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## **INFLUENCE OF LECITHINS ON DISORDERS OF COGNITIVE FUNCTIONS OF ANIMALS CAUSED BY TETRACHLOROMETHANE**

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**Ключевые слова:** *лецитины сои и подсолнечника, когнитивные функции, тетрахлорметан*

**Abstract. Influence of lecithins on disorders of cognitive functions of animals caused by tetrachloromethane. Svirgun I.S., Mohammed Adab, Koshelev O.S., Drozdov O.L.** Nowadays the study of the influence of soya and especially sunflower lecithin as one of the natural monopolies in Ukraine, on the state of cognitive functions is relevant. Specified neurotropic activity of lecithin is characterized by the obstacle to the development of behavioral manifestations of neurotoxic action of carbon tetrachloride, prevention of inhibition of mobility, research, unconditional reflex activity. In this article the determination of the effects of soy lecithin (L), and sunflower lecithin (SL) on a state of cognitive processes in rats showed that there were no significant differences between them. Changes in memory were judged by conventional passive-defensive reactions. Conditional reaction of passive avoidance (passive avoidance reaction) was produced on the basis of a single electrodermal support. We proposed modified method of assessing the presence of individually obtained memory trace and a group of genetically fixed form of memory. The establishment of this fact enables to make a comparative analysis of changes caused by the two lecithins in reproduction of individually obtained memory trace. Lecithin, derived from both plants in conditions of intoxication with carbon tetrachloride prevents and improves reproduction of conditional reaction of passive avoidance. Soy lecithin and sunflower lecithin prevent the development of behavioral manifestations of neurotoxic action of carbon tetrachloride, preventing inhibition of mobility, research, unconditional reflex activity and cause expressive anti-amnesic effect contributing to the course of protective instinctive behavior in recognition of new circumstances as a safe. Both lecithins of plant origin exhibit the improving effect on the course of cognitive processes and their neuro-hormonal mechanisms in conditions of poisoning with carbon tetrachloride. Sunflower lecithin has more antidepressant, nootropic effect whereas soy lecithin has been demonstrated to have significant anti-amnesic effect.

**Реферат. Влияние лецитинов на ростройство когнитивных функций животных, вызванное тетрахлолметаном. Свиргун И.С., Мухаммед Адаб, Кошелев О.С., Дроздов О.Л.** В наше время актуальным является изучение влияния лецитина сои и особенно лецитина подсолнечника, как одной из естественных монополий Украины, на состояние когнитивных функций. Указанная нейротропная активность лецитина характеризуется препятствием развития поведенческих проявлений нейротоксического действия четыреххлористого углерода, предотвращением угнетения подвижности, исследовательской, безусловно-рефлекторной активности. В данной статье определение влияния лецитина (Л) сои и лецитина подсолнечника на состояние когнитивных процессов у крыс показало, что между ними не имеется существенных различий. Об изменениях памяти судили по условной пассивно-защитной реакции. Условную реакцию пассивного избегания (УРПИ) производили на основе одноразового электрокожного подкрепления. Нами предложен модифицированный метод оценки соотношения наличия индивидуально приобретенного памятного следа (УРПИ) и групповой генетически закрепленной формы памяти. Установление этого факта позволяет провести сравнительный анализ изменений, вызванных двумя лецитинами в воспроизведении индивидуально приобретенного памятного следа. Лецитин, полученный из обоих растений, в условиях интоксикации четыреххлористым углеродом предотвращает и улучшает воспроизведение условной реакции пассивного избегания. Лецитин сои и лецитин подсолнечника препятствуют развитию поведенческих проявлений нейротоксического действия четыреххлористого углерода, предотвращая угнетение подвижности, исследовательской, безусловно-рефлекторной активности, оказывает выразительный антиамнестический эффект и способствует течению защитного инстинктивного поведения по распознаванию новых обстоятельств в качестве безопасных. Оба лецитина растительного происхождения проявляют улучшающее влияние на ход когнитивных процессов и их нейро-гормональные механизмы в условиях отравления тетрахлолметаном. Лецитин подсолнечника обладает больше антидепрессивным, ноотропным эффектом, тогда как лецитин сои продемонстрировал более значимый антиамнестический эффект.

Nowadays experts of the World Health Organization propose to define nootropic drugs as those that have a direct activating effect on learning processes, improve memory and mental activity, as well as increase the resistance of the brain to aggressive influences [9].

Today, this group, together with medicinal substances, includes herbal medicines with their impurities, functional food products and food impurities, primarily lecithin (L), nutraceuticals, which mostly contain various herbal components, vitamins, fatty acids, phospholipids, antioxidants, amino acids, minerals, etc. [8].

Among the identified biological properties of L, attention is drawn primarily to its ability both to

maintain the morphological structure of cell membranes [4] and to regulate their density, permeability to ions and low- and medium-molecular substances, as well as the level of secondary messengers, including  $Ca^{+2}$  or phosphatidylinositol [7]. The ability to change the permeability of cytoplasmic membranes, spreading to platelets, increases the sensitivity of these cells to the influence of aggregating agents [10], and in relation to DP to show a penetrating effect.

Such fundamental properties of L may indirectly indicate the possibility of neurotropic effects, especially under the influence of extreme, in particular toxic, factors.

A significant achievement of today is the recognition of the presence in a diverse group of drugs of 5 leading pharmacodynamic mechanisms of nootropic action. Such identified processes include: increasing blood circulation to the brain, increasing level of neurotransmitters and functioning of their systems in CNS, increasing intensity of energy metabolism in nervous tissue, restoring the functional activity of nerve cells, reducing free radical metabolism and lipid peroxidation, and damage to the membranes of nerve elements by listed above [1, 2].

In this regard, the aim of our work was to determine the effect of L on individually acquired memory in rats under conditions of carbon tetrachloride intoxication.

#### MATERIALS AND METHODS OF RESEARCH

Observations were performed on 96 white sexually mature rats weighing 170.0-240.0 g. Rats were kept in standard conditions with free access to water and food in the vivarium settings of "DMA". All experiments were performed in accordance with the rules of ethical treatment of animals, approved by the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1986), as well as the requirements of the commission on bioethics of SE "DMA" of HM of Ukraine, protocol N 6 dated 4.10.2019).

In the experiments carbon tetrachloride (CTC, CCl<sub>4</sub>), GOST 20288-74, manufactured by JSC "Reakhim" (RF), dry non-fat sunflower lecithin (LSF), Ukrainian production, dry fatless food soy lecithin SOLEC (LS), manufactured by SOLAE LLC (USA) were used.

The state of the nervous system of animals was judged by changes in the conditioned response of passive avoidance (CRPA).

CRPA was performed using a disposable electrodermal reinforcement, repeatedly mentioned earlier [6]. The experimental unit consisted of two chambers connected by a round opening: a large illuminated and a small dark one with an electrified floor. To produce a conditioned response (CR), the rat was placed in the middle of the illuminated chamber with its tail up to the passage into the dark part. Exploring space, the animal found an opening to the dark chamber and penetrated into it. The latent period of the CRPA covered the time from the moment the animal was placed in the unit until it completely moved to the dark compartment. In 15 seconds alternating current (50 Hz, 2-3 s, 10 ms) was applied to the lattice floor of the chamber, the value of which was determined individually for each animal. The rat which ran to the illuminated com-

partment was under observation for 3 minutes and if it did not attempt to return to the dark room, the CRPA was considered to have been produced in one combination. Animals that re-entered the dark chamber during 3 minutes were excluded from the experiment [5]. A model of endogenous intoxication was created by intragastric administration of CTC diluted twice in olive oil at a dose of 2.5 g / kg on day 1, 3 and 7 of observations [3].

A group of rats with a model of intoxication intragastrically received a 20% suspension of soy or sunflower lecithin at 2.5 g/kg of body weight. A control volume of isotonic sodium chloride solution was administered daily intragastrically to the control group of rats.

In these groups of animals, the manipulations were performed in 3 hours and then in 30 minutes, the rats were again tested for the preservation of the CRPA.

Statistical processing of results for quantitative indicators was performed taking into account the Student's t-test, for qualitative – by comparing the radians of the indicators, data processing was also performed using a personal computer using software STATISTICA 6.1 (StatSoftInc., Serial N AGAR909E415822FA) and Microsoft Excel (Microsoft Office 2016 Professional Plus, Open License 67528927).

#### RESULTS AND DISCUSSION

To determine the presence of neurotropic activity in L, we studied changes in the cognitive functions of the brain in rats (behavior and individually acquired species memory) under conditions of CTC poisoning.

Comparison of latent periods (LP) (Tables 1, 2) of penetration into the dark compartment in both amnesized with electric current (hereinafter) animals and those that have preserved CRPA after electroconvulsive exposure (in groups to determine the effects of LS and LSF), showed the absence of significant differences between them. Establishing this fact allows for a comparative analysis of the changes caused by both lecithins in the reproduction of an individually acquired memory trace.

Under the influence of electric current in animals that lost the CRPA, the time of "entry" to the dark burrow probably decreased by 33.9% (Table 1). The use of LS already in 30 minutes led to the restoration of CRPA in 33.3% ( $p < 0.05$ ) of rats and a significant prolongation of its LP by 107.9%. Subsequently, the anti-amnesic effect of this L increased, achieving an improvement in skill reproduction in 67.0% ( $p < 0.05$ ) of animals and an increase in the time of movement to the dark chamber of the labyrinth by 62.5% ( $p < 0.05$ ).

Table 1

**Impact of soy lecithin on reproduction of CRPA in rats under conditions of carbon tetrachloride intoxication**

Series of research		Animals amnesized		Animals with preserved CRPA	
		% of animals with CRPA	LP of entry into opening (sec.)	% of animals with CRPA	LP of entry into opening (sec.)
Learning	M	0	16.62	0	13.15
	±m	-	2.19	-	1.57
After electric shock	M	0	11.04 *	100.0	0
	±m	-	1.43	-	-
30 min. after usage	M	33.3 **	34.55 **	25.0 **	27.33
	±m	-	1.86	-	4.60
day 7 after usage	M	50.0 * **	28.83	25.0 **	32.50
	±m	-	7.05	-	4.30
day 14 after usage	M	67.0 * **	27.00 **	30.0 **	69.00
	±m	-	3.47	-	6.10

Note: \* – p<0.05 when compared with learning; \*\* – p<0.05 when compared with LP after electric shock.

Another effect of LS was on the preservation of memory engrams in non-amnesized rats. A significant increase in the CRPA decrement in relation to the effects of electric current was observed on day 1,

7 and 14 of the experiments, when only 25.0%, 25.0% and 30.0% of animals retained conditional individual skill, respectively, and LP reactions tended to increase, not changing significantly.

Table 2

**Impact of soy lecithin on reproduction of CRPA in rats under conditions of carbon tetrachloride intoxication**

Series of research		Animals amnesized		Animals with preserved CRPA	
		% of animals with CRPA	LP of entry into opening (sec.)	% of animals with CRPA	LP of entry into opening (sec.)
Learning	M	0	21.00	0	17.00
	±m	-	2.43	-	2.59
After electric shock	M	0	18.29	100.0	0
	±m	-	1.93	-	-
30 min. after usage	M	11.1	20.18	71.4 * ●	11.00 *
	±m	-	4.14	-	0.71
day 7 after usage	M	46.6 * **	42.0	85.7 * ●	60.00 * ●
	±m	-	7.50	-	5.73
day 14 after usage	M	53.3 * **	13.64 *	71.4 *	68.5
	±m	-	1.52	-	15.27

Note: \* – p<0.05 when compared with learning; \*\* – p<0.05 when compared with LP after electric shock, ● – p<0