УДК 615.451.1.074:615.322-06:616.379-008.64:615.357.099]-092.9
DOI 10.11603/mcch.2410-681X.2021.i2.12233

A. I. Dub, I. M. Klishch, L. V. Vronska, I. P. Stechyshyn
I. HORBACHEVSKY TERNOPIL NATIONAL MEDICAL UNIVERSITY

STUDY OF THE SPECIFIC ACTIVITY OF THE PHYTOCOMPOSITION ON THE DEXAMETHASONE-INDUCED INSULIN RESISTANCE

Introduction. *Type 2 diabetes mellitus (DM2) has recently become an epidemic in the population. There are approximately 463 million patients in the world, and according to experts from the International Diabetes Federation, it is expected to increase to 700 million people by 2045, of which more than 90 % will fall on DM2. Despite the significant progress made in studying the pathogenesis of DM, the presence of a wide range of antidiabetic drugs, diabetes remains an acute medical and social problem.*

The aim of the study *– to investigate the specific activity of the phytocomposition, which contains dry extracts of white mulberry leaves (Morus alba L.), common beans shells (Phaseolus vulgaris L.), bilberry sprouts (Vaccinium myrtillus L.) in the experimental model of insulin resistance caused by dexamethasone injections.*

Research Methods. *The experiments were performed on male rats aged three months and weight (200±20) g. Experimental animals were divided into the following groups: negative and positive control, two reference groups, which received Arfazetin and metformin respectively, and experimental group, which received phytocomposition. Insulin resistance was modeled by intramuscular administration of glucocorticosteroid dexamethasone (0.125 mg/kg daily for 13 days in the morning). The state of glucose homeostasis was assessed by changes in basal glycemia and under oral glucose tolerance test, short insulin and adrenalin test. Functional glycemic coefficients were also calculated. Statistical processing was performed using computer programs IBM SPSS Statistics v.10.1 and MS Excel 2010.*

Results and Discussion. *Basal glycemia after modeling insulin resistance in the experimental group, which received the phytocomposition, was significantly lower by 19.0 % from the positive control group and did not differ from the activity of metformin. During the oral glucose tolerance test, the phytocomposition significantly inhibited the growth of glycemia in all studied periods relative to the indicators of the positive control group. Functional glycemic coefficients, which were obtained based on test data, did not exceed the norm. Insulin sensitivity under the influence of phytomedicine increased by 16.2 % above the positive control group, indicating inhibition of insulin resistance development under its influence. The studied phytocomposition inhibited the development of adrenaline glycemia by 42.9, 70.2 % after 30 and 90 min, respectively, relative to the positive control group, which corresponds to the indicators of the negative control group and reference group, which received Arfazetin, but this decrease is not enough to exceed the effect of metformin.*

Conclusions. *The obtained results indicate that the studied phytocomposition inhibits the development of insulin resistance and carbohydrate tolerance in the conditions of insulin resistance caused by the introduction of dexamethasone.*

KEY WORDS: **diabetes mellitus; insulin resistance; hypoglycemic activity; white mulberry; common bean; bilberry.**

INTRODUCTION. Type 2 diabetes mellitus (DM2) has recently become an epidemic in the population. There are approximately 463 million patients in the world, and according to experts from the International Diabetes Federation, it is expected to increase to 700 million people by 2045, of which more than 90 % will fall on DM2 [1]. Progressive hyperglycemia, which develops in patients with DM, stimulates various glycolysis-dependent pathological pathways, potentially contributes to tissue damage. Causing destruction of pancreatic cells, reduced insulin synthesis, and secretion, reduces insulin sensitivity of peripheral head tissues, and causes the development of complications of DM. The combination of insulin resistance (IR) and hyperinsulinemia is the starting point for many metabolic disorders [2].

The goal of treating patients with DM2 is to achieve the maximum reduction of the total risk of complications by achieving and maintaining the target level of metabolic parameters [3]. Traditional tactics for the treatment of DM2 involve a gradual transition from diet therapy and lifestyle changes to drug therapy, which, in turn, necessarily involves the use of antidiabetic drugs (oral drugs or insulin)

[2]. However, in DM of both types, an important role is played by the prescription of drugs, which is directly aimed at correcting metabolic processes. Without diminishing the role of synthetic drugs, it should be noted that plants have polyvalent properties, mild but at the same time long-lasting. Today, herbal medicine is becoming an essential part of the treatment of patients with DM. It can be used for certain types and stages of the disease as monotherapy combined with diet therapy and adjunctive therapy, given the importance of preventing complications in DM – in combination with antihyperglycemic agents and insulin [4].

