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## THE EFFECT OF THE ANTIDIABETIC COMPOSITION ON THE FUNCTIONAL CONDITION OF THE RAT LIVER IN THE EXPERIMENTAL DIABETES

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*Key words: diabetes mellitus; hepatopathy; medicinal plants; antidiabetic composition*

*On the model of diabetes mellitus in rats induced by the 18-days subcutaneous administration of dexamethasone in the dose of 0.125 mg/kg the hepatoprotective properties of a new antidiabetic composition based on medicinal plants have been investigated. The antidiabetic composition and the reference drug – officinal composition "Arphasetinum" were introduced intragastrically as a decoction in the dose of 18 ml/kg simultaneously with dexamethasone. According to the data obtained the antidiabetic composition exhibited a significant hepatoprotective and general metabolic effect. Under the effect of the composition studied the normalization of the basal glycemic level, recovery of the lipid balance and the bile secretory function of the liver, decrease of activity of cytolysis and inflammatory marker enzymes were observed. By its effect on the majority of the indices studied the new antidiabetic composition exceeded the reference composition "Arphasetinum".*

In the last decades a sharp increase in incidence of diabetes mellitus (DM) is observed in most of countries of the world. Almost 90% of cases are accounted for DM type 2. Due to affection of almost all organs and systems, particularly the gastro-intestinal tract, DM becomes a serious medical and social problem [6, 7]. Hyperglycemia, hyperlipidemia, disorders of other links of metabolism are tightly connected with disturbance of the functional activity of the liver – the central organ for metabolism. Numerous clinical trials are the evidence for occurrence of diabetic hepatopathy in patients with DM type 2. In development of the hepatic functional disorders the main role belongs to insulin resistance, which occurs during prediabetes [3]. Taking into account the abovementioned it is reasonable to use drugs, which along with antidiabetic properties have the hepatoprotective activity.

The aim of the work was to investigate the effect of a new antidiabetic composition of medicinal plants on the functional activity of the liver in the experimental diabetes type 2 in rats. The antidiabetic composition contains *Silybum marianum*; *Polygonum aviculare* L.; *Vaccinium vitis-idea* L.; *Linum usitatissimum* L.; *Cichorium intybus* L.; *Zea mays* L.

### Materials and Methods

The experiments were conducted on 49 white male rats of old age (18.5 months) with the body mass of 350-400 g. During the experiment animals were kept in standard conditions at 18-24°C, 50-60% of humidity, "day-night" natural light regime, a balanced diet with free access to water. All procedures with animals were conducted according to the principles of the "European convention for the protection of vertebrate animals used for experimental and other scientific purposes" (Strasbourg, 1986), according to the GLP standards [1]. The experimental diabetes was provoked by subcutaneous in-

roduction of dexamethasone in the dose of 0.125 mg/kg for 18 days [4]. The antidiabetic composition was introduced intragastrically as a decoction in the dose of 18 ml/kg simultaneously with dexamethasone once a day [5]. The officinal composition "Arphasetinum" administered in the similar regimen was chosen as a reference drug. The animals were divided into the following groups: intact group (IG); control group (CG); groups of animals that received the antidiabetic composition or a reference composition "Arphasetinum". On day 19 the bile secretory function of the liver was assessed (the bile secretion rate was calculated within 3 hours in mg/min·100-1g) [2]. Afterwards animals were removed from the experiment by decapitation under chloroform anaesthesia. The level of glucose was determined in the rats' blood. The functional condition of the liver was estimated by biochemical measurements in the blood serum: the activity of such enzymes as alanine aminotransferase (ALT), aspartate transferase (AST), alkaline phosphatase (AF), the cholesterol level, triglycerides (TG), high density lipoproteins (HDL) and low density lipoproteins (LDL) using test kits of "Lachema" company (Czech Republic). The relative mass of liver was determined.

### Results and Discussion

Introduction of dexamethason to old rats (18.5 months) caused a moderate basal hyperglycemia (Table) that was accompanied by expressive lipid disbalance. According to the data obtained the statistically significant increase in the cholesterol level, TG, LDL and decrease in HDL were observed in the blood serum of animals in CG. It indicates development of atherogenic processes under conditions of the experimental diabetes. A relative liver mass increase by 47% compared to IG is the evidence of circulatory dynamics disorder. This disorder occurs as a result of increasing hepatic tissue edema. Increase of alkaline phosphatase in the blood serum almost twice and

Table

A comparative study of the effect of the antidiabetic composition and the composition "Arphasetinum" on the functional condition of the rat liver in dexamethasone diabetes (n = 7)

