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The study of antidiabetic action of the phlomis pungens extract

Topicality. Despite the rather large arsenal of antidiabetic drugs, the main goal of DM pharmacotherapy, aimed at reducing hyperglycemia and progress of diabetic vascular complications, still remains far from practical implementation. In this regard, the expansion of antidiabetic drugs spectrum due to natural biologically active substances is actual and promising.

Aim. To study the antidiabetic action of phlomis pungens extract.

Materials and methods. Trials were performed on 33 rats. Experimental diabetes was caused by a single intravenous alloxan injection at a dose of 70 mg/kg to females weighing 200-250 g. The extract of the Phlomis Pungens (PP) was injected once a day intragastrically at doses of 25 and 50 mg/kg daily for three weeks prior to modeling of experimental diabetes, and for 30 days of the experiment. Control animals received water in a similar regime. Metformin was used as a reference preparation in a dose of 100 mg/kg. Intraperitoneal glucose tolerance test was performed as follows: after night fasting (16-18 hours) rats intraperitoneally injected glucose solution at a dose of 3 g/kg in the morning.

Results and discussion. Experimental diabetes was caused by a single intravenous alloxan injection at a dose of 70 mg/kg to females weighing 200-250 g. Basal glycemia was determined in dynamics: baseline level and after alloxan injection - at the 3rd (period of acute development of hyperglycemia), 1, 2 and 4 weeks of the trial. As a result of the trial it was established that the extract of the Phlomis Pungens (PPE) demonstrates a hypoglycemic effect in a dose of 25 m 50 mg/kg for 4 weeks of the trial. The most pronounced hypoglycemic effect of PPE demonstrated by the end of the trial, i.e. at 4 weeks and significantly reduced the blood glucose level in comparison with the control pathology (CP) by 40 %. According to hypoglycemic activity, the extract of Phlomis Pungens in 2 doses of 25 and 50 mg/kg demonstrated almost the same effect and did not differ significantly between each other.

Conclusions. The Phlomis Pungens Extract demonstrated a pronounced hypoglycemic effect against the background of exudate alloxan diabetes of moderate severity. Against the backdrop of a glucose load, the Phlomis Pungens extract reduces the level of basal glycemia by decreasing insulin resistance and exceeds the activity of metformin at a dose of 50 mg/kg.

Key words: *Phlomis pungens; antidiabetic action; basal glycemia*

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Вивчення антидіабетичної дії екстракту зопника колючого

Актуальність. Незважаючи на досить великий арсенал протидіабетичних препаратів, головна мета фармакотерапії ЦД, спрямована на зниження гіперглікемії і прогресування діабетичних судинних ускладнень, ще залишається далекою від практичної реалізації. У зв'язку з цим розширення спектра антидіабетичних засобів за рахунок природних біологічно активних речовин є актуальним і перспективним.

Мета роботи. Метою даної роботи є вивчення антидіабетичної дії екстракту зопника колючого.

Матеріали та методи. Досліди проводилися на 33 щурах. Експериментальний цукровий діабет викликали шляхом одноразового внутрішньовенного введення алоксану в дозі 70 мг/кг щурам самицям масою 200-250 г. Екстракт зопника колючого (ЕЗК) вводили один раз на день внутрішньошлунково в дозах 25 і 50 мг/кг щодня впродовж трьох тижнів до моделювання експериментального діабету і впродовж 30 днів експерименту. Контрольні тварини отримували воду в аналогічному режимі. Як препарат порівняння використовували Метформін у дозі 100 мг/кг. Внутрішньоочеревинний тест толерантності до глюкози проводили наступним чином: після нічного голодування (16-18 годин) щурам вранці внутрішньоочеревинно вводили розчин глюкози в дозі 3 г/кг.