Despite the significant progress made in studying the pathogenesis of DM, the presence of a wide range of antidiabetic drugs, diabetes remains an acute medical and social problem. Therefore, based on the above, the search for new herbal medicines that could be used with dignity in medical practice remains relevant.

Several promising plants were selected to create a phytocomposition, namely white mulberry, beans, and bilberry, the hypoglycemic and hypolipidemic properties confirmed in previous studies [5, 6].

The aim of the study – to investigate the specific activity of the phytocomposition, which contains dry extracts of white mulberry leaves (*Morus alba* L.), common beans shells (*Phaseolus vulgaris* L.), bilberry sprouts (*Vaccinium myrtillus* L.) in the experimental model of insulin resistance caused by dexamethasone injections.

RESEARCH METHODS. The experiments were performed on male rats aged three months and weight (200±20) g with normal carbohydrate homeostasis, which was assessed by basal glycemia.

Experimental animals were divided into the following groups:

1–2 – Negative control (NC) (n = 8), Positive control (PC) (n = 10) – received an equivalent amount of distilled water as a placebo.

3–4 – Reference group, that received infusion of the plant collection Arfazetin (n=10) (12 ml/kg) ("Liktravy", Ukraine) and a suspension of synthetic hypoglycemic agent metformin (n=10) (150 mg/kg) ("Diaformin", "Farmak", Ukraine). Doses were calculated according to the instructions for the drugs use, taking into account the coefficient of species endurance according to Yu. Yu. Rybolovliev [7].

5 – Experimental group (n = 10) – received phytocomposition at a dosage of 100 mg/kg based on a dry extract of white mulberry leaves, which was experimentally determined in previous studies [8].

Oral administration of distilled water, Arfazetin infusion, metformin suspension, and an aqueous solution of phytocomposition were performed intragastrically through a thin metal atraumatic probe simultaneously with dexamethasone injections.

Insulin resistance (IR) was modeled by intramuscular administration to rats of groups 2–5 of glucocorticosteroid dexamethasone ("KRKA Ukraine", Slovenia) at a dose of 0.125 mg/kg daily for 13 days in the morning. This regimen in young rats leads to the development of glucose intolerance, IR, and hyperinsulinemia, but unlike older rats does not cause changes in basal glycemia, i.e., reproduces the state of prediabetes [8].

Blood for research was obtained from the tail vein of rats by distal resection of the tail. The concentration of glucose in the blood was determined by the biosensor electrochemical method (using test strips, glucometer "Accu-Chek Performa Nano" ("Roche Diagnostics", Germany)). The glucose level in the blood was determined on an empty stomach to avoid the effect of food on the absorption of the studied drugs and expressed in absolute and relative values. The first determination was performed before the start of the experiment, and the second was after inducing the IR and introducing appropriate solutions. The state of glucose homeostasis was assessed by changes in basal glycemia, using an oral glucose tolerance test (OGTT) and a short insulin test.

Under OGTT [7], all groups of animals were subjected to "glucose load" by intragastric administration of 40 % glucose solution (based on glucose 3 g/kg body weight). After 30, 60, 90, 120, and 180 min, the blood glucose level of all groups' animals was determined [5].

Functional glycemic coefficients were also calculated, which is considered to be no less important than detecting the dynamics of changes in glucose concentration after its introduction [9–11]:

Hyperglycemic Baudouin's coefficient (BC) – the ratio of glucose levels after 60 min to basal glycemia; normally less than 1.7;

Postglycemic (hypoglycemic) Rafalsky's coefficient (RC) – the ratio of the patient's blood glucose level after 120 minutes to basal glycemia); normally less than 1.3;

Sokolnikov's coefficient (SC) – the ratio of the difference between the maximum and basal to the difference between the maximum and minimum glycemia; normally less than or equal to 1.0.

The sensitivity of peripheral tissues to the action of insulin was studied in the short insulin test, the result of which was presented as the insulin sensitivity coefficient, which shows the percentage reduction in glycemia 30 min after intraperitoneal administration of exogenous insulin (1 MU/kg body weight, "Actrapid" "Novo Nordisk", Denmark)) regarding basal glycemia (after night fasting) [7].

