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ВЕСТНИК

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НАН РК сообщает, что научный журнал «Вестник НАН РК» был принят для индексирования в Emerging Sources CitationIndex, обновленной версии Web of Science. Содержание в этом индексировании находится в стадии рассмотрения компанией Clarivate Analytics для дальнейшего принятия журнала в the Science Citation Index Expanded, the Social Sciences Citation Index и the Arts & Humanities Citation Index. Web of Science предлагает качество и глубину контента для исследователей, авторов, издателей и учреждений. Включение Вестника НАН РК в Emerging Sources Citation Index демонстрирует нашу приверженность к наиболее актуальному и влиятельному мультидисциплинарному контенту для нашего сообщества.

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HOW *THALICTRUM FOETIDUM* EXTRACT INFLUENCES THE LIPID PEROXIDE OXIDATION AND ANTIOXIDANT SYSTEM IN RATS SUBJECTED TO CHRONIC IMMOBILISATION STRESS

Abstract. The experiment showed a potential correction of the free radical oxidation in the rats' membrane lipids by means of oral injection of *Thalictrum Foetidum* aqueous extract, contains a complex of natural antioxidants.

The experimental animals were divided into 6 groups (6 animals per group). The experimental animals from group 1 and the animals from group 2, which had been subjected to stress by immobilization for 5 hours, were given 1.5 ml of distil water orally/intragastrically. The animals from group 3, 4, 5 and 6 were given 0.5 ml, 1,0 ml, 1,5 ml and 2,0 ml correspondingly of *Thalictrum Foetidum* extract orally/intragastrically every day an 1 hour before stress exposition. The animals from all the groups were decapitated under ether anesthetic 5 hours after simulating immobilization stress, notably in the condition of the maximum stress exposition. Blood serum was used for the experiment. There was estimated lipid peroxide oxidation and the condition of the antioxidant system by the spectrophotometric method. For some chances to be observed in the indicators under research, the latter were determined in the control and experimental animals after 5, 15 and 30 days.

According to the experimental results, only the 15th and the 30th day, i. e. under chronic stress, show a statistically credible reduction in these indicators as to immobilization stress, approximating the control groups.

Analyzing the results of the experiment, we may conclude that *Thalictrum Foetidum* liquid extract has a rather gentle effect on the lipid peroxide oxidation and antioxidant system under immobilization stress.

Key words: *Thalictrum Foetidum*, liquid extract, immobilization stress, antioxidant system, lipid peroxide oxidation.

Introduction. Stresses, especially if they are frequent and long-term, have a negative impact not only on psychological state, but also on physical health. They serve as major risk factors in the development and exacerbation of many diseases. Of the most frequent diseases one can find those of the cardiovascular system (myocardial infarction, stenocardia, hypertension), the gastrointestinal tract (gastritis, stomach and duodenal ulcer), depressed immunity [1-3].

Moreover, stress, including the immobilization one, leads to intensive free radical peroxide oxidation (FRPO), resulting in oxidizing cell corruption, that can also provoke the development of gastroduodenal erosions and ulcers. This testifies to the necessity of prescribing antioxidants in the treatment and prevention of diseases of the nervous system [4].

As a rule, such medicaments as sedatives and neuroleptics are prescribed to solve problems, involving nervous disorder. This approach, however, does not always bring positive results, as it is important to remove the factors, which have provoked this state in a person. When the symptoms of nervous exhaustion are discovered, the treatment should be all-embracing and systematic, directed at removing the cause of diseases, which provoke disorders of the nervous system. Therefore, treating

patients, suffering from cerebrovascular diseases, with herbal drugs is one of the alternative methods of the therapy, which promotes normalization of the functions of the nervous system [5,6].

The *Thalictrum Foetidum* contains triterpene saponins, up to 2.2% of alkaloids (berberine, fetidin, thalictrine, isotetrandrine, berbamine), tannin (1.63-5.45%), flavonoids (rutin, glucoramnine, kaempferol, quercetin, flavestsin, ranunkuletin), cardenolides, volatile oil and organic acids. The tincture of *Thalictrum Foetidum* is used as a sedative, bactericide, anti-inflammatory, blood-stanching, diuretic and antiemetic agent. Apart from that, the infusion of herb is used in case of neuroses and convulsions, over tension, indigestion and diarrhea, diseases of the liver and the gall bladder, edema and dropsy and in case of internal and external bleedings [7-9].

