ISSN NO: 2770-0003
Date of Publication: 10-10-2022

Biochemical study of the effect of hypoglycemic collection on the intensity of glucose neoformation under conditions of adrenaline hyperglycemia

Malikova G.Y
Department of Toxicological Chemistry
Tashkent Pharmaceutical Institute
Tashkent city, Uzbekistan
gulchekhramalikova.70@gmail.com

Annotation Unfortunately, diabetes today is still one of the most important medical and social problems worldwide. This disease is often accompanied by hyperglycemia, that is, high blood glucose levels, which in turn leads to damage to many body systems. Of course, at the moment there are methods of effective control and treatment of the disease. Against this background, over the past decade, there has been a marked increase in interest in the methods of complementary and alternative medicine. Some researchers report that up to 72.8% of people with diabetes have used herbal medicine, dietary supplements, and other complementary-alternative medicine methods, in most cases as an adjunct to conventional medical treatment. Many herbal remedies have antioxidant properties that can reduce the level of oxidative stress, one of the key pathogenetic factors in the development of diabetes [1].

Key words: Diabetes, high blood glucose

Relevance. Unfortunately, diabetes today is still one of the most important medical and social problems worldwide. This disease is often accompanied by hyperglycemia, that is, high blood glucose levels, which in turn leads to damage to many body systems. Of course, at the moment there are methods of effective control and treatment of the disease. Against this background, over the past decade, there has been a marked increase in interest in the methods of complementary and alternative medicine. Some researchers report that up to 72.8% of people with diabetes have used herbal medicine, dietary supplements, and other complementary-alternative medicine methods, in most cases as an adjunct to conventional medical treatment. Many herbal remedies have antioxidant properties that can reduce the level of oxidative stress, one of the key pathogenetic factors in the development of diabetes [1].

With insufficient secretion of insulin or its inadequate action on the target, diabetes mellitus develops. In 1981. The WHO Expert Committee defined diabetes mellitus as a syndrome of chronic hyperglycemia that develops as a result of absolute or relative insulin deficiency and manifests itself as glucosuria, polyuria, polydipsia, lipid, protein and mineral metabolism disorders and the development of characteristic complications (acute and chronic) [2].

Type 1 diabetes mellitus (DM1) is a polyetiological syndrome caused by an absolute deficiency of insulin, leading to a violation of carbohydrate and then other types of metabolism. DM1 develops as a result of autoimmune destruction of insulin-producing pancreatic cells (autoimmune variant) or spontaneously (idiopathic variant) [3].

The most important function of gluconeogenesis is to maintain blood glucose levels in the face of reduced food intake and glycogen stores. Gluconeogenesis, as a fundamental process that occurs in the liver and is directly related to carbohydrate metabolism, has not been sufficiently studied in the pharmacobiochemical aspect in various diseases. As a result, the study of the rate of glucose formation from non-carbohydrate compounds is relevant, because gluconeogenesis can serve as a source of additional amounts of glucose for energy supply of a number of essential protective and adaptive phenomena: compensatory hyperfunction of the heart [4], plastic processes (synthesis, RNA, DNA), especially for brain activity. De novo synthesis of glucose from non-carbohydrate precursors, mainly from amino acids and metabolites of intermediate metabolism, is a specific function of hepatocytes and cells of the cortical layer of the kidneys [6].

ISSN NO: 2770-0003
Date of Publication: 10-10-2022

A large number of experimental studies have been carried out to elucidate the state, intensity of the course and hormonal control of gluconeogenesis both in intact animals and with hepatic pathology in an isolated perfused liver.

It is essential for this work that the hypoglycemic effect of a number of oral antidiabetic drugs, sulfonylurea and biguanides, is associated with their inhibitory effect on the processes of cAMP-dependent enzyme. Enzymes of gluconeogenesis are cAMP dependent, their state is important in the regulation of carbohydrate metabolism.

Herbal preparations contain a significant amount of active ingredients that affect different parts of the pathogenesis of diabetes, which provides a multifactorial mechanism of action on metabolism (Kar A. et al., 2003). The low economic component of therapy based on herbal remedies and the minimum number of side effects in the course of treatment serve as an additional justification for the expediency of their use [5].

The main oral agents in the treatment of diabetes are sulfonamides and biguanides, but due to the fact that side effects are detected after treatment, toxicity and addiction make us look for new adjuvant treatments. Therefore, the use of a herbal preparation with a hypoglycemic effect that normalizes metabolic processes in diabetes mellitus remains relevant. This prompted us to study the hypoglycemic activity of local plants, namely the extract of plantain leaves and white mulberry leaves.

Objective: To investigate the effect of collection on the rate of de novo formation of glucose from its precursors under conditions of hyperglycemia of adrenaline origin in the liver.