The state of carbohydrate reserves in the body was assessed by the degree and rate of rising of the glycemic curve in the adrenaline test by intramuscular injection of 0.18 % solution of adrenaline hydrotartrate a dose of 0.5 mg/kg (based on adrenaline hydrochloride). After 30 and 90 minutes, the blood glucose concentration was determined [12–13].

All manipulations were carried out following the general ethical principles of animal experiments, regulated by the provisions of the European Convention for the Protection of Vertebrate Animals Used for Experimental and other Scientific Purposes (European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes, Strasbourg, 1986, as amended, 1998) and the Law of Ukraine "On the Protection of Animals against Cruel Treatment" (No. 1759-VI of December 15, 2009) and the EU Directive 2010/10/63 EU on animal experiments.

Statistical processing of the results was performed by methods of variation statistics using Mann-Whitney U-test and Student's test using computer programs IBM SPSS Statistics v.10.1, and MS Excel 2010 and presented as comparative tables with the results of different groups. To assess the probability of the obtained results took the significance level $p \leq 0.05$.

RESULTS AND DISCUSSION. Before starting IR modeling, basal glycemia of different groups did not differ significantly (Table 1). Still, after 13 days of dexamethasone administration, it is possible to notice its growth in the PC group by 27.6 %, in the reference group, which received Arfazetin and metformin – by 12.8 and 6.4 %, respectively.

In the experimental group, which received phytocomposition, fasting glucose concentration increased by 8.6 %, significantly lower by 19.0 % than the PC group. However, according to modern criteria for the diagnosis of DM [14], the rate of basal glycemia in venous blood is – 4.0–6.1 mmol/l, which does not indicate the development of carbohydrate metabolism in groups 2–5, which were administered dexamethasone.

Carbohydrate tolerance tests allow correctly assessing the therapeutic effect of the compound on glucose utilization, which is especially important in the absence of a significant impact on basal glucose blood levels [7].

It is known that the "glucose load" test (OTTG) since 1999 is considered the "gold standard" for the diagnosis of not only DM but also the detection of carbohydrate metabolism disorders [15].

During the OTTG, the following data were obtained, presented in Table 2.

In the analysis of the obtained values (Table 2), it was taken into account that the first rise in glucose levels after oral administration reflects the strength of the reflex stimulation of the sympathetic nerves, which occurs when glucose enters the gastrointestinal tract. Thus, in healthy individuals, 15–20 minutes after glucose intake, there is an increase in blood glucose concentration, which reaches its maximum up to 60 min, which is associated with the rate of carbohydrate absorption (determined, in particular, the condition of the intestinal wall) and liver function [9–10]. After that, the glucose level begins to fall, and up to 120 minutes of observation, the blood glucose concentration should be below 7.8 mmol/l (for capillary blood) and 6.7 mmol/l (for venous blood) [14, 16], and after 150–180 min

Table 1 – **The changes in basal glycemia before and after inducing insulin resistance**

Experimental group	The basal glycemia, mmol/l	
	Before the injection	After the injection
Negative control (NC)	4.71±0.19	4.50±0.15
Positive control (PC)	4.65±0.09	5.91±0.10
	$p_1>0.10$	$p_1\leq0,001$
Reference group (Arfazetin)	4.73±0.15	5.32±0.13
	$p_1>0.10$	$p_1\leq0.001$
	$p_2>0.10$	$p_2\leq0.01$
Reference group (Metformin)	4.70±0.10	5.00±0.11
	$p_1>0.10$	$p_1\leq0.05$
	$p_2>0.10$	$p_2\leq0.001$
Experimental group (Phytocomposition)	4.64±0.0	5.03±0.08
	$p_1>0.10$	$p_1\leq0.01$
	$p_2>0.10$	$p_2\leq0.001$
	$p_3>0.10$	$p_3\leq0.10$
	$p_4>0.10$	$p_4>0.10$

Note. p_1 – significantly relative to the NC group;
p_2 – significantly relative to the PC group;
p_3 – significantly relative to the reference group (Arfazetin);
p_4 – significantly relative to the reference group (Metformin).