Результати та їх обговорення. Експериментальний цукровий діабет (ЦД) викликали шляхом одноразового внутрішньовенного введення алоксану в дозі 70 мг/кг щурам самицям масою 200-250 г. Базальну глікемію визначали в динаміці: вихідний рівень і після введення алоксану – на 3-ій (період гострого розвитку гіперглікемії), 1, 2 і 4 тижні експерименту. В результаті експерименту було встановлено, що екстракт зопника колючого (ЕЗК) проявляє гіпоглікемічну дію в дозі 25 м 50 мг/кг впродовж 4 тижнів експерименту. Найбільш виражену гіпоглікемічну дію ЕЗК проявив до кінця експерименту, тобто на 4 тижні і достовірно зменшував рівень глюкози в крові в порівнянні з контрольною патологією (КП) на 40 %. За гіпоглікемічною активністю екстракт зопника колючого в 2-х дозах – 25 і 50 мг/кг проявляв майже однаковий ефект і результати достовірно не відрізнялися між собою.

Висновки. Екстракт зопника колючого чинить виражену гіпоглікемічну дію на тлі ексудального алоксанового діабету середньої тяжкості. На тлі глюкозного навантаження екстракт зопника колючого знижує рівень базальної глікемії за рахунок зниження інсулінорезистентності і перевищує за активністю метформін у дозі 50 мг/кг.

Ключові слова: *зопник колючий; антидіабетична дія; базальна глікемія*

А. Т. Бадалова

Изучение антидиабетического действия экстракта зопника колючего

Актуальность. Несмотря на достаточно большой арсенал противодиабетических препаратов, главная цель фармакотерапии СД, направленная на снижение гипергликемии и прогрессирования диабетических сосудистых осложнений, еще остается далекой от практической реализации. В связи с этим расширение спектра антидиабетических средств за счет природных биологически активных веществ является актуальным и перспективным.

Цель работы – изучение антидиабетического действия экстракта зопника колючего.

Материалы и методы. Опыты проводились на 33 крысах Экспериментальный сахарный диабет (СД) вызывали путем одноразового внутривенного введения аллоксана в дозе 70 мг/кг крысам самкам массой 200-250 г. Экстракт зопника колючего (ЭЗК) вводили один раз в день внутрижелудочно в дозах 25 и 50 мг/кг ежедневно на протяжении трех недель до моделирования экспериментального диабета и на протяжении 30 дней эксперимента. Контрольные животные получали воду в аналогичном режиме. В качестве препарата сравнения использовали Метформин в дозе 100 мг/кг. Внутрибрюшинный тест толерантности к глюкозе проводили следующим образом: после ночного голодания (16-18 часов) крысам утром внутрибрюшинно вводили раствор глюкозы в дозе 3 г/кг.

Результаты и их обсуждение. Экспериментальный сахарный диабет вызывали путем одноразового внутривенного введения аллоксана в дозе 70 мг/кг крысам самкам массой 200-250 г. Базальную гликемию определяли в динамике: исходный уровень и после введения аллоксана – на 3-ю (период острого развития гипергликемии), 1, 2 и 4 недели эксперимента. В результате эксперимента было установлено, что экстракт зопника колючего (ЭЗК) проявляет гипогликемическое действие в дозе 25 м 50 мг/кг на протяжении 4 недель эксперимента. Наиболее выраженное гипогликемическое действие ЭЗК проявил к концу эксперимента, т. е. на 4 неделе и достоверно уменьшал уровень глюкозы в крови в сравнении с контрольной патологией (КП) на 40 %. По гипогликемической активности экстракт зопника колючего в 2-х дозах – 25 и 50 мг/кг проявляли почти одинаковый эффект и достоверно не отличались между собой.

Выводы. Экстракт зопника колючего проявляет выраженное гипогликемическое действие на фоне экссудального аллоксанового диабета средней тяжести. На фоне глюкозной нагрузки экстракт зопника колючего снижает уровень базальной гликемии за счет снижения инсулинорезистентности и превышает по активности метформин в дозе 50 мг/кг.

Ключевые слова: *зопник колючий; антидиабетическое действие; базальная гликемия*

INTRODUCTION

Diabetes mellitus is a global medical and social problem of the 21st century and ranks seventh among the leading causes of death in most countries of the world. According to the estimates of the World Health Organization and the International Diabetes Association, the number of people with diabetes mellitus (DM) is projected to reach 380 million in 2025, of which 95 % are patients with type 2 diabetes [1, 2].

