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Phytocorrection Of Metabolic Disorders In Glucocorticoid Hyperglycemia

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I. INTRODUCTION

Type 2 diabetes is one of the main causes of the development of systemic organ pathology due to severe metabolic abnormalities and is one of the most common and severe pathologies in the modern world, in which the corrected risk factors play a leading role [9,10]. At the same time, risk factors are clearly defined, interrelated and interdependent - an excessive high-calorie diet, leading to excess body weight and a sedentary lifestyle. stressor factor. This "death quartet" triggers the development of irreversible development of systemic organ damage, especially cardiovascular diseases, in the late stages [17,18].. In the early stages, structural disturbances are reversible and the period of the "therapeutic" window avoids fatal violations, provided that the risk factors, especially those of nutritional value, are corrected. Correction of drug disorders in diabetes mellitus is not effective enough, it is associated with the risk of side effects, but their rapid correction in emergency conditions is necessary. The leading role of the food risk factor in the development of metabolic disorders allows the use of non-medicament us methods of correction, changing the structure of everyday nutrition by including functional products of plant origin, forming a habit of a healthy lifestyle. The peculiarities of the food habits of the population of different countries, the inclusion in the daily diet of plant origin, are associated with the possibility of correcting metabolic disorders of the diabetic nature. Experimental studies of models of type 1 and type 2 diabetes confirm the observations of traditional folk medicine [2,3]. Given the contribution of the hormonal factor, it is of interest to study phytopreparations in the modeling of glucocorticosteroid glycaemia as one of the factors of stressful effects with pronounced dismetabolic disorders such as hyperglycemia, dysproteinemia, dyslipidemia with a high risk of developingsteroid diabetes.

II. SUMMARY

Administration of aqueous extracts of herbs Cymbopogon proximus, Acacia nilotica and Trigonella foenumgraecum., Lupinus luteus, Solenostemma argel prevents fasting hyperglycaemia and 2 hours after loading with glucose in rats with dexamethasone hyperglycaemia. High doses of glucocorticosteroids cause damage to hepatocytes, as evidenced by an increase in activity of cytolysis enzymes of ALT by 312.5%. Aquatic extracts of all herbs, except for Acacia nilotica, have a hepatoprotective effect, which is manifested in the correction of the growth of cytolysis enzymes of ALT. More favorable effect on the functional indexes of the kidneys of aqueous extracts of Trigonella foenumgraecum, in the application of which there was no increase in urea and creatinine in the serum, on the contrary, against the background of the introduction of extracts of Acacia nilotica, the increase in urea and creatinine was the maximum of all herbs used, and in combination with high indices ALT, low values of albumins and total protein, these results can be regarded as a consequence of the toxic effect of plant components.

KEY WORDS: dexamethasone hyperglycemia, water extracts of herbs Cymbopogon proximus, Acacia nilotica and Trigonella foenumgraecum., Lupinus luteus, Solenostemma argel.

Goal.

The purpose of this study was to study the pharmacological effects of phytopreparations of various medicinal herbs Cymbopogon proximus, Acacia nilotica and Trigonella foenumgraecum., Lupinus luteus, Solenostemma argel, grown and collected in the Northern Sudan on the model of dexamethasone hyperglycemia in rats.

