background of hyperglycemia, a more significant effect was observed at the 60th minute. The level of sugar in the blood in the 60th

ISSN: 2309-5288 (Print)
ISSN: 2309-6152 (Online)
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minute decreases by 29.3%, respectively; 42.7% and 37% in relation to the control (Table 3.1)

Table1

Drugs	Doses, mg/kg	Intact, mmol/l	Time after the drug administration		
			30 min	60 min	120 min
Physical solution	1ml	4, 65 ± 0,3	8,5±0,3* (82)	8,9±0,45* (91)	6,6±0,25** (42)
Glipil	50 mg/kg		6,7±0,2^* (44)	6,3±0,32*^ (35.5)	5,5±0,4**^ (18.3)
Diaglycon	50 mg/kg		5,8±0,2*^, ^^ (24,7)	5,1±0,3^,^^ (12)	4,9±0,2**^ (5,3)
Glucair	100 mg/kg		6,1±0,25*^,^^^ (31, 1)	5,6±0,4*^ (20.4)	5,3±0,2 **^ (13,9)

The effect of diaglycon, glucair and glipil on the blood glucose level in rats during experimental hyperglycemia (mmol/l). n=6

Note:

* - the significance of differences ($p<0.05$) when comparing the results with the initial data obtained from intact animals in group I; ** - the same compared with the result after 30 minutes;

*** - the same compared with the result after 60 minutes;

^ the same ($p<0.05$) when comparing the results with the data obtained in group II after the introduction of phys

^^ - the same ($p<0.05$) when comparing the results with the data obtained in group III after the introduction of the drug "Glipil"

^^^ - the same ($p<0.05$) when comparing the results with the data obtained in group III after the introduction of the drug "Diaglicon"

Therefore, diaglycon has a pronounced hypoglycemic effect and is not inferior to the reference drugs in terms of activity.

Next, we studied the effect of diaglycon on the blood sugar level of laboratory animals with "alloxan hyperglycemia" and compared its activity with glypil and glucair.

The results of the experiments are given in the table 2. The results of the experiments revealed that in a mild form, diaglycon reduces blood sugar levels after 20 days by 35.5% in relation to the initial data and 17.6% in relation to the parallel control value, glypil, respectively, by 37.4% and 23.7%, glucair by 41.5% and 30.6%, and with moderate severe form diaglycon by 38.9% and 18.3%, glypil by 33.9% and 22.7%, glucair by 37.7 % and 23.2%.

Consequently, the drug diaglycon has a pronounced hypoglycemic effect in experimental alloxan hyperglycemia and in this respect is not inferior to glypil and glucair.

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Table 2 The effect of diaglycon, glipil and glucair on the content of sugar (glucose) in the blood in alloxan hyperglycemia, mmol/l

Groups	Initial data	Blood glucose after alloxan administration, n=6	Day after the drug administration			
			10th		20th	
			abc, n=6	%	abc, n=6	%
Easy current						
Phys, 1ml	4,8±0, 2	12,4±0,7*	11,5±1,1*	100%	10,8±1,1*	100%
Diaglycon, 50 mg/kg		13,8±1,3*	10,6±1,6*	76,8 92,2	8,9±0,9 *,**	64,5 82,4
Glipil, 50 mg/kg		13,1±1,5*	11,2±0,8*	85,5 97,4	8,2±0,7 *,**,***	62,6 76,3
Glucair, 100 mg/kg		12,6±0,9*	10,4±1,2*	82,9 90,9	7,5±0,6 *,**	58,5 69,4
Moderately severe form						
Phys, 1ml	5,1±0,4	23,3±1,4*	21,9 ±1,3*	100%	18,1±1,2 *, **	100%
Diaglycon, 50 mg/kg		24,2±1,8*	20,3±0,7*	83,8 92,6	14,8±0,8 *,**,***	61,1 81,7
Glipil, 50 mg/kg		23,9±0,9*	20,7±1,0*, **	86,6 94,5	15,8±1,3 *,**,***	66,1 87,3
Glucair, 100 mg/kg		22,3±1,2*	19,8±1,9*	88,8 90,4	13,9±1,5 *, **, ***	62,3 76,8

Note. In the numerator, the percentage in relation to the original, and in the denominator to the parallel control value:

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* - the significance of differences ($p<0.05$) when comparing the results with the initial data obtained from intact animals in group I;

** - the same as compared with the result after the introduction of alloxan;

*** - the same compared with the result after the introduction of alloxan on the 10th day;

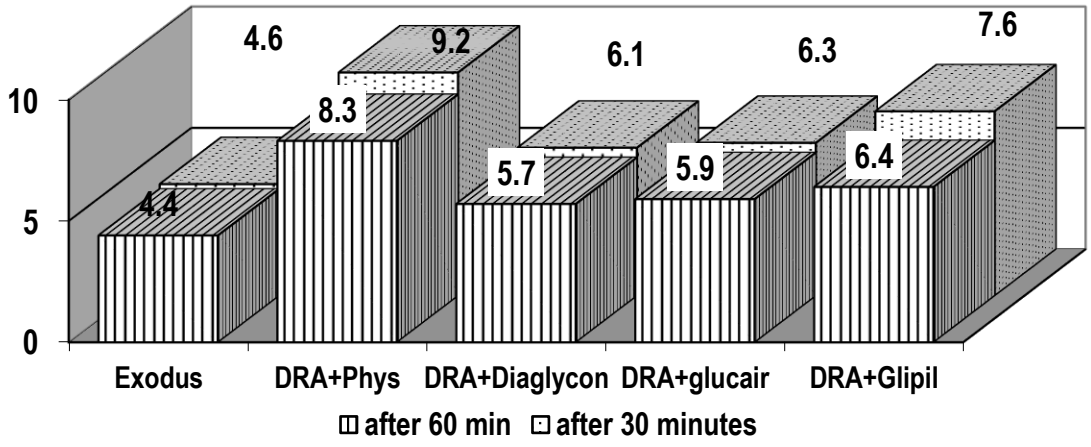
^ the same ($p<0.05$) when comparing the results with the data obtained in group II after the introduction of phys:

^^ - the same ($p<0.05$) when comparing the results with the data obtained in group III after the introduction of the drug "Diaglicon"

^^^ - the same ($p<0.05$) when comparing the results with the data obtained in group III after the introduction of the drug "Glipil"

Reliability $P<0.05$

Given that one of the mechanisms for the development of hyperglycemia is stress and an increased release of adrenaline, it was of interest to study the hypoglycemic properties of herbal preparations on the model of adrenaline hyperglycemia. The drugs were administered 30 minutes before the administration of adrenaline. Studies have shown that the administration of diaglycon at a dose of 50 mg/kg leads to a significant decrease in blood glucose from 9.2±0.21 mmol/l to 6.1±0.1 mmol/l 30 minutes after administration. adrenaline, from 8.3 ± 0.4 mmol / l to 5.7 mmol / l - after 60 minutes, i.e. the affect of the drug is 33.7% and 34.4%, respectively. The introduction of Glucair at a dose of 100 mg/kg, the blood glucose level was 6.3 ± 0.4 and 5.9 ± 0.5 mmol/l 30 and 60 minutes after the model was reproduced (affect 31.5% and 29. 0%. With the introduction of glipil at a dose of 50 mg/kg, the level of glucose in the blood after 30 and 60 minutes was 7.6 ± 0.3 and 6.4 ± 0.5 mmol / l (affect 17.4% and 22.9%) (Fig. 1).



Note: * - differences relative to the data of the intact group are significant (* - $P<0.05$) Fig. 1. Changes in blood glucose in animals under the influence of drugs in adrenaline hyperglycemia

Therefore, diaglycon and glucair effectively reduce adrenaline-induced hyperglycemia. At the same time, glipil shows a slight effect.

When studying the biological activity of drugs against the background of oxyquinoline hyperglycemia, the following results were obtained: the level of glycemia in the control group on the 15th and 30th days of the study was 13.2 ± 0.6 and 11.4 ± 0.7 mmol / l. With the introduction of diaglycon at a dose of 50 mg/kg, the level of glucose in the blood after 15 and 30 days decreased by 25.8% and by 41.3% (9.8±0.2 and 6.7±0.5 mmol/l) ($P<0.05$). The drug at a dose of 100 mg/kg at the same time reduced glycemia by 29.5% and 43.5%, respectively. Glucair at a dose of 100 mg/kg did not reduce glycemia by 21.0% and by 28.5% (Fig. 2).