Table 2 – **The results of oral glucose tolerance test (OGTT)**

Experimental group	The basal glycemia, mmol/l	The blood glucose concentration, mmol/l				
		after 30 min	after 60 min	after 90 min	after 120 min	after 180 min
Negative control (NC)	4.5±0.15	6.68±0.21	7.03±0.18	6.30±0.17	5.59±0.12	4.44±0.08
Positive control (PC)	5.91±0.10 $p_1 \leq 0.001$	10.54±0.12 $p_1 \leq 0.001$	10.82±0.16 $p_1 \leq 0.001$	9.82±0.10 $p_1 \leq 0.001$	8.64±0.11 $p_1 \leq 0.001$	6.32±0.06 $p_1 \leq 0.001$
Reference group (Arfazetin)	5.32±0.13 $p_1 \leq 0.001$ $p_2 \leq 0.01$	8.90±0.18 $p_1 \leq 0.001$ $p_2 \leq 0.001$	9.32±0.12 $p_1 \leq 0.001$ $p_2 \leq 0.001$	8.09±0.14 $p_1 \leq 0.001$ $p_2 \leq 0.001$	7.07±0.17 $p_1 \leq 0.001$ $p_2 \leq 0.001$	5.29±0.10 $p_1 \leq 0.001$ $p_2 \leq 0.001$
Reference group (Metformin)	5.00±0.11 $p_1 \leq 0.05$ $p_{2\leq} 0.001$	7.68±0.10 $p_1 \leq 0.001$ $p_2 \leq 0.001$	7.99±0.10 $p_1 \leq 0.001$ $p_2 \leq 0.001$	7.34±0.09 $p_1 \leq 0.001$ $p_2 \leq 0.001$	6.44±0.07 $p_1 \leq 0.001$ $p_2 \leq 0.001$	5.07±0.08 $p_1 \leq 0.001$ $p_2 \leq 0.001$
Experimental group (Phytocomposition)	5.03±0.08 $p_1 \leq 0.01$ $p_2 \leq 0.001$ $p_3 \leq 0.10$ $p_4 > 0.10$	7.90±0.17 $p_1 \leq 0.001$ $p_2 \leq 0.001$ $p_3 \leq 0.001$ $p_4 > 0.10$	7.96±0.11 $p_1 \leq 0.001$ $p_2 \leq 0.001$ $p_3 \leq 0.001$ $p_4 > 0.10$	7.02±0.11 $p_1 \leq 0.01$ $p_2 \leq 0.001$ $p_3 \leq 0.001$ $p_4 \leq 0.05$	6.41±0.13 $p_1 \leq 0.001$ $p_2 \leq 0.001$ $p_3 \leq 0.01$ $p_4 > 0.10$	4.99±0.04 $p_1 \leq 0.001$ $p_2 \leq 0.001$ $p_3 \leq 0.05$ $p_4 > 0.10$

Note. p_1 – significantly relative to the NC group;
p_2 – significantly relative to the PC group;
p_3 – significantly relative to the reference group (Arfazetin);
p_4 – significantly relative to the reference group (Metformin).

should return to the initial level, or below [17]. This segment of the curve (after 60 min) is called the hypoglycemic phase and reflects insulin production, and mainly depends on the functional state of the parasympathetic nervous system and the pancreas function. [10–11].

Thus, in the NC group, the glucose concentration increased by 48.6, 56.6, 40.4, and 24.6 % after 30, 60, 90, and 120 min, respectively, on an empty stomach and returned to baseline to 180 min. On the other hand, in the PC group, blood glucose levels increased by 78.6, 83.3, 66.5, and 46.5 % after 30, 60, 90, and 120 min, respectively, and were 7.1 % higher by 180 min relative to basal glycemia, which is significantly higher than the indicators of the NC group in all studied time intervals. Therefore, guided by the criteria for the diagnosis of DM 2 according to [15] the results of OGTT, it is possible to interpret the impaired glucose tolerance (prediabetes) in the PC group.

The introduction of the reference drug "Arfazetin" restrained the increase in glycemia by 10.9, 7.5, 13.7, 13.1 % after 30, 60, 90, 120 minutes relative to the PC group and returned to baseline by 180 minutes. However, analyzing the absolute values, the blood glucose level for 120 min was high, which according to [14], is interpreted as impaired glucose tolerance (prediabetes) due to the effect of this drug is not enough to curb the development of glycemia in experimental diabetes.

According to [14] the first-line drug for treating patients with DM 2 and overweight is metformin, which remains the most studied in terms of efficacy and safety of monotherapy. Under OGTT in the group, which received metformin, the following results were obtained: the glycemia after 30, 60, 90, 120 min was significantly lower by 24.4, 22.8, 19.0, 17.3 %, respectively, than the PC group and did not differ from the indicators of the NC group.