The indices studied	Groups of animals			
	Intact group	Control group (dexamethasone)	Antidiabetic composition 18 ml/kg + dexamethasone	"Arphasetinum" 18 ml/kg + dexamethasone
Basal glycemia, mmol/l	4.35±0.30	7.15±0.35*	4.38±0.22**	4.03±0.35**
cholesterol, mmol/l	1.47±0.17	2.61±0.25*	1.87±0.15**	1.96±0.15**
LDL, mmol/l	0.38±0.02	0.52±0.02*	0.39±0.04**	0.44±0.05
CL-HDL, mmol/l	2.27±0.28	1.39±0.16*	2.48±0.19**	1.97±0.19†
TG, mmol/l	0.40±0.06	0.63±0.04*	0.43±0.03**/**	0.64±0.05
AP, mmol/l	18.51±6.34	36.35±3.35†	18.97±4.63	17.11±3.90†
ALT, mmol/l-h	0.47±0.01	0.63±0.04*	0.47±0.03**	0.52±0.04**
AST, mmol/l-h	0.42±0.02	0.56±0.04*	0.39±0.03**/**	0.54±0.03*
Bile secretory rate, ml/h·100 <sup>-1</sup>	3.56±0.21	2.28±0.29	3.23±0.40	3.03±0.40
Liver relative mass, %	2.30±0.19	3.38±0.21*	2.46±0.20**/†2	3.02±0.16†2

Notes: 1.\* – differences statistically significant compared to the intact group, p<0.05; 2.\*\* – differences statistically significant compared to the control group, p<0.05; 3.\*\*\* – differences statistically significant compared to the reference drug, p<0.05.

the activity of cytolysis markers of hepatocytes (ALT and AST) in 1.3 times was statistically significant. It is the evidence of development of inflammation in the liver (Table). Destructive consequence in hepatocytes was the bile secretory dysfunction (Table).

Introduction of the antidiabetic composition and the reference drug contributed to normalization of the basal glycemic level. However, compared to the composition "Arphasetinum" under the effect of the antidiabetic composition the more expressive recovery of general trophic processes in the liver and decrease in symptoms of atherogenesis were observed. Dynamics of the relative organ mass and indices of the lipid metabolism was similar to the dynamics in the intact group. The level of cytolitic enzymes and alkaline phosphatase decreased to the physiological level (Table). The bile secretory function

of the liver was restored (Table). Under these conditions the composition "Arphasetinum" exhibited a bit inferior activity. The level of ALT and cholesterol decreased significantly in the group of the reference drug. There was a tendency to normalization of the level of CL-HDL and alkaline phosphatase. However, the content of TG, LDL, AST activity and a relative liver mass were in the same range that in the control group. As a result, the recovery of the bile secretory rate had a character only of an inexpressive tendency (Table).

#### CONCLUSIONS

Thus, under conditions of the experimental diabetes mellitus induced by dexamethasone it has been found that a new antidiabetic composition exhibits a significant hepatoprotective action due to suppression of inflammation and the positive effect on metabolic processes in the liver.

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**ВПЛИВ АНТИДІАБЕТИЧНОГО ЗБОРУ НА ФУНКЦІОНАЛЬНИЙ СТАН ПЕЧІНКИ ЩУРІВ ПРИ ЕКСПЕРИМЕНТАЛЬНОМУ ДІАБЕТИ****О.Ю.Кошова**

**Ключові слова:** цукровий діабет; гепатопатії; лікарські рослини; антидіабетичний збір

На моделі цукрового діабету у щурів, викликаного 18-денним підшкірним введенням дексаметазону у дозі 0,125 мг/кг, досліджували гепатопротекторні властивості нового збору лікарських рослин, який виявляє антидіабетичні властивості. Антидіабетичний збір та препарат порівняння офіційний збір «Арфазетин» вводили внутрішньошлунково у вигляді відвару (1:10), у дозі 18 мл/кг одночасно з дексаметазоном. Відповідно до отриманих даних антидіабетичний збір виявив виразну гепатопротекторну та загальнометаболичну дію. Під впливом засобу спостерігалась нормалізація рівня базальної глікемії, відновлення ліпідного профілю та жовчосекреторної функції печінки, зниження активності маркерних ферментів цитолізу та запалення. За впливом на більшість досліджуваних показників новий збір переважав препарат порівняння збір «Арфазетин».

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**ВЛИЯНИЕ АНТИДИАБЕТИЧЕСКОГО СБОРА НА ФУНКЦИОНАЛЬНОЕ СОСТОЯНИЕ ПЕЧЕНИ КРЫС ПРИ ЭКСПЕРИМЕНТАЛЬНОМ ДИАБЕТЕ****Е.Ю.Кошова**

**Ключевые слова:** сахарный диабет; гепатопатии; лекарственные растения; антидиабетический сбор

На модели сахарного диабета у крыс, вызванного 18-дневным подкожным введением дексаметазона в дозе 0,125 мг/кг исследовали гепатопротекторные свойства нового сбора лекарственных растений с антидиабетическими свойствами. Антидиабетический сбор и препарат сравнения официальный сбор «Арфазетин» вводили внутривенно в виде отвара (1:10) в дозе 18 мл/кг одновременно с дексаметазоном. Согласно полученным данным, антидиабетический сбор оказывал выраженное гепатопротекторное и общеметаболическое действие. Под воздействием сбора наблюдалась нормализация уровня базальной гликемии, восстановление липидного профиля и желчсекреторной функции печени, снижение активности маркерных ферментов цитолиза и воспаления. По влиянию на большинство изученных показателей новый антидиабетический сбор превосходил препарат сравнения сбор «Арфазетин».