Materials and methods. The experiment was conducted on 36 WAG-line rats with an average weight of 210-230 g. The stress-simulating action was studied on the prototype of chronic neuromuscular tension, reconstructed for 5, 15 and 30 days. Immobilization stress was simulated by keeping rats in plastic "cages-cases" every day for 5 hours. The experimental animals were divided into 6 groups (6 animals per group). The animals from group 1 (the so-called intact animals of a conditional norm) were given 1.5 ml of distil water orally and intragastrically through the probe. The animals from group 2 were subjected to stress by immobilization for 5 hours and given 1.5 ml of distil water orally and intragastrically through the probe. The animals from group 3, 4, 5 and 6 were given 0.5 ml, 1.0 ml, 1.5 ml and 2.0 ml correspondingly of *Thalictrum Foetidum* aqueous liquid extract though the probe orally and intragastrically every day an hour before stress exposition.

For some quantitative chances to be observed in the indicators under research, the latter were determined in the control and experimental animals in action after 5, 15 and 30 days.

The animals from all the groups were decapitated under ether anesthetic 5 hours after simulating immobilization stress, notably in the condition of the maximum stress exposition. Blood serum was used for the experiment to estimate lipid peroxide oxidation (LPO), namely: the level of primary oxidation products – conjugated dienes (CD), and secondary products – malondialdehyde (MDA), as well as the condition of the antioxidant system, namely: catalase activity and superoxide dismutase [10] by the spectrophotometer method [11,12].

Results and discussion. The results of the experiment are presented in table. The LPO was estimated according to the number of peroxide products: CD and thiobarbituric acid active products (TBA-AP), which amount to 14.00 ± 0.64 mmol/l and 4.65 ± 0.10 mmol/l correspondingly in the intact animals.

Neurotropic and antioxidant activity of *Thalictrum Foetidum* liquid extract

Indicator	Term of the experiment	Intact animals (n = 6)	Immobilization stress (n = 6)	Immobilization stress + 0.5 ml of *Thalictrum Foetidum* extract (n = 6)	Immobilization stress + 1 ml of *Thalictrum Foetidum* extract (n = 6)	Immobilization stress + 1.5 ml of *Thalictrum Foetidum* extract (n = 6)	Immobilization stress + 2 ml of *Thalictrum Foetidum* extract (n = 6)
DC, mmol/l	5 days	14.16 ± 0.64	30.72 ± 1.06*	29.15 ± 0.12*	27.24 ± 0.01*	28.09 ± 1.43*	25.45 ± 0.32*
	15 days		34.85 ± 0.85*	24.18± 0.44*,**	23.18 ± 0.10*,**	24.01 ± 0.90*,**	21.21 ± 0.1*,**
	30 days		37.85 ± 0.12*	15.11 ± 1.12**	15.67 ± 0.03**	15.23 ± 0.09**	14.54 ± 0.07**
MDA, mkmol/l	5 days	4.65 ± 0.10	6.94 ± 0.16*	6.02 ± 0.21*	6.13 ± 0.11*	5.98 ± 0.04**	5.67 ± 0.06**
	15 days		7.15 ± 0.45*	5.11 ± 0.01**	5.16 ± 0.10**	5.06 ± 0.56**	4.89 ± 0.17**
	30 days		7.56 ± 0.78*	4.21 ± 0.23**	4.34 ± 0.05**	4.56 ± 0.34**	4.23 ± 0.23**
SOD, standard unit	5 days	3.59 ± 0.11	6.93 ± 0.49*	5.33 ± 0.12*	5.16± 0.30*	5.09 ± 0.12*,**	4.87 ± 0.07*,**
	15 days		6.98 ± 0.23*	4.21 ± 0.16**	4.13 ± 0.04**	4.22 ± 0.02*,**	4.08 ± 0.67*,**
	30 days		7.13 ± 0.89*	3.42 ± 0.34**	3.47 ± 0.05**	3.47 ± 0.57**	3.32 ± 0.07**
Catalase, standard unit	5 days	5.10 ± 0.13	5.88 ± 0.26*	5.74 ± 0.11	5.73 ± 0.16	4.97 ± 0.25	4.86 ± 0.03**
	15 days		6.03 ± 0.21*	4.97 ± 0.02**	5.02 ± 0.09**	4.67 ± 0.43**	4.54 ± 0.78**
	30 days		6.23 ± 0.03*	4.75 ± 0.67 **	4.98 ± 0.21**	4.78 ± 0.06**	4.66 ± 0.01**