In the experimental group, which received phytocomposition, the glucose concentration was lower than the PC group by 21.4, 24.8, 26.7, 18.9, 7.8 % after 30, 60, 90, 120, and 180 min, respectively, which significantly exceeded the effect "Arfazetin" for 30, 60, 90 min, and did not significantly differ from the indicators of the NC group and the reference group, which received metformin, at all studied periods.

Based on OGTT results, glycemic coefficients were calculated, which are used to interpret glycemic curves and are presented in Figure.

After analyzing the coefficients, it can be seen that in the PC group Baudouin's and Rafalsky's coefficients exceeded the norm. Also, it was found that the same coefficients exceeded the norm in the reference group, which received Arfazetin, which indicates inadequate absorption of glucose from the intestine and insufficient release of insulin in response to "glucose load" [10–11]. The same indicators corresponded to the norm in the reference group, which received metformin and experimental group, which received phytocomposition. Sokolnikov's coefficient, which reflects a violation of the relationship between glucose resorption and utilization, indicates insufficient insulin release and confirms the lack of an adequate hypoglycemic phase [10–11].

Short insulin test allows assessing the sensitivity of both the liver and peripheral tissues to the action of insulin, given the inhibition of glucose production in the liver and increased utilization of glucose by muscle due to the effect of the hormone

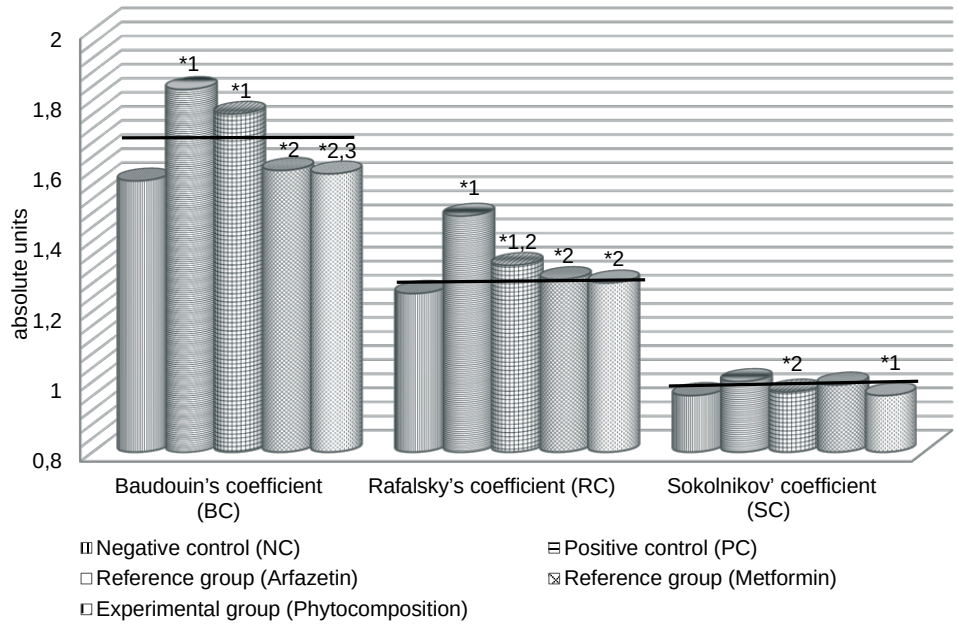

Figure. Functional glycemic coefficients obtained from oral glucose tolerance test (OGTT).
Note. The line marks the upper limit of the norm for each coefficients.
* 1 – significantly relative to the NC group;
* 2 – significantly relative to the PC group;
* 3 – significantly relative to the reference group (Arfazetin);
* 4 – significantly relative to the reference group (Metformin).

[7]. The test (Table 3) revealed a significant decrease in insulin sensitivity by 23.0 % in the PC group relative to the NC group, which confirms IR development. In the reference groups, which received Arfazetin and metformin, insulin sensitivity significantly increased by 8.2 and 11.4 % respectively, relative to the PC group.

In the experimental group, which received phytocomposition, the insulin sensitivity coefficient was 45.7 %, which is 16.2 % higher than in the PC group, significantly higher than the indicator in the reference group, which received Arfazetin, and did not differ statistically from the reference group, which received metformin and NC group. This indicates inhibition of IR development under the influence of phytocomposition at the level of the effect of metformin.