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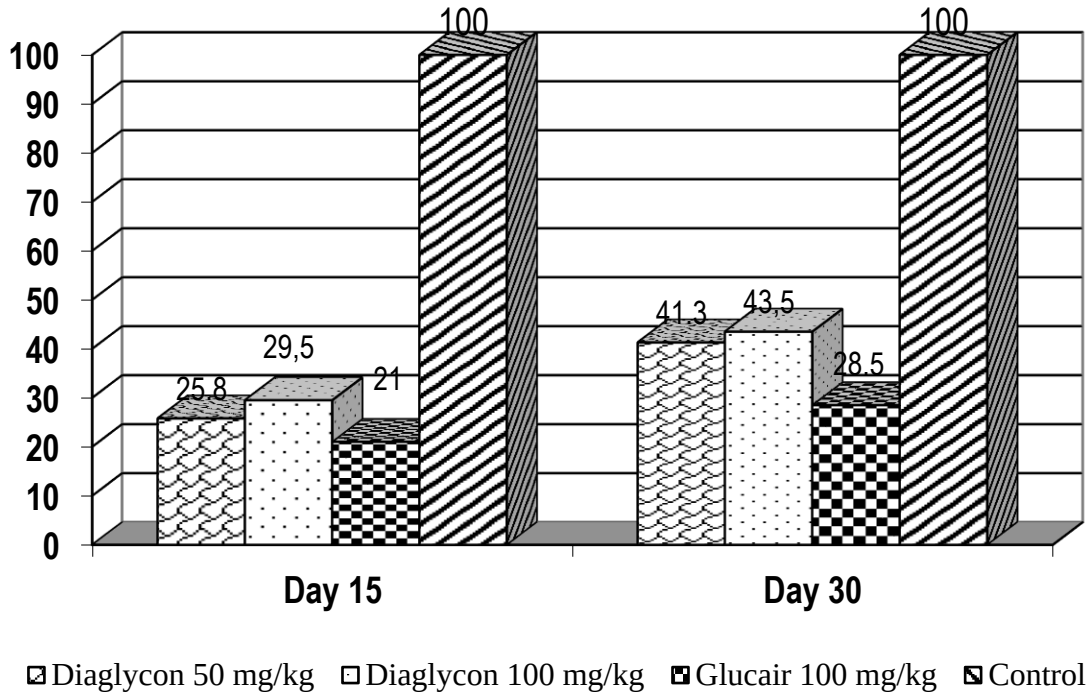

Fig. 2. Hypoglycemic effect of diaglycon and glucair in the oxyquinoline model of hyperglycemia

Thus, diaglycon has a positive effect on the course of zinc-deficient forms of hyperglycemia and in this respect is significantly superior to the drug Glucair.

§3.2. Study of some mechanisms of the hypoglycemic action of diaglycon

To elucidate some aspects of the mechanism of action, the level of C-peptide in the blood serum, the content of glycogen in the liver, and the activity of hexokinase and phosphorylase enzymes in the liver and muscles of animals were studied.

It is known that preproinsulin is synthesized by pancreatic β-cells, from which pro-insulin remains after signal peptide cleavage, and then, when insulin matures, C-peptide is cleaved from it. The C-peptide is always secreted into the blood in equivalent amounts to insulin, that is, it can be an indicator of the activity of β-cells and the level of insulin. Therefore, in recent years, a method for determining the C-peptide has been introduced in clinical endocrinology, along with the determination of insulin in the blood serum.

The studies carried out in this regard showed a marked decrease in the secretion of C-peptide by the pancreas of rats with alloxan hyperglycemia due to the developed necrosis of β-cells. In the control group, the level of C-peptide after 7 and 14 days of alloxan administration was 0.35±0.06 pg/ml and 0.31±0.03 pg/ml.

The use of diaglycon at a dose of 50 mg/kg for 7 and 14 days led to an increase in the secretion of C-peptide from 0.44±0.05 pg/ml and 0.52±0.07 pg/ml (the effectiveness of the drug was 25, 7% and 67.7% With an increase in the dose of the drug by 100 mg/kg, the level of C-peptide on days 7 and 14, respectively, was 0.57±0.08 pg/ml and 0.61±0.05 pg/ml (efficiency 62.8% and 96.7%).