III. MATERIALS AND METHODS OF RESEARCH

The study was carried out on 40 mature adult albino rats of the Wistar line weighing 25-300 g in spring and summer on the basis of the Vivarium FGBOU VO "National Research Mordovian State University. N.P.Ogaryova ".. The animals were obtained from the nursery" Stolbovaya ", FGBU" Scientific Center for Biomedical Technologies "of RAMS. All experiments, care and maintenance were carried out in accordance with Directive No. 63 of September 22, 2010 of the Presidium and the Parliament of Europe "On the Protection of Animals Used for Scientific Research", "Sanitary Rules for the Device, Equipment and Maintenance of Experimental Biological Clinics of 06.04.1993 and Order of the Ministry of Health of the Russian Federation No. 267 of 19.06.2003 "On approval of the rules of laboratory practice". In accordance with the "Guidelines for experimental (preclinical) study of new pharmacological substances" [2005], the maximum permissible intravenous fluid injection to white non-linear rats is 2.0 ml / kg. Laboratory animals were randomly divided into 8 groups of 5 individuals. Group 1 - intact animals. 2-ydexamethasone 800 μg/kg for 4 days IM, in subsequent series against dexamethasone 800 μg laboratory animals were injected intraperitoneally with 2 ml of water herb extracts at a concentration of 1:10 for 5 days: 3rd aqueous extract of Lupinus luteus, 4th group - gad-gad, 5th group of Trigonella foenumgraecum (seeds), 6th - Cymbopogon proximus, 7th - Acacia nilotica (seeds), 8th - Solenostemma argel. Aqueous extracts were prepared from a powder of dry raw material followed by treatment with an Ultra-Turrax T-18 homogenizer, (Germany) at a speed of 12,000 rpm. Within 5 minutes, centrifuged for 5 minutes in a centrifuge at 3000 rpm, filtered and the supernatant was examined.
On the 5th day of the experiment, a glucose tolerance test was performed, injecting 1 g of glucose as a 40% solution with the study of glucose in capillary blood from the tail vein test with Accu-Chek Active strips. At the end of the experiment, the animals were removed from the experiment by ether anesthesia in a chamber followed by decapitation. Biochemical studies were carried out in the blood serum on an automatic biochemical analyzer of the firm "HUMASTAR 600, Germany". In the serum of rats, the content of total protein, albumins, transaminase activity - ALT, AST, total cholesterol, triglycerides, urea and creatinine was determined by a set of reagents for the analyzer.

The results of the study are processed by statistics using the STATISTICA statistical software package, the statistical indicators are indicated by the following symbols: M - average; m - error of the mean, Pi - difference from the similar index of intact animals; Pc - the difference from the similar index of the control group. To assess the reliability of the difference, the Student's T-test was used. Differences at $p < 0.05$ were considered significant.
Theresults of the study and their discussion

Against the background of dexamethasone injection in rats,fasting hyperglycemia develops, the glucose level exceeds the data of intact animals by 71% (Table 1). The introduction of herbal extracts Lupinus luteus, Gad-Gad, Solenostemma argel and Cymbopogon proximus prevents the development of fasting hyperglycaemia. The extracts of Acacia nilotica do not correct the increase in blood glucose. One hour after loading with glucose, the level of glycemia increased in 162% in intact rats, in the control series by 202%, in batches with herb extracts by an average of 200% compared to intact fter 2 hours of glucose tolerance test in intact rats, the indices exceeded initial values by 73%, in control with dexamethasone by 179%, against the background of application of Lupinus luteus by 80%, Gad-Gad and Solenostemma argel did not differ from intact animals. Extracts of Lupinus luteus, Cymbopogon proximus, Acacia nilotica and Trigonella foenumgraecum corrected glycemia in 2 hours by 44% compared with the data from the control series. Thus, two phytocompositions Gad-Gad and Solenostemma argel completely corrected hyperglycemia according to the glucose tolerance test.

The introduction of dexamethasone causes systemic metabolic shifts in the body, presented in Table 2. A tendency has been found to increase the total serum protein. Against the backdrop of the introduction of aqueous extracts, this trend persisted, with the exception of the series with Acacia nilotica, where the total protein values were below intact by 15%. Dexamethasone stimulates the albumin-synthetical function of the liver, as evidenced by an increase in the values of this indicator by 29.52% compared to intact animals. This trend persists in all the series with extracts of herbs, except forAcacia nilotica, in which the serum albumin levels remain intact and below the control by 22%. Against the background of the introduction of Trigonella foenumgraecum, Acacia nilotica Solenostemma argel, an increase in total serum cholesterol was found to be 172% -182% compared to intact animals. Aqueous extracts of Lupinus luteus and Cymbopogon proximus increase the serum cholesterol values by 152% and 114% to the data of intact animals. The lowest values of cholesterol were revealed when using water extracts Gad-gad.The growth of triglycerides of blood serum with the introduction of herbs such as Gad-gad - by 143%, Acacia nilotica - 176%. Water extracts of Trigonella foenumgraecum, Lupinus luteus, Solenostemma argel and Cymbopogon proximus correct the development of hypertriglyceridemia in the glucocorticoid load. Thus, the maximum increase in the level of triglycerides was detected with the introduction of aqueous extracts of Acacia nilotica.