Materials and Methods: To determine the nature of changes in carbohydrate metabolism under the action of an extract of local plants (Morus alba, Plantago major) white mulberry leaves and greater plantain leaves, studies were conducted in intact animals in normal and pathological conditions of carbohydrate metabolism. The experiments were carried out on 9 white mature rats, weighing 100-120 g, kept on a normal diet. The animals were divided into 3 groups of 3 each: the first group was an intact control, the second group was a control pathology (animals with experimental diabetes introduced into saline alloxan hydrate), the third group was a control pathology (animals with experimental diabetes + extract of local plants) [7]. The plant extract was administered to diabetic animals once a day for 1,3,7 days at a dose of 50 mg/100 g and oranil in the amount of 100 mg/kg administered orally. The general condition of the animals was monitored for one week in a vivarium. The task of the study was to determine the intensity of gluconeogenesis in sections of the liver tissue (the formation of glucose from its precursors under conditions of hyperglycemia in the liver). To solve this problem, studies were carried out in the norm in intact animals, as well as in control and experimental animals with diabetes under the influence of hypoglycemic collection.

After 7 days, the rats were decapitated and the blood sugar level was determined at intervals of 15 minutes, that is, after 30, 45 and 60 minutes. Determination of glucose in the blood was carried out using glucose oxidase methods (on the example of using the traditional methodological approach associated with the use of certified reagent kits (according to the kits of NTPC "Analysis-X", Belarus) [7,8].

The rate of gluconeogenesis in liver tissue sections was determined [4] by incubation of liver sections in Krebs-Rieger bicarbonate buffer pH – 7.4 with the addition of one of the substrates (alanine, α-ketoglutaric acid, pyruvic acid, succinic acid) at a final concentration of 0.01 M . Incubation was carried out under aerobic conditions at 37°C and constant shaking for 1 h [6].

The rate of gluconeogenesis was expressed in mg of newly formed glucose per 1 hour per 1 g of raw liver tissue.

Results and Discussion: In insulin deficiency, epinephrine is known to cause higher hyperglycemia and reduce glucose uptake in tissues. Therefore, the study of the effect of epinephrine in rats treated for several days with the collection is of particular interest in the interpretation of the insulin-like action of the collection, which prevents the production of glucose, and thus blocking the effect of adrenaline on gluconeogenesis. The regulation of gluconeogenesis by adrenaline has some peculiarities. In particular, in rats adrenaline stimulates gluconeogenesis to a greater extent than glucagon. This is due to the fact that adrenaline, unlike glucagon, enhances glycogenolysis in muscles and the production of lactate, one of the main substrates of gluconeogenesis in the liver [9] . The collection has, along with hypoglycemic and

ISSN NO: 2770-0003
Date of Publication: 10-10-2022

antigluconeogenic effect. The continuation of these studies was to study the effect of collection on the rate of gluconeogenesis in the liver of rats, stimulated by the administration of adrenaline (table 1).

Table 1.

Formation of glucose by liver sections from endogenous sources
kov when administering epinephrine to alloxandiabetic rats treated with the collection (in mg glucose/1g tissue/1 hour, n=6)

Group Options without substrate	Single injection	Triple Introduction	Sevenfold Introduction
I.control (intact)	0,545±0,060	0,537±0,063	0,547± 0,054
II. control+adrenaline	0,666±0,043	0,618±0,049	0,635±0,082
II. gathering+adrenaline	0, 533±0,049	0,527±0,043	0,446±0,041
	p II-III›0,05	p II-III›0,05	pII-III<0,05

Under experimental conditions without introducing exogenous substrates into the incubation medium, adrenaline stimulates the formation of glucose from endogenous sources. The administration of the mixture to animals not only inhibited the formation of glucose from tissue substrates, but even reduced its level to control values. This is especially noticeable when the collection is administered within 3-7 days. The results of the experiments are given in table. 2. confirm the idea that alanine is the most beneficial source of neoglucogenesis precursors in the liver tissue. Indeed, the substrate supply of gluconeogenesis with the introduction of adrenaline far exceeded other sources, the percentage of which was almost 50% more than the control value. The distribution of substrates according to their use as a source of glucose in descending order had the following sequence: alanine > succinate > pyruvate > α-ketoglutarate. These data are consistent with the importance of substrates in the provision of gluconeogenesis in the liver shown in the literature.