Note. 1. * - statistically significant difference compared to group of intact control; ** - statistically significant difference compared to group of stimulated by immobilization stress, $p \leq 0.05$.

2. All date were presented as Mean ± SE.

Table shows a considerable increase of these indicators, subjected to immobilization stress for 5 days. The level of CD approaches 30.72 ± 1.06 mmol/l, doubly exceeding the norm, whereas TBA-AP makes 6.94 ± 0.10 mmol/l, surpassing the control in 1.5 times.

On the 15th day the level of CD makes 34.85 ± 0.85 mmol/l, exceeding the norm in 2.5 times; TBA-AP comes to 7.15 ± 0.10 mmol/l, twice surpassing the control. After 30 days the CD level runs to 37.85 ± 0.12 mmol/l, thrice exceeding the norm; TBA-AP approaches 7.56 ± 0.78 mmol/l, twice surpassing the control.

According to the data from table, at the 5-day stage *Thalictrum Foetidum* liquid extract of in doses of 0.5 ml, 1 ml, 1.5 ml and 2 ml does not reduce the level of CD and TBA-AP statistically significantly relative immobilization stress.

Liquid extract of *Thalictrum Foetidum* has lowered the level of CD and TBA-AP in all the doses under research statistically significantly as regards to immobilization stress on the 15th day. Thus, under immobilization stress the level of CD in *Thalictrum Foetidum* liquid extract in doses of 0.5 ml, 1 ml, 1.5 ml and 2 ml makes 24.18 ± 0.44 mmol/l, 23.18 ± 0.10 mmol/l, 24.01 ± 0.90 mmol/l and 21.21 ± 0.10 mmol/l accordingly. Though statistically veritable as to the animals' group, which have undergone immobilization stress 34.85 ± 0.85 ($P \leq 0.05$), these indicators do not come close to the control. Under immobilization stress the level of TBA-AP in *Thalictrum Foetidum* liquid extract in doses of 0.5 ml, 1 ml, 1.5 ml and 2 ml amounts to 5.11 ± 0.01 mmol/l, 5.16 ± 0.10. mmol/l, 5.06 ± 0.56 mmol/l and 4.89 ± 0.17 mmol/l correspondingly. These indicators are veritable as regards to immobilization stress 7.15 ± 0.45 mmol/l ($P \leq 0.05$).

The 30th day showed *Thalictrum Foetidum* liquid extract in all the doses under research decreasing the level of CD and TBA-AP according to statistical significance as regards to immobilization stress and approaching the control.

Thus, under immobilization stress the level of CD in *Thalictrum Foetidum* liquid extract in doses of 0.5 ml, 1 ml, 1.5 ml and 2 ml made 15.11 ± 1.12 mmol/l, 15.67 ± 0.03 mmol/l, 15.23 ± 0.09 mmol/l and 14.54 ± 0.07 mmol/l correspondingly. These indicators are statistically significant as to the animals' group, subjected to immobilization stress 37.85 ± 0.12 mmol/l ($P \leq 0.05$). Under immobilisation stress the level of TBA-AP in *Thalictrum Foetidum* liquid extract in doses of 0.5 ml, 1 ml, 1.5 ml and 2 ml amounts to 4.21 ± 0.23 mmol/l, 4.34 ± 0.05 mmol/l, 4.56 ± 0.34 mmol/l and 4.23 ± 0.23 mmol/l correspondingly. These indicators are statistically significant as to immobilization stress 7.56 ± 0.78 mmol/l ($P \leq 0.05$).