High doses of glucocorticosteroids cause damage to hepatocytes, as evidenced by an increase in activity of cytolysis enzymes of ALT by 312.5%. Extracts of Lupinus luteus correct the cytotoxic effect of high doses of dexamethasone while maintaining ALT values at the level of intact animals (Table 2.). A similar effect is exhibited by extracts of Solenostemma argel and Gad-gad, against which the growth of ALT activity was minimal - by 24% with respect to intact animals. Hepatotoprotective activity of extracts of Trigonella foenumgraecum and Cymbopogon proximus is somewhat less pronounced, however it remained at a sufficiently high level in comparison with the control group. Acacia nilotica did not limit the growth of cytolysis enzyme activity.

High doses of dexamethasone have a cardiotoxic effect, as evidenced by an increase in the activity of the enzyme AST by 46% of the values of intact animals. Phytoextracts of all used herbs do not correct the growth of activity of this enzyme. Introduction Acacia nilotica increases the values of this indicator to 93%.from the values of intact animals.

Extracts of plants increase the level of urea in the serum of Acacia nilotica by 177%, Lupinus luteus by 146%, Cymbopogon proximum by 135%, Gad-gad. - by 67%, from the initial values, Solenoste-mma argel- by 82%, Trigonella foenumgraecum does not change the values of this indicator.

Creatinine values increase in all series, maximally by 67% against the background of Acacia nilotica, with the appA study of the pharmacological effects of the grasses studied by us is devoted to the work of many authors who are unanimous in confirming the positive metabolic effects of Acacia nilotica. Acacia nilotica lowered the systemic load of glucose in diabetic mice, reduced (35%) insulin resistance without any significant effect on insulin sensitivity. The antihyperglycemic properties of Acacia nilotica were manifested by a decrease in HbA1c) and improved glucose use. Extracts corrected the development of pathological complications of alloxan diabetes - hepato- and nephrotoxicity. The drug prevented the development of oxidative stress by increasing the activity of catalase and peroxidase in the liver, kidneys and skeletal muscles, which resulted in a 32% reduction in MDA levels in serum [12,13].

Aqueous extract of the A. nilotica crust bark contains tannins, complete phenols, flavonoids, saponins and alkaloids. In aqueous extracts of the A. nilotica cortex, sodium, chloride, potassium, calcium, titanium, vanadium, chromium, manganese, iron, copper, zinc, arsenic, nickel, lead and cadmium. It was found that condensed tannins isolated from selected Kenyan products exhibit antidiabetic activity by inhibiting the enzymes α-amylase and α-glucosidase [10,11]. In addition, commercially available tannic acid was found to induce phosphorylation of the insulin receptor (IR) and cause the translocation of glucose transporter 4 (GLUT 4) [10,11].

Trigonella foenum-graecum L.Fenugreek fenugreek - one of the oldest medicinal plants originating from India and North Africa [9]. Experimental studies in animals suggest possible hypoglycemic and anti-hyperlipidemic properties of fenugreek seed powder. Mucilagin fiber, present in fenugreek seeds, can bind bile acids, which reduces the level of cholesterol and lipids in the blood. The vegetable protein in fenugreek can exert a diminishing effect on lipids. Steroid saponins, alkaloids and 4-hydroxyisoleucine can promote glucose metabolism and inhibit the absorption of cholesterol. In addition, some chemical components of fenugreek can directly stimulate the secretion of insulin from B cells, leading to a decrease in blood sugar levels. These cardioprotective effects are explained by its modulating effect on blood lipid levels and antioxidant properties [2,3,4,6].

In the Arab countries, Saudi Arabia and Iraq [2,4,6] fenugreek has been recognized as one of the most common herbs used among people with diabetes. Studies in animals suggest hypoglycemic effects of fenugreek [4,6]. The antidiabetic effect of fenugreek is due to the formation of a colloid in the stomach and intestines due to hydration and swelling of the mucilaginous seeds, which slows the absorption of glucose from the gastrointestinal tract [17].