The last stage of research was to study the effect of phytocomposition on the development of adrenaline hyperglycemia, which is to activate

Table 3 – **The results of short insulin test**

Experimental group	The basal glycemia, mmol/l	The blood glucose concentration after 30 min, mmol/l
Negative control (NC)	4.78±0.08	2.26±0.07
Positive control (PC)	5.98±0.08 $p_1 \leq 0.001$	4.21±0.16 $p_1 \leq 0.001$
Reference group (Arfazetin)	5.23±0.10 $p_1 \leq 0.01$ $p_2 \leq 0.001$	3.25±0.09 $p_1 \leq 0.001$ $p_2 \leq 0.001$
Reference group (Metformin)	5.36±0.11 $p_1 \leq 0.001$ $p_2 \leq 0.001$	3,17±0.18 $p_1 \leq 0.001$ $p_2 \leq 0.001$
Experimental group (Phytocomposition)	5.12±0.09 $p_1 \leq 0.05$ $p_2 \leq 0.001$ $p_3 > 0.10$ $p_4 > 0.10$	2,77±0.11 $p_1 \leq 0.01$ $p_2 \leq 0.001$ $p_3 \leq 0.01$ $p_4 \leq 0.10$

Note. p_1 – significantly relative to the NC group;
p_2 – significantly relative to the PC group;
p_3 – significantly relative to the reference group (Arfazetin);
p_4 – significantly relative to the reference group (Metformin).

under its influence glycogenolysis in the liver. The degree and rate of rising of the glycemic curve after adrenaline injection characterize the state of carbohydrate reserves in the body and can be used as an indicator of impaired carbohydrate metabolism [7, 13]. The results of adrenaline test are presented in Table 4.

The concentration of glucose in the blood in the NC group increased by 46.8 and 81.7 % after 30 and 90 min after the introduction of adrenaline relative to basal glycemia. On the contrary, in the PC group, there was a statistically more significant increase in glycemia compared with NC group by 50.3 and 75.9 %, which indicates a substantial increase in sensitivity to the stimulating effect of adrenaline on gluconeogenesis in induced IR and once again confirms the profound deviations in carbohydrate metabolism under the influence of dexamethasone [12].

In the reference group, which received Arfazetin, glycemia was significantly lower by 31.5 and 61.6 % after 30 and 90 min, respectively, from the beginning of adrenaline test, and at 90 min corresponded to NC group. In the reference group, which received metformin, the glycemic level was significantly lower than in the PC group by 61.4, 98.3 %, and by 11.1, 22.4 % from the NC group in 30 and 90 min, respectively, after the injection of adrenaline.

Table 4 – **The results of adrenaline test**

Experimental group	The basal glycemia, mmol/l	The blood glucose concentration, mmol/l	
		After 30 min	After 90 min
Negative control (NC)	4.41±0.09	6.46±0.13	8.00±0.15
Positive control (PC)	5.63±0.11 $p_1 \leq 0.001$	11.07±0.17 $p_1 \leq 0.001$	14.48±0.25 $p_1 \leq 0.001$
Reference group (Arfazetin)	5.47±0.07 $p_1 \leq 0.001$ $p_2 > 0.10$	9.05±0.25 $p_1 \leq 0.001$ $p_2 \leq 0.001$	10.71±0.36 $p_1 \leq 0.001$ $p_2 \leq 0.001$
Reference group (Metformin)	5.05±0.09 $p_1 \leq 0.001$ $p_2 \leq 0.001$	6.87±0.30 $p_1 > 0.10$ $p_2 \leq 0.001$	8.03±0.16 $p_1 > 0.10$ $p_2 \leq 0.001$
Experimental group (Phytocomposition)	5.19±0.08 $p_1 \leq 0.001$ $p_2 \leq 0.01$ $p_3 \leq 0.05$ $p_4 > 0.10$	7.98±0.20 $p_{1\leq} 0.001$ $p_2 \leq 0.001$ $p_3 \leq 0.01$ $p_4 \leq 0.01$	9.73±0.26 $p_1 \leq 0.001$ $p_2 \leq 0.001$ $p_3 \leq 0.05$ $p_4 \leq 0.001$

The studied phytocomposition inhibited the development of glycemia by 42.9, 70.2 % after 30 and 90 min, respectively, relative to the PC group, which corresponds to the indicators of NC group and reference group, which received Arfazetin. Still, this decrease is not enough to exceed the effect of metformin.

CONCLUSIONS. 1. Basal glycemia after modeling insulin resistance in the experimental group, which received the phytocomposition, was significantly lower by 19.0 % from the positive control group and did not differ from the activity of metformin.