With the introduction of Glucair, the level of C-peptide after 7 and 14 days was 0.43±0.06 pg/ml and 0.46±0.04 pg/ml, respectively (efficiency 22.8% and 48.3% (Fig. .3). Therefore, the studied new drug diaglycon at doses of 50 mg/kg and 100 mg/kg significantly increases the secretion of C-peptide by pancreaticβ-cells.

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ISSN: 2309-6152 (Online)
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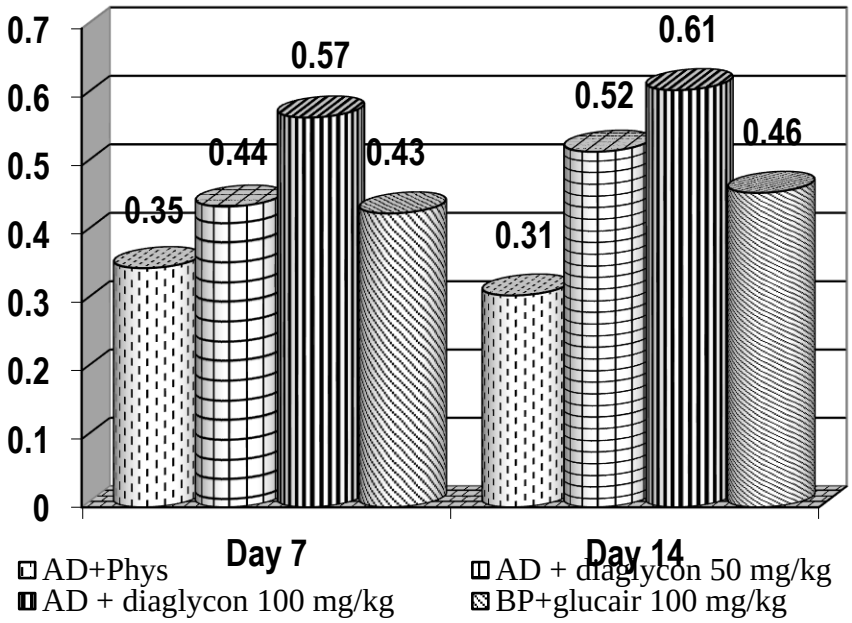

Note: - differences relative to the data of the control group are significant (* - P<0.05)

Fig. 3. Dynamics of changes in the level of C-peptide in the blood serum of rats with alloxan hyperglycemia under the influence of diaglycon and glucair.

It can be assumed that, at the same time, insulin secretion also increases, causing the hypoglycemic effect of the drugs. Glucair has little effect on the secretory function of insulinocytes.

We also studied the content of glycogen in the liver and muscles of experimental animals. Against the background of alloxan hyperglycemia, glycogen stores in the studied tissues are markedly reduced. The studied hypoglycemic drugs significantly increased the glycogen content in the studied tissues (Table 3). Diaglycon at a dose of 50 mg/kg after 7 days increased the glycogen content in the liver and muscles by 61% and 35% compared with the control. At a dose of 100 mg/kg, the effect of diaglycon was 82% and 46.8%. With the introduction of Glucair, the glycogen content in the liver and muscles increased by 48.2% and 25.6% compared with the control.

Table3 The effect of diaglycon on the content of glycogen in the liver and muscles in alloxan hyperglycemia

Drugs	Glucose level in blood, mmol/l	Glycogen content, mg/g tissue	
		In the liver	In the muscles
Intact, n=6	4,58±0,30	38,50±1,60	19,05±1,45
Alloxan hyperglycemia + physical solution, n=6	17,3±1,15^	20,34±1,19^	12,60±1,08^
Alloxan hyperglycemia + diaglycon, 50 mg/kg, n=6:	13,10±0,83^,^^	32,83±2,11^^	17,01±1,20^^
Alloxan hyperglycemia + diaglycon, 100 mg/kg, n=6	11,24±1,07^,^^	37,02±1,13^^	18,50±1,82
Alloxan hyperglycemia + Glucair 100 mg/kg (n=6)	12,40±0,63^,^^	30,14±1,16 ^,^^,^^^^	15,83±1,50

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ISSN: 2309-6152 (Online)
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Note

^ - the significance of differences ($p<0.05$) when comparing the results with data obtained from intact animals;

^^ - the same ($p<0.05$) when comparing the results with data obtained in the group with alloxan hyperglycemia and treated with physical. solution"

^^^ - the same ($p<0.05$) when comparing the results with data obtained in the group with alloxan hyperglycemia and treated with diaglycon

Therefore, diaglycon significantly restores the glycogen content in the liver and muscles. In this direction, diaglycon is more effective than the comparative drug Glucair.