Despite the rather large arsenal of antidiabetic drugs, the main goal of DM pharmacotherapy, aimed at reducing hyperglycemia and progression of diabetic vascular complications, still remains far from practical implementation. In this regard, the expansion of the spectrum of antidiabetic drugs due to natural biologically active substances is actual and promising [3, 4].

Compared with synthetic drugs, phyto-drugs have a greater similarity to the animal and human organism and are less toxic. This ensures their greater bioavailability at the systemic, organ and cellular levels, which is physiologically implanted in the body. Natural compounds are suitable for long-term use because of a less pronounced sensitizing effect on the body. All this forms the prerequisites for creating promising phyto-drugs for the treatment of diabetes.

Flora of Azerbaijan is rich in species composition. Plants are an indispensable source for obtaining medicines of various pharmacological actions. However, to date, these sources are not used rationally because of the lack of study [5].

The genus *Phlomis* comprises perennial plants from the family *Lamiaceae.* Several Phlomis species possess various types of activity such as anti-inflammatory, anticonvulsant, antitumor, antiallergic, antimicrobial and antidiabetic effects [6].

The aim of this work that to study of antidiabetic action of extract of phlomis pungens.

MATERIALS AND METHODS

Trials were performed on 33 rats. Experimental diabetes was caused by a single intravenous injection of alloxan at a dose of 70 mg/kg to females weighing 200-250 g [4]. The extract of the Phlomis Pungens (PP) was injected once a day intragastrically at doses of 25 and 50 mg/kg daily for three weeks prior to modeling of experimental diabetes, and for 30 days of the experiment. Control animals received water in a similar regime. Metformin was used as a reference preparation in a dose of 100 mg/kg.

Intraperitoneal glucose tolerance test was performed as follows: after night fasting (16-18 hours) rats intraperitoneally injected glucose solution at a dose of 3 g/kg in the morning. The blood glucose concentration that was obtained from the animal tail vein was determined before the administration of glucose and after 20, 40, 60, 90 and 120 minutes through glucose oxidase method [7].

RESULTS AND DISCUSSION

Experimental diabetes was caused by a single intravenous injection of alloxan at a dose of 70 mg/kg to females weighing 200-250 g [1]. The mechanism of cyto-

Table 1

DYNAMICS OF BASAL GLYCEMIA OF AN EXTRACT OF A PHLOMIS PUNGENS AT INTRAGASTRIC INTRODUCTION TO RATS WITH AN ALLOXAN DIABETES (M ± m)

Animal groups	n	Dose, mg/kg	Concentration of glucosis, mmol/l			
			1st week	2rd week	3rd week	4th week
Intact control	5	–	4.68 ± 0.45	4.45 ± 0.14	4.44 ± 0.41	3.50 ± 0.31
Control pathology	7		11.11 ± 1.96*	10.33 ± 1.65*	12.78 ± 1.47*	9.87 ± 2.06*
PPE	7	25	6.43 ± 1.77**	9.00 ± 1.26	8.93 ± 2.37**	6.00 ± 0.39**
	7	50	4.92 ± 1.45**	9.3 ± 1.42	7.5 ± 0.49**	6.8 ± 0.62**
Metformin	7	100	4.97 ± 1.49**	10.00 ± 0.55**	9.3 ± 0.14**	7.5 ± 0.62**

Note: * – the differences are significant relative to the intact control, $p < 0.05$; ** – the differences are significant relative to the control pathology, $p < 0.05$; n is the number of animals in each group.

toxic action of alloxan is caused by destructive action of hydroxyl and superoxide radicals, which are formed as a result of pancreatotoxin enhancement of free radical and peroxide oxidation in biomebranes of B cells. After administration in the body, alloxane binds to the membranes of the ß-cells of the prostate, which leads to a rapid decrease in the secretion of insulin [4, 8].

The test specimen (Phlomis Pungens extract (PPE) was injected once daily intravenously at doses of 25 and 50 mg/kg daily for three weeks prior to modeling of experimental diabetes, and for 30 days of the experiment. Control animals received water in the same manner. Metformin was used as a reference preparation in a dose of 100 mg/kg.