2. During the oral glucose tolerance test, the phytocomposition significantly inhibited the growth of glycemia in all studied periods relative to the indicators of the positive control group. However, functional glycemic coefficients, which were obtained based on the same test data, did not exceed the norm.

3. Insulin sensitivity under the influence of phytomedicine increased by 16.2 % above the positive control group, indicating inhibition of insulin resistance development under its influence.

4. The studied phytocomposition inhibited the development of adrenaline glycemia by 42.9, 70.2 % after 30 and 90 min, respectively, relative to the positive control group, which corresponds to the indicators of the negative control group and reference group, which received Arfazetin, but this decrease is not enough to exceed the effect of metformin.

5. The obtained results indicate that the studied phytocomposition inhibits the development of insulin resistance and carbohydrate tolerance in the conditions of insulin resistance caused by the introduction of dexamethasone.

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А. І. Дуб, І. М. Кліщ, Л. В. Вронська, І. П. Стечишин
ТЕРНОПІЛЬСЬКИЙ НАЦІОНАЛЬНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ ІМЕНІ І. Я. ГОРБАЧЕВСЬКОГО МОЗ УКРАЇНИ

ДОСЛІДЖЕННЯ СПЕЦИФІЧНОЇ АКТИВНОСТІ ФІТОКОМПОЗИЦІЇ ПРИ ІНСУЛІНОРЕЗИСТЕНТНОСТІ, СПРИЧИНЕНІЙ ДЕКСАМЕТАЗОНОМ

Резюме

Вступ. *Цукровий діабет 2 типу (ЦД 2) останнім часом набуває епідемічного характеру поширення. У світі налічується приблизно 463 млн хворих, а за прогнозами експертів Міжнародної федерації діабету, до 2045 р. передбачається збільшення їх кількості до 629 млн осіб, з яких понад 90 % припадатиме на ЦД 2. Незважаючи на значний прогрес у вивченні патогенезу ЦД, широкий спектр протидіабетичних препаратів, це захворювання залишається гострою медичною та соціальною проблемою.*

Мета дослідження *– вивчити специфічну активність фітокомпозиції, що містить сухі екстракти листя шовковиці білої (Morus alba L.), стулок квасолі звичайної (Phaseolus vulgaris L.) та пагонів чорниці звичайної (Vaccinium myrtillus L.), за умов експериментальної моделі інсулінорезистентності, спричиненої дексаметазоном.*

Методи дослідження. *Експерименти проводили на тримісячних щурах-самцях масою (200±20) г. Піддослідних тварин розподілили на такі групи: негативний та позитивний контроль, 2 референс-групи, які отримували арфазетин і метформін відповідно, й експериментальну групу, яка одержувала фітокомпозицію. Інсулінорезистентність моделювали шляхом внутрішньом'язового введення глюкокортикостероїду дексаметазону (0,125 мг/кг щодня впродовж 13 днів уранці). Стан вуглеводного гомеостазу оцінювали за змінами базальної глікемії та за допомогою орального тесту толерантності до глюкози, короткого інсулінового й адреналінового тесту. Також було розраховано функціональні глікемічні коефіцієнти. Статистичну обробку проводили за допомогою комп'ютерних програм IBM SPSS Statistics v.10.1 та MS Excel 2010.*

Результати й обговорення. *Глікемія натще після моделювання інсулінорезистентності в експериментальній групі, яка отримувала фітокомпозицію, була значно нижчою – на 19,0 % від групи позитивного контролю і не відрізнялася від активності метформіну. Під час орального тесту толерантності до глюкози фітокомпозиція суттєво пригнічувала зростання глікемії в усі досліджувані періоди щодо показників групи позитивного контролю. Функціональні глікемічні коефіцієнти, одержані на основі даних тесту, не перевищували норми. Чутливість до інсуліну під впливом фітокомпозиції збільшилась на 16,2 % порівняно з групою позитивного контролю, що свідчило про пригнічення розвитку інсулінорезистентності під його впливом. Досліджувана фітокомпозиція пригнічувала розвиток адреналінової глікемії на 42,9 і 70,2 % через 30 та 90 хв відповідно щодо групи позитивного контролю, що відповідало показникам групи негативного контролю та референс-групи, яка отримувала арфазетин, але цього зниження недостатньо, щоб перевищити ефект метформіну.*