The following studies showed that the activity of muscle phosphorylase in rats with alloxan hyperglycemia increased significantly. This indicates the activation of glycogenolysis in the tissues of experimental animals, which is characteristic of hyperglycemia, causing the development of hyperglycemia (Table 4). Diaglycon at a dose of 50 mg/kg reduces the activity of phosphorylase during incubation for 30 and 60 minutes by 28% and 30.4%. With the introduction of the drug at 100 mg / kg, the efficiency was 32.8% and 34.3%

Table 4 The activity of muscle phosphorylase in experimental animals after administration of diaglycon

Drugs	**Glycogen content, mg/g tissue**	
	30 min	**60 min**
Intact, n=6	15,85±1,20	24,50±1,65*,^
Alloxan hyperglycemia + physical solution, n=6	25,43±1,42^	38,95±2,15*,^
Alloxan hyperglycemia + diaglycon 50 mg/kg, n=6	18,40±1,30^^	27,10±1,32*^^
Alloxan hyperglycemia + diaglycon 100 mg/kg, n=6	17,10±1,25 ^^,^^	25,60±1,40*,^^

Note.

* - the significance of differences ($p<0.05$) when comparing the results with blood glucose levels;

^ the same ($p<0.05$) when comparing the results with data obtained from intact animals;

^^ - the same ($p<0.05$) when comparing the results with data obtained in the group with alloxan hyperglycemia and treated with physical. solution"

^^^ - the same ($p<0.05$) when comparing the results with data obtained in the group with alloxan hyperglycemia and treated with diaglycon

Therefore, diaglycone reduces the sharp activation of muscle phosphorylase in rats with alloxan hyperglycemia. Based on the results, it can be assumed that the increase in the level of glycogen in the liver and muscles of rats with alloxan hyperglycemia under the influence of diaglycon is associated with a slowdown in the breakdown of glycogen due to a decrease in phosphorylase activity. One of the regulatory enzymes of glucose metabolism is hexokinase. Studies have shown that in rats with alloxan hyperglycemia, the activity of enzymes in the liver and muscles is markedly reduced, which indicates a slowdown in glucose metabolism in tissues. Diaglycon at a dose of 50 mg/kg activates glucokinase in the liver and hexokinase in muscles by 32.8% and by 58.3% compared with the control. With the introduction of 100 mg/kg, the drug increased the activity of enzymes in the tissues of the liver and muscles by 39.6% and 63.2% compared with the control group (Table 5).

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Table 5 The activity of hexokinase in the liver and muscles of experimental animals with the introduction of diaglycon

Drugs	Phosphorylase activity (IU) after incubation	
	liver glucokinase (IU)	muscle hexokinase (ME)
Intact	128,10±4,50	118,95±3,25
Alloxan hyperglycemia + Phys	105,80±2,70^	98,70±4,10^
Alloxan hyperglycemia + diaglycon 50 mg/kg	140,55±3,45^^	156,30±2,30*^,^^
Alloxan hyperglycemia + diaglycon 100 mg/kg	147,69±6,20^,^^	161,10±3,68^,^^

Note.

* - the significance of differences ($p<0.05$) when comparing the results with blood glucose levels;

^ the same ($p<0.05$) when comparing the results with data obtained from intact animals;

^^ - the same ($p<0.05$) when comparing the results with data obtained in the group with alloxan hyperglycemia and treated with physical. solution"

^^^ - the same ($p<0.05$) when comparing the results with data obtained in the group with alloxan hyperglycemia and treated with diaglycon. Therefore, diaglycon significantly activates liver glucokinase and, especially, muscle hexokinase. Based on the data obtained, it can be said that the mechanism of hypoglycemic action also includes the accelerated formation of a metabolically active form of glucose, which leads to an increase in glucose metabolism by tissues.

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