Basal glycemia was determined in dynamics: baseline level and after alloxan injection - at the 3rd (period of acute development of hyperglycemia), 1, 2 and 4 weeks of the trial.

The state of glucose homeostasis of animals against the background of model pathology was assessed by the level of basal glycemia and glucose tolerance, which was determined using an intraperitoneal glucose tolerance test (IPGTT).

Intraperitoneal glucose tolerance test was performed as follows: after night fasting (16-18 hours) rats intraperitoneally injected glucose solution at a dose of 3 g/kg in the morning. The blood glucose concentration that was obtained from the animal tail vein was determined before the administration of glucose and after 20, 40, 60, 90 and 120 minutes through glucose oxidase method [7].

The obtained data are presented in Tab. 1 and 2.

As a result of the trial it was established that the extract of the Phlomis Pungens (PPE) demonstrates a hypoglycemic effect in a dose of 25 m 50 mg/kg for 4 weeks of the trial. The most pronounced hypoglycemic effect of PPE demonstrated by the end of the trial, i.e. at 4 weeks and significantly reduced the blood glucose level in comparison with the control pathology (CP) by 40 %.

According to hypoglycemic activity, the extract of Phlomis Pungens in 2 doses of 25 and 50 mg/kg demonstrated almost the same effect and did not differ significantly between each other. The metformin comparison

Table 2

EFFECT OF PPE ON THE DEVELOPMENT OF HYPERGLYCEMIC REACTION IN RATS WITH ALLOXAN DIABETES ON CARBOHYDRATE LOAD (IPGTT, GLUCOSE 3 g/kg, M ± m)

Time of observation	Animal groups				
	Intact control (n = 5)	Control pathology (Alloxan, n = 7)	PPE		Metformin, 100 mg/kg (n = 6)
			25 mg/kg (n = 6)	50 mg/kg (n = 6)	
Initial data	3.50 ± 0.31	9.87 ± 2.06*	4.00 ± 0.46**	4.77 ± 0.65**	4.54 ± 0.62**
20 min	14.12 ± 0.94	24.82 ± 1.64*	15.23 ± 1.71**	13.48 ± 0.65**	14.90 ± 1.37**
40 min	7.30 ± 0.77	22.25 ± 2.27*	13.43 ± 1.58*/**	12.74 ± 0.89*/**	15.61 ± 1.38*/**
60 min	5.45 ± 0.49	22.02 ± 2.20*	12.70 ± 0.34*/**	9.92 ± 1.01*/**	11.74 ± 2.52**
90 min	4.21 ± 0.53	18.10 ± 2.48*	10.92 ± 1.77**	9.17 ± 2.31**	9.10 ± 1.24**
120 min	4.25 ± 0.49	14.71 ± 1.12*	8.40 ± 1.11*/**	8.42 ± 0.68*/**	7.00 ± 0.80

Notes: * – the differences are significant relative to the intact control, $p < 0.05$; ** – the differences are significant relative to the control pathology, $p < 0.05$; n – is the number of animals in each group.

drug also demonstrated a pronounced hypoglycemic effect, but was less active at all stages of the trial compared to the studied extract.

Effect of ppe on basal glycemia under conditions of glucose load

The introduction of the extract in 2 doses and metformin in the prophylactic dosage prevented a significant increase in basal glycemia during the glucose load in comparison with CP. This is indicated by a decrease in glucose level for 20 min exposure, when studying animals receiving PPE in doses of 25 mg by 39.6 % and 50 mg by 45.3 %, respectively. A similar trend in the group of animals receiving PPE was observed throughout the entire trial. Against the backdrop of a glucose load, the most pronounced hypoglycemic effect was demonstrated by the extract of the *Phlomis Pungens* in a dose of 50 mg/kg and exceeded the activity of metformin.

CONCLUSIONS

1. Extract of the *Phlomis Pungens* demonstrated a pronounced hypoglycemic effect against the background of exudate alloxan diabetes of moderate severity.
2. Against the backdrop of a glucose load, the extract of the *Phlomis Pungens* reduces the level of basal glycemia by decreasing insulin resistance and exceeds the activity of metformin at a dose of 50 mg/kg.

Conflict of interests: authors have no conflict of interests to declare.

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