Висновок. *Отримані результати вказують на те, що досліджувана фітокомпозиція пригнічує розвиток інсулінорезистентності та толерантності до вуглеводів за умов інсулінорезистентності, спричиненої введенням дексаметазону.*

КЛЮЧОВІ СЛОВА: **цукровий діабет; інсулінорезистентність; фітокомпозиція; гіпоглікемічна активність; шовковиця біла; квасоля звичайна; чорниця звичайна.**

А. И. Дуб, И. Н. Клищ, Л. В. Вронска, И. П. Стечишин
ТЕРНОПОЛЬСКИЙ НАЦИОНАЛЬНЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ ИМЕНИ И. Я. ГОРБАЧЕВСКОГО МОЗ УКРАИНЫ

ИССЛЕДОВАНИЕ СПЕЦИФИЧЕСКОЙ АКТИВНОСТИ ФИТОКОМПОЗИЦИИ ПРИ ИНСУЛИНОРЕЗИСТЕНТНОСТИ, ВЫЗВАННОЙ ДЕКСАМЕТАЗОНОМ

Резюме

Вступление. *Сахарный диабет 2 типа (СД 2) в последнее время приобретает эпидемический характер распространения. В мире насчитывается примерно 463 млн больных, а по прогнозам экспертов Международной федерации диабета, в 2045 г. предполагается увеличение их количества до 629 млн человек, из которых более 90 % будет приходиться на СД 2. Несмотря на значительный прогресс в изучении патогенеза СД, широкий спектр противодиабетических препаратов, это заболевание остается острой медицинской и социальной проблемой.*

Цель исследования *– изучить специфическую активность фитокомпозиции, содержащей сухие экстракты листьев шелковицы белой (Morus alba L.), створок фасоли обыкновенной (Phaseolus vulgaris L.) и побегов черники обыкновенной (Vaccinium myrtillus L.), в условиях экспериментальной модели инсулинорезистентности, вызванной дексаметазоном.*

Методы исследования. *Эксперименты проводили на трехмесячных крысах-самцах весом (200±20) г. Подопытных животных распределили на следующие группы: негативный и позитивный контроль, 2 референс-группы, получавшие арфазетин и метформин соответственно, и экспериментальную группу, которая получала фитокомпозицию. Инсулинорезистентность моделировали путем внутримышечного введения глюкокортикостероида дексаметазона (0,125 мг/кг ежедневно в течение 13 дней утром). Состояние углеводного гомеостаза оценивали по изменениям базальной гликемии и с помощью орального теста толерантности к глюкозе, короткого инсулинового и адреналинового теста. Также были рассчитаны функциональные гликемические коэффициенты. Статистическую обработку проводили с помощью компьютерных программ IBM SPSS Statistics v.10.1 и MS Excel 2010.*

Результаты и обсуждение. *Гликемия натощак после моделирования инсулинорезистентности в экспериментальной группе, получавшей фитокомпозицию, была значительно ниже – на 19,0 % от группы положительного контроля и не отличалась от активности метформина. Во время орального теста толерантности к глюкозе фитокомпозиция существенно подавляла возрастание гликемии во все исследуемые периоды относительно показателей группы положительного контроля. Функциональные гликемические коэффициенты, полученные на основе данных теста, не превышали нормы. Чувствительность к инсулину под влиянием фитокомпозиции увеличилась на 16,2 % по сравнению с группой положительного контроля, что свидетельствовало об угнетении развития инсулинорезистентности под его влиянием. Исследуемая фитокомпозиция подавляла развитие адреналиновой гликемии на 42,9 и 70,2 % через 30 и 90 мин соответсвенно относительно группы положительного контроля, что соответствовало показателям группы отрицательного контроля и референс-группы, получавшей арфазетин, но этого снижения недостаточно, чтобы превысить эффект метформина.*

Вывод. *Полученные результаты указывают на то, что исследуемая фитокомпозиция подавляет развитие инсулинорезистентности и толерантности к углеводам в условиях инсулинорезистентности, вызванной введением дексаметазона.*

КЛЮЧЕВЫЕ СЛОВА: **сахарный диабет; инсулинорезистентность; фитокомпозиция; гипогликемическая активность; шелковица белая; фасоль обыкновенная; черника обыкновенная.**

Received 17.03.21

Address for correspondence: *A. I. Dub, I. Horbachevsky Ternopil National Medical University, Maidan Voli, 1, Ternopil, 46001, Ukraine, e-mail: dub_aih@tdmu.edu.ua.*