As can be seen from Table 2, the rate of glucose formation in liver sections of animals subjected to the action of two factors - hypoglycemic collection and adrenaline, lags far behind in comparison with that with the introduction of only the hormone. At the same time, long-term administration of the mixture to rats led not only to a significant decrease in the intensity of stimulated gluconeogenesis by adrenaline, from all studied substrates, but also to a decrease in the rate of glucose synthesis from endogenous precursors (see control after a sevenfold introduction). Based on these data, it can be assumed that the collection has a direct inhibitory effect on gluconeogenesis in the liver.

Table 2

Formation of glucose by liver sections from various substrates
when administering adrenaline to alloxandiabetic rats
against the backdrop of the collection. (glucose mg per 1g tissue/1 hour n=6)
*II –III -p<0.05

Substrates	Group Options	Single injection	Triple Introduction	Sevenfold Introduction
Alanine	I control	0,622±0,061	0,613±0,041	0,675±0,044
	II control+ adrenaline	0,935±0,084	0,900±0,038	0,927±0,067
	IIIcollection+ adrenaline	0,766±0,082	0,598±0,068*	0,541±0,048*
Private	I control	0,623±0,092	0,630±0,072	0,650±0,066
	II control+ adrenaline	0,705±0,064	0,673±0,036	0,712±0,065
	IIIcollection+ adrenaline	0,628±0,037	0,593±0,047	0,475±0,074*
Succinate	I control	0,637±0,050	0,620±0,050	0,632±0,038
	II control+adrenaline	0,802±0,072	0,762±0,060	0,800±0,061

ISSN NO: 2770-0003
Date of Publication: 10-10-2022

	IIIcollection+ adrenaline	0,665±0,050	0,503±0,030*	0,572±0,043*
Ketoglutarate	I control IIcontrol+adrenaline IIIcollection+ adrenaline	0,630±0,021 0,660±0,057 0,622±0,040	0,633±0,016 0,652±0,047 0,528±0,047	0,640±0,021 0,670±0,042 0,554±0,051*

It is known that the main intracellular mediator of gluconeogenesis in hepatocytes (and in the cells of the cortical layer of the kidneys) is cyclic c-AMP, which is a universal regulator of metabolic processes and, therefore, the analysis of hormonal regulation of cellular processes is reduced to identifying the relationship of cyclic nucleotides. Therefore, in the effect of collection on gluconeogenesis, deviations in the c-AMP regulated mechanism of action of adrenaline can be tolerated.

Thus, the hypoglycemic effect of the collection consists of its ability to increase glucose consumption in muscle tissue, inhibit gluconeogenesis in the liver, activate glucose phosphorylation by hexokinase and glycogen synthesis, and reduce glycogen breakdown by phosphorylase. Therefore, the mechanism of action of the collection is based on hypoglycemia, due to a combination of inhibition of gluconeogenesis and increased consumption of glucose in peripheral tissues. Gluconeogenesis inhibitors are also sulfonamides and biguanides, which are widely used in the clinic as oral therapy for diabetes.

The results of our research allow us to consider the collection as an effective anti-diabetic agent, absolutely non-toxic when used orally.

References

1. Dedov, T.JI. Kuraeva, O.V. Remizov and others. /Genetics of sugar diabetes in children and adolescents: a guide for doctors / I.I. - M., 2003. 72 p.
2. V.N.Bochkov, A.B.Dobrovolsky, N.E. Kushlinsky et al., Clinical biochemistry: textbook / ed. V.A.Tkachuka-3rd ed., GEOTAR, 2008.-p.307
3. Clinical guidelines and pharmacological reference / Ed. I.N.Denisova, Yu.L.Shevchenko, F.G.Nazirov.-M.: GEOTAR-Media, 2005.-S.-328.
4. Simon I. LI-Maghrabi M., Raafat, C. Thomas H. Hormanal regulation of hepatic
5. Ajit Kar 1, B K Choudhary, N G Bandyopadhyay. /Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan diabetic rats. Ethnopharmacol. 2003 Jan;84(1):105-8. doi:10.1016/s0378-8741(02)00144-7. gluconeogenesis and flicolysis.//Ann.Rev.Biochem.-1988.-v.57.-hh.755-783.
6. Mirzaev B.G. Dynamics of gluconeogenesis in the liver in myocardial infarction.// abstract. Candidate diss., Tashkent.1985.-p.21
7. 7.Jamshid Mohammadi. Evolution of hypoglycemic effect of Morus alba in an animal model /Jamshid Mohammadi,Prakash R.Naik//Indian J.of Pharmacology-February 2008.Vol.40.P.15-18
8. Methods of clinical laboratory research: textbook / ed. V.S.Kamyshnikova.-3rd ed., revised. And extra. - M. : MEDpress-inform, 2009. -540s.
9. Pilkis S. Hormonal regulation of hepatic gluconeogenes//Annu. Rev. Bioch.-1988.-v.57.-hh.755-783.