Section A-Research paper

INFLUENCE OF HYPOGLYCEMIC EXTRACT COLLECTION ON GLYCOLYSIS UNDER CONDITIONS OF HYPERGLYCEMIA

Gulchekhra Yu. Malikova – Assistant professor, Department of Toxicological biochemistry, Tashkent Pharmaceutical Institute, 45 Aybek Street, Tashkent, 100015, Uzbekistan
Zumrad U. Usmanaliyeva – Assistant professor, Head of department of the Toxicological biochemistry, Tashkent Pharmaceutical Institute, 45 Aybek Street, Tashkent, 100015, Uzbekistan
Dinara M. Khashirbaeva – Assistant professor, Head of department of the General hygiene, Tashkent Pharmaceutical Institute, 45 Aybek Street, Tashkent, 100015, Uzbekistan
Dilafruz B. Akhmedova - PhD, Department of Normal and pathological physiology, Tashkent Medical Academy, Farabi 2 Tashkent, 100109, Uzbekistan
Khabibulla Kh. Pulatov - PhD, Associate professor, Department of Human anatomy and OXTA, Tashkent Medical Academy, Farabi 2 Tashkent, 100109, Uzbekistan

Abstract
The treatment of hyperglycemia - diabetes mellitus, herbal medicinal substances clearly differ from synthetic chemical preparations in that they have few side effects and can be used for a long time. But since the effect is relatively weak, the possibility of using them at the right time is relatively small. The most oral preparations are mainly xenobiotics, their use is somewhat limited due to side effects. To isolate hypoglycemic substances from medicinal plants, to create effective antidiabetic drugs on their basis by identifying the mechanisms of influence on biochemical processes are given in this article.
Keywords: white mulberry, large plantain, hyperglycemia, hexokinase, oranil.

Introduction

Abu Ali Husayn ibn Abdullah ibn Sina (August 16, 980 - June 18, 1037) wrote works not only on medicine, but also on theology, philosophy, astronomy and the history of religion.

A number of sources mention more than 450 works of Ibn Sina, in which only 242 of them have come down to us. Over 100 herbal products are listed in Ibn Sina's treatise for the treatment of diabetes.

One of the most widely used herbal raw materials in diabetes mellitus are the leaves of the white mulberry (Morus alba) and the greater plantain (Plantago major).

Ibn Sina stated that the raw materials of these plants are highly effective in diabetes, not only when used separately, but also when combined [1].

Unfortunately, diabetes is one of the most important medical and social problems of the modern world. This disease is often accompanied by hyperglycemia, that is, a high level

of glucose in the blood, which in turn causes damage to many body systems. Of course, there are currently effective methods for controlling and treating diseases.

Against this backdrop, there has been significant interest in complementary and alternative medicine in the last decade. Some researchers have found that up to 72.8% of people with diabetes have used herbal medicine and other complementary and alternative medicine methods, and in many cases, medication as traditional supplements.

There are many plant products with antioxidant properties that can reduce the level of oxidative stress, one of the main pathogenetic factors in the development of diabetes [2].

The number of antidiabetic drugs used to treat diabetes is on the rise worldwide. Since most oral preparations are mainly xenobiotics, their use is somewhat limited due to side effects. The most widely used synthetic drugs are biguanides and sulfonylureas, which cause more and more complications [3]. Considering the above, the staff of the Department of Pharmacognosy and Botany of the Tashkent Pharmaceutical Institute created a new hypoglycemic composition based on the raw materials of local medicinal plants - white mulberry leaves (Morus alba) and large plantain (Plantago major), studied its chemical composition and determined quantitative parameters [4]. For the application of this collection in scientific medicine, it is considered desirable to study carbohydrate metabolism.

These days, in the treatment of hyperglycemia - diabetes mellitus, herbal medicinal substances clearly differ from synthetic chemical preparations in that they have few side effects and can be used for a long time. But since the effect is relatively weak, the possibility of using them at the right time is relatively small [5].

Purpose of the research

The purpose of the research is to isolate hypoglycemic substances from medicinal plants, to create effective antidiabetic drugs on their basis by identifying the mechanisms of influence on biochemical processes.

Materials and Methods

The rate of glycolysis increasing is achieved by stimulating glucose uptake and activation of hemokinase, followed by pyruvate oxidation in the Krebs cycle in muscles and some other tissues. In addition, the role of the h-pentose phosphate pathway in skeletal muscle is negligible and does not play a role in energy production. Experiments with fixed glucose have shown that the label is about 70% after several hours of parenteral administration in mice and rats. Glucose is oxidized to carbon dioxide, up to 12% protein, 8% to glycogen, up to 5% lipids, and 5% is found in the urine as various oxidized compounds. Therefore, amino acid biosynthesis is the main pathway for intermediate glucose metabolism in the normal body [7].

In order to determine the nature of changes in carbohydrate and lipid metabolism under the influence of hypoglycemic collection, studies were carried out against the background of the pathology of carbohydrate metabolism when alloxan was administered to intact animals. The experiments were carried out on 6 white mature rats weighing 120-140 g with normal nutrition. Animals were divided into two groups [7]. In the first group of 6 rats, the normal state of carbohydrate-lipid metabolism was studied, and in the second group (6 animals), the parameters studied under conditions of diabetes mellitus were studied. The development of diabetes mellitus was observed with an increase in the level of glucose in the blood of at least 17-20 mmol/l, an increase in water consumption; lose weight. The hypoglycemic compound was taken orally once a day for 1, 3, 7 days at the same dose as the compound extract. The choice of this dose and study time is due to the fact that

pharmacologists studied the effect of the compound at this dose and during this time [6]. During the experiment, the animals were divided into groups, the first - intact, the second - an alloxan-diabetic rat, the third - an alloxan-diabetic animal that received 50 mg/100 g of the plant extract orally and oranil 100 mg/kg. for 7 days. After 7 days, the amount of glucose in the blood of rats, the amount of lactate (lactic acid), pyruvate (pyruvic acid) [7], and the activity of the hexokinase enzyme [8] in the liver and muscle tissues were simultaneously determined. According to the results presented in Table 1, plant extracts induced the activation of the hexokinase enzyme in the liver, without significantly affecting the activity of the enzyme in the muscles.

Results and Discussion

The results of the experiment showed that the extract of plants Morus alba, Plantago major can be used as a hypoglycemic agent in diabetes mellitus.Analyzed the amount of glucose in the blood. Simultaneously with the study of the amount of glucose in the liver and muscle tissues, the activity of hexokinase, the main key enzyme of the glycolysis process, was studied. It has been established that pyruvate, which is the end product of the anaerobic metabolism of carbohydrates in the blood and tissues, has the ability to increase the rate of oxidation and reduce the amount of lactate. The metabolism of pyruvate and lactate, which are the last metabolites of carbohydrate metabolism, was studied in combination with Oranil, a drug belonging to the group of antidiabetic sulfonylurea, in conditions of alloxan diabetes. Sulfonamide preparations, on the one hand, increase the amount of lactate in the blood and tissues by effectively reducing the amount of sugar, and on the other hand, plant extracts reduce lactic acidosis. The combined use of these two drugs, according to the ratio of lactate and pyruvate, also prompted this work, which creates the possibility of their use in tissue energy.

An increase in the rate of glycolysis in muscles and some other tissues is achieved by stimulating glucose uptake and activation of hemokinase, followed by pyruvate oxidation in the Krebs cycle. In addition, the role of the h-pentose phosphate pathway in skeletal muscle is negligible and does not play a role in energy production. Experiments with fixed glucose have shown that the label is about 70% after several hours of parenteral administration in mice and rats. glucose is oxidized to carbon dioxide, 12% to protein, 8% to glycogen, 5% to lipids, and 5% is found in the urine as various oxidized compounds. Therefore, the biosynthesis of amino acids is considered the main pathway for the intermediate metabolism of glucose in the normal body. In conditions of alloxan diabetes, although the amount of glucose in the blood is much higher, there is a sharp decrease in the activity of the enzyme in the liver, which indicates that it occurred as a result of a decrease in the synthesis of hexokinase [9].

Table 1

Influence of the hypoglycemic combined extract on the activity of the hexokinase enzyme in the tissues of the alloxan-diabetic rat (n=6)

Experimental groups	Blood glucose mmol/l	Hexokinase activity (ME)	
		muscles	liver
Intact animals	3.9±0.12	41.0±2.3	284.0±15
Diabetes	17.3±2.0	45.0±2.5	205.0±260
Diabetes+extract	10.4±1.6	39.0±3.7	274.0±130
P	<0.02	>0.2	<0.05
%	-40	-13	34

According to the results of the experiment, the plant extract reduced the amount of sugar in the blood of diabetic rats by forty percent. In the liver and muscles, glycogen is formed from glucose by phosphorylation with the help of the hexokinase enzyme, the amount of glycogen in the liver increases, and in the muscles its amount does not change [9].

Based on the objectives of the study, the activation of the glycolysis process with a combined extract of plants Morus alba, Rlantago major allows the use of the primary metabolite glucose as an energy source in the liver. experiments caused in rats with alloxan-induced diabetes, a significant decrease in insulin production due to alloxan-induced damage to pancreatic β-cells. The metabolism of the pyruvate substrate has also been studied experimentally. At the same time, the activity of pyruvate dehydrogenase, an enzyme closely associated with the coenzyme thiamine pyrophosphate during the oxidation of pyruvate, causes the accumulation of pyruvate, especially lactate, in the tissues of the blood, muscles and liver.

In diabetes mellitus, oranil was administered orally separately and an antidiabetic drug - oranil with the addition of a plant extract. This case was carried out for 7 days, and the amount of pyruvate and lactate in the tissues was studied. According to the results of the experiment, it was noticed that when only the plant extract was introduced, the amount of lactate decreased slightly, the amount of pyruvate increased significantly, and the ratio of lactate to pyruvate was higher than the control level.

Quantitative results of metabolites are presented in Table 2, Table 3 and Table 4.

Table 2

Effect of hypoglycemic combined extract and oranil on the amount of lactate and pyruvate in the blood (n=6)

Indicators	Experiment conditions		
	Diabetes I	Diabetes + oranil II	Diabetes+Oranil+Extract III
In blood			
Lactate, micron/mol/l	2.06±0.30	2.03±0.08	1.88+0.13
Pyruvate, micron / mol / l	0.32±0.06	0.23+0.03	0.31+0.001*
Lactate/pyruvate, micron/mol/l	7:01	9:01	6:01

It has been established that the combined effect of the hypoglycemic extract and oranil is significantly higher than with their joint administration. According to the results of the experiment, the antidiabetic drug oranil itself does not significantly affect the ratio of lactate and pyruvate in the liver tissue. When co-administered with a hypoglycemic pooled extract, a significant increase in lactate in hepatic effusion was observed.

Table 3

The effect of hypoglycemic combined extract and oranil in muscles on the amount of lactate and pyruvate (n=6)

Indicators	Experiment conditions		
	Diabetes I	Diabetes + oranil II	Diabetes+Oranil+Extract III
in the muscles			
Lactate, micron/mol/l	1.90±0.26	3.89±0.21	2.13+0.10
Pyruvate, micron / mol / l	0.65+0.04	0.74±0.02	0.50±0.02*
Lactate/pyruvate, micron/mol/l	3:01	5:1	4:01

Table 4

Effect of hypoglycemic combined extract and oranil in the liver on the amount of lactate and pyruvate (n=6)

Indicators	Experiment conditions		
	Diabetes I	Diabetes + oranil II	Diabetes+Oranil+Extract III
in the liver			
Lactate, micron/mol/l	1.57±0.08	1.51±0.01	0.95±0.01*
Pyruvate, micron / mol / l	0.56±0.02	0.45±0.05	0.51 ±0.02
Lactate/pyruvate, micron/mol/l	3:01	3:01	4:01

Differences between groups I and II; II and III, P<005.

Based on the results of the effect of hypoglycemic compound extract and oranil on lactate and pyruvate in muscle and liver, this fact may be due to two different processes, i.e. the combination of the compound extract and the antidiabetic drug oranil. accelerates glycolysis in the liver tissue or the liver extracts lactate from the blood at a high level.

Under physiological conditions, the transport of glucose to all tissues determines its intracellular metabolism, which is judged by the oxidation of glucose to carbon dioxide. It is clear that transport is the main reaction that limits the rate of glucose utilization by cells, because in the absence of insulin, the flux of transported glucose is always lower than the rate of glucose phosphorylation. The intensity of the main pathways of glucose metabolism depends on the structural and functional features of individual tissues, for example, the highest level of glucose transport is observed in human erythrocytes and in the liver of animals, which is approximately an order of magnitude higher than the corresponding values in other tissues, as a result of which glucose transport in the liver does not limit consumption. Glucose phosphorylation is the limiting reaction of glucose utilization in these tissues.

Regardless of how the above processes proceed, in experiments, the combined extract of the extract with oranil causes a decrease in the amount of lactate in muscle tissue and a slight increase in the amount of pyruvate.

A decrease in the amount of lactate in the cell, on the contrary, such a change in pyruvate in the cell means that its use as an energy source has increased. Based on this, pyruvate determines a number of oxidation-phosphorylation processes in mitochondria.

Acceleration of glucose catabolism - the process of glycolysis, lactate-pyruvate metabolism activates the use of substrates for energy purposes of the body, causes the disappearance of complications of hyperacidemia in diabetic conditions.

The use of herbal extracts in combination with oranil in diabetes has been shown to have a positive effect in this condition.

Conclusion

1. Alloxan significantly lowers blood sugar levels when a hypoglycemic compound is orally administered to diabetic rats.
2. Stimulates the activity of the hexokinase enzyme in the liver tissue.
3. Hypoglycemic pooled blood reduced the amount of lactate in tissues. significantly reduces experimental diabetes.
4. Oranil has been shown to increase the amount of lactate in muscle tissues, as it has the property of reducing the amount of sugar.

References

1. Malikova G.Yu., Juraeva A.A., Tashmatova M.A. Effect of the hypoglycemic compound extract from the works of Ibn Sino on glycolysis in hyperglycemia conditions: International Scientific Practical video conference ABU ALI IBN SINO (AVICENNA): HUMAN HEALTH AND ECOLOGY November 11th, pp.262
2. Dedov, T.JI. Kuraeva, O.V. Remizov et al. / Genetics of diabetes mellitus in children and adolescents: a guide for doctors / I.I. - M., 2003. pp.72.
3. Kim S.M., Turchin I.S., Kim V.S., Burdievskaya L.M. // Medical business. 1987. No. 11-pp. 7-10.
4. N.T. Farmonova, F.F. Urmanov, N.M. Sultanbaeva. Standardization of the new hypoglycemic collection // Farmasevtika jurnali. – Tashkent, 2013.-№1. – 40 – 42
5. Almagambetova N.A., Belovalova I.M., Perelygina A.A. // Prob. endocrine. 1991. V. 37. No. 3. pp. 38-39.
6. Baranov V.G., Sokoloverova I.M., Gasparyan E.G. and others. Experimental diabetes mellitus. L., 1983.
7. Methods of biochemical research / Under. edited by Prokhorova. L.: LGU, 1982. pp.272.
8. Hexokinase test for the diagnosis of gastric cancer and some tumor diseases of the blood system: Method. instruction / S.A. Neifakh. I.F. Sin, N.K. Monakhov, Z.N. Maleev. L., 1969. pp.11.
9. Zhuraeva A.A., Abidov A.A., Babaev T.A. // Kimyo va pharmacy. 1999. No. 1. pp. 31-32.