Thus, after studying the indicators of LPO we can draw the conclusion that at the five-day stage the characteristics of TBA-AP and CD cannot be corrected significantly as regards to immobilization stress [13]. Only at the 15-day and 30-day stages the liquid extract of *Thalictrum Foetidum* in all the doses under research reduces the level of CD and TBA-AP according to statistical significance as to immobilization stress, thus approaching the control group. Moreover, we have established that increasing the dose of *Thalictrum Foetidum* liquid extract of has an insignificant effect on the indicators of TBA-AP and CD.

The condition of the antioxidant system was estimated according to the number of products of catalase and superoxide dismutase (SOD), amounting in the intact rats to 5.10 ± 0.13 standard unit and 3.59 ± 0.11 standard unit correspondingly. The data from table show a considerable increase of these indicators under immobilization stress. At the 5-day stage the level of catalase comes to 5.88 ± 0.26 standard unit under immobilization stress, thus exceeding the norm significantly ($P \leq 0.05$). SOD runs to 6.93 ± 0.49 standard unit, surpassing the control twice. At the 15-day stage the level of catalase comes to 6.03 ± 0.21 standard unit, exceeding the norm in 1.5 times. Meanwhile, SOD indicators make 6.98 ± 0.23 standard unit, twice surpassing the control. The 30th day sees the level of catalase amounting to 6.23 ± 0.03 standard unit, thus surpassing the norm twice. SOD indicators ran to 7.13 ± 0.89 standard unit, thus exceeding the control in 2.5 times.

According to table, at the 5-day stage the liquid extract of *Thalictrum Foetidum* in doses of 0.5 ml, 1 ml, 1.5 ml and 2 ml does not lower the level of catalase and SOD significantly as to immobilization stress.

At the 15-day stage the liquid extract of *Thalictrum Foetidum* in all the doses decreases the level of catalase and SOD significantly as to immobilization stress, approaching the control group. Thus, under immobilization stress the level of catalase in the liquid extract of *Thalictrum Foetidum* in doses of 0.5 ml, 1 ml, 1.5 ml and 2 ml amounted to 4.97 ± 0.02 standard unit, 5.02 ± 0.09 standard unit, 4.67 ± 0.43 standard unit and 4.54 ± 0.78 standard unit accordingly. These indicators correspond to statistical significance as regards to the animals' group, subjected to immobilization stress 6.03 ± 0.21 standard unit ($P \leq 0,05$). Under immobilization stress the level of SOD in the liquid extract of

Thalictrum Foetidum in doses of 0.5 ml, 1 ml, 1.5 ml and 2 ml came to 4.21 ± 0.16 standard unit, 4.13 ± 0.04 standard unit, 4.22 ± 0.02 standard unit and 4.08 ± 0.67 standard unit correspondingly. These indicators are significant as to immobilization stress 6.98 ± 0.23 standard unit and the control group of 3.59 ± 0.11 standard unit ($P \leq 0,05$). On the 30th day we observed similar dynamics for all the doses of *Thalictrum Foetidum* liquid extract under research. Thus, under immobilization stress the level of catalase in the liquid extract of *Thalictrum Foetidum* in doses of 0.5 ml, 1 ml, 1.5 ml and 2 ml ran to 4.75 ± 0.67 standard unit, 4.98 ± 0.21 standard unit, 4.78 ± 0.06 standard unit and 4.66 ± 0.01 standard unit accordingly. These indicators correspond to statistical significance as regards to the animals' group, subjected to immobilization stress 6.23 ± 0.03 standard unit ($P \leq 0.05$). Under immobilization stress the level of SOD in the liquid extract of *Thalictrum Foetidum* in doses of 0.5 ml, 1 ml, 1.5 ml and 2 ml came to 3.42 ± 0.34 standard unit, 3.47 ± 0.05 standard unit, 3.47 ± 0.57 standard unit and 3.32 ± 0.07 standard unit correspondingly. This is veritable as regards to immobilization stress 7.13 ± 0.89 standard unit ($P \leq 0.05$).

Conclusions. Thus, according to the results of the experiment on the LPO indicators (CD and TBA-AP), we have determined that under chronic immobilization stress these indicators cannot be corrected significantly as to the control group during a 5-day period. At the 15-day and 30-day stages the liquid extract of *Thalictrum Foetidum* in the doses under study lowered the level of CD and TBA-AP according to statistical significance as to immobilization stress, approaching the control. Moreover, it has been established that increased doses of the liquid extract of *Thalictrum Foetidum* exert an insignificant effect on the LPO indicators in the rats' blood.