The antilipidemic effects of fenugreek were caused by the inhibition of cholesterol absorption in the intestine due to the formation of a saponin-cholesterol complex, an increase in bile loss through fecal excretion due to saponin-bile complexes, thereby increasing cholesterol in the bile of the liver [5]. The insulinotropic action of fenugreek is due to the discovery in the seeds of the new amino acid 4-idroxyleucine [14].

IV. THE CONCLUSION

Thus, the administration of high doses of dexamethasone 800 μg / kg promotes the development of hyperglycemia and impaired glucose tolerance in rats. The introduction of aqueous extracts of the studied herbs prevents the development of hyperglycemia and normalizes the TSH values, in addition to the extracts of Acacia nilotica. A high level of glucocorticosteroids has a stimulating effect on the parameters of total protein and albumins, as a consequence, a possible increase in the antitoxic function of the liver. All studied herbs, except for Acacia nilotica, retain the positive effects of corticosteroids. Interest in the phenomenon of growth in the values of total cholesterol and especially triglycerides against the background of the application of herbs, the most pronounced with the use of Acacia nilotica and Gad-gad, which is probably due to the specificity of their chemical composition. The hepatoprotective effect of water extracts of all herbs, except for Acia nilotica, is unambiguously positive. which

is manifested in the correction of growth of cytolysis enzymes ALT. As a positive, we can also consider the growth of urea function of the liver, which characterizes the stimulation of liver function against the background of excessively catabolic effect of corticosteroids. The increase in the level of creatinine is hardly worth considering as a factor of nephrotoxicity, but rather as a phenomenon of accelerating the inactivation of catabolism products against the background of systemic effects of corticosteroids. It should be noted a more favorable effect on the renal functional indexes of the aqueous extracts of Trigonella foenumgraecum, with the use of which there was no increase in urea and creatinine in the blood serum; on the contrary, with the introduction of Acacia nilotic extracts, the increase in urea and creatinine was the largest of all herbs used, and in combination with high ALT, low values of albumins and total protein, these results can be regarded as a consequence of the toxic effect of plant components.

Contribution of authors:
Inchin VI - the author of the idea, the organization of the experiment.
Abdalhamid_Huseyn MA - providing phytopreparations, preparing extracts, conducting experiments,
conducting laboratory studies. statistical processing of data
Conflict of interest: the authors declare that there are no obvious and potential conflicts of interest related to the publication of this article.

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Table 1

Test for glucose tolerance in white laboratory rats against the background of dexamethasone 800 µg/kg IM for 4 days, corrected with water extracts of herbs in a concentration of 1:10 in a volume of 2 ml intra peritoneum from the first day of Dexamethasone (M±м)

№	Series of experiments	Fasting	After 1 hour	After 2 hours
1	Intact	4,9±4,93	12,88±2,65	1 28,66±12,58
2	Control (Dexamethasone 800 µg/kg	8,4 ±1,57	25,68±6,04 Pi<0,001	24,17±3,91 Pi<0,001
3	Dexamethasone 800µg/kg + Tromus grassLupinus luteus	5,26 ±1,87 Pi>0,05 Pc<0,001	21,3±5,51 Pi<0,01 Pc>0,05	15,64 ±4,46 Pi<0,001 Pc<0,01
4	Dexamethasone 800 µg/kg + Gad- Gad	4,76 ±1,06 Pi>0,05 Pc<0,001	24,44 ±6,29 Pi<0,001 Pc>0,05	9,6 ±3,05 Pi<0,001 Pc<0,001
5	Dexamethasone800µg/kg + hargal Solenostemma argel	5,05 ±0,144 Pi>0,05	20,42 ±6,46 Pi<0,001 Pc>0,05	7,95 ±0,74 Pi>0,05 Pc<0,001
6	Dexamethasone800 µg/kg + Cymbopogon proximus lemon grass	5,13±-1,16 Pi>0,05 Pc<0,001	21,69 ±10,18 Pi>0,05 Pc>0,05	13,59 ±5,00 Pi<0,01 Pc<0,01
7	Dexamethasone800µg/kg + Acacianilotica	12,04 ±2,54Pi<0,05	25,6 ±5,19 Pi<0,001 Pc>0,05	11,2 ±3,81Pi<0,03 Pc<0,001
8	Dexamethasone 800µg/kg + bread Trigonellafoenumgraecum	6,65 ± 0,49 Pi<0,01 Pc<0,03	25,6 ±6,4 Pi<0,001 Pc>0,05	15,2 ±1,82 Pi<0,001 Pc<0,01

The reliability of the difference in Pi is determined with respect to the indicates of intact, Pc- control animals

The values of some biochemical parameters of blood serum of white rats against the background of 800 µg/kg of Dexamethasone for 5 days and water extracts of the studied herbs in a concentration of 1:10

N	Indicator	Intact	Control Dexamethasone 800 µg/kg	Dexamethasone +Lupinus luteus	Dexamethasone + Gad-gad	Dexamethasone+ Trigonella foenumgraecum	DexamthasoneCymbopogon proximum	Dexamethasone + Acacianilotica	Dexamethasone +Solenoste-mmargel
1	Total Protein,g/l	66,4±4.	71±7,1 Pi>0,05	68±8,2 Pi>0,05 Pc>0,0	65,75±2,62 Pi>0,05 Pc>0,05	72,25±4,64Pi>0,05 Pc>0,05	65,4±3,20Pi>0,05 Pc>0,05	57,14±,5,0Pi<0,05 Pc<0,007	71,5±8,22Pi>0,05 Pc>0,05
2	Albumin, g/l	34,6±	44,8±3,96Pi<0,001	41,5±5,80 Pi<0,002 Pc>0,34	44±0,81 Pi<0,001 Pc>0,05	42,5±1,73 Pi<0,001 Pc>0,05	44,8±2,77 Pi<0,001 p_c>0,05	35±3,25 p_c>0,05 Pc<0,001	43,25±1,89 Pi<0,001 Pc>0,05
3	Total cholesterol, mm/l	0,68±0,08	1,14±0,49Pi>0,05	1,72±0,62Pi<0,04 Pc>0,05	0,95±0,36Pi>0,05 Pc>0,05	1,85±0,20 Pi<0,002 Pc<0,001	1,46±0,27Pi<0,05 Pc>0,05	1,91±0,35 Pi<0,002 Pc<0,001	1,92±0,52 Pi<0,01 Pc<0,02
4.	Triglycerides, mm/l	0,69±0,16	0,84±0,36Pi<0,001	0,89±0,07Pi>0,05Pc>0,05	1,685±0,61Pi<0,001 Pc<0,001	0,89±0,01Pi>0,05 Pc>0,05	0,98±0,17Pi<0,001Pc>0,05	1,94±0,43Pi<0,001Pc<0,001	0,91±0,14Pi<0,001Pc>0,05
5.	ALT, unit	55,8±7,12	230,4±93,81 Pi<0,001	62±7,78 Pi>0,05 Pc>0,05	77,5±1,73Pi<0,001 Pc<0,001	93,4±12,26Pi<0,001 Pc<0,001	105,4±12,58Pi<0,001 p_c<0,001	164,5±38,82 Pi<0,001 Pc>0,05	71,25±9,39Pi>0,05 p_c<0,001
6	AST, unit	165,83±14,2	242,2±38,23 Pi<0,001	256,25±13,91Pi<0,001 Pc>0,05	270,75±41,27Pi<0,001 Pc>0,05	243,2±47,98Pi<0,001Pc>0,05	261,2±39,76Pi<0,001Pc>0,05	320,28±35,19 Pi<0,001 Pi<0,001	260,25±32,25Pi<0,001Pc>0,05
7	Urea, mm/l	4,92±1,1	6,06±0,77 Pi>0,05	12,15±3,01Pi<0,001Pi<0,001	8,25±1,88Pi<0,001Pc>0,05	5,32±0,93Pi<0,001 Pi<0,001	11,58±0,91Pi<0,001 Pi<0,001	13,67±3,8 Pi<0,001 Pi<0,001	9,125±2,31Pi<0,05 Pc<0,001
8.	Ccreatinine, mg/dl	0,053±0,001	0,056±0,007Pi>0,05	0,076±0,01Pi<0,001Pi<0,001	0,073±0,01Pi<0,01 Pi<0,01	0,06±0,01Pi>0,05 Pc>0,05	0,080±0,004Pi>0,05 Pi<0,01	0,09±0,04Pi<0,01Pc<0,05	0,089±0,02Pi<0,01 Pi<0,01

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