Taking into consideration the experimental results of the antioxidant system (catalase and SOD) under chronic immobilization stress, we may draw the conclusion that these indicators cannot be corrected significantly as regards to the control within a 5-day period. Only a 15-day stage and 30-day stage saw the liquid extract of *Thalictrum Foetidum* in the doses under research lower the level of catalase and SOD significantly as to immobilization stress, approaching the control group.

Analyzing the results of the experiment, we can come to the conclusion that the liquid extract of *Thalictrum Foetidum* exerts a very gentle effect on the LPO and antioxidant system under immobilization stress. This holds true as the experimental results show that only at the 15-day and 30-day period, namely under chronic stress, these indicators decrease significantly as to immobilization stress, approaching the control group.

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СОЗЫЛМАЛЫ ҚИМЫЛСЫЗДАНДЫРУ СТРЕСС ЖАҒДАЙЫНДА ЕГЕУҚҰЙРЫҚТАҒЫ ЛИПИДТЕРДІҢ ТОТЫҒУ КҮЙІНЕ ЖӘНЕ АНТИОКСИДАНТТЫ ЖҮЙЕГЕ РУТВИЦА САСЫҚ СЫҒЫНДЫСЫНЫҢ ӘСЕРІН ЗЕРТТЕУ

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ИССЛЕДОВАНИЕ ВЛИЯНИЯ ЭКСТРАКТА РУТВИЦЫ ВОНЮЧЕЙ НА СОСТОЯНИЕ ПЕРЕКИСНОГО ОКИСЛЕНИЯ ЛИПИДОВ И АНТИОКСИДАНТНОЙ СИСТЕМЫ У КРЫС В УСЛОВИЯХ ХРОНИЧЕСКОГО ИММОБИЛИЗАЦИОННОГО СТРЕССА

Аннотация. В экспериментальных условиях исследована возможность коррекции свободнорадикального окисления липидов мембран крыс путем перорального введения водного экстракта рутвицы вонючей, содержащего комплекс природных антиоксидантов.

Для проведения эксперимента животные были разделены на 6 групп по 6 животных в каждой группе. Животным 1-й группы – интактные (условная норма), и животным 2-й группы, которые подвергались стрессу путем иммобилизации в течение 5 часов, перорально внутрижелудочно через зонд вводили дистиллированную воду объемом 1,5 мл. Животным 3-й, 4-й, 5-й и 6-й групп перорально внутрижелудочно через

зонд вводили по 0,5 мл, 1,0 мл, 1,5 мл и 2,0 мл соответственно экстракта рутвицы вонючей каждые сутки за 1 час до экспозиции стресса. Иммобилизационный стресс моделировали путем каждодневного удерживания крыс в течение 5 часов в пластиковых клетках-пеналах. Животных всех групп декатировали под эфирным наркозом через 5 часов после моделирования иммобилизационного стресса, то есть на фоне максимальной экспозиции стресса. Для эксперимента использовали сыворотку крови. Определяли перекисное окисление липидов, а именно: уровень первичных продуктов окисления – диеновых конъюгатов и вторичных продуктов – малонового диальдагида и состояние антиоксидантной системы, а именно: активность каталазы и супероксиддисмутазы спектрофотометрическим методом. С целью выявления изменений исследуемых показателей, их определяли у контрольных и экспериментальных животных через 5, 15 и 30 суток.

Анализируя результаты исследования, можно сделать вывод, что жидкий экстракт рутвицы вонючей оказывает очень мягкое воздействие на состояние перекисного окисления липидов и антиоксидантной системы в условиях иммобилизационного стресса, потому что по результатам эксперимента только на этапе 15-ти и 30-ти суток, то есть в хроническом стрессе, эти показатели статистически достоверно снижаются относительно иммобилизационного стресса, приближаясь к контролю.

Ключевые слова: рутвица вонючая, жидкий экстракт, иммобилизационный стресс, антиоксидантная система, перекисное окисление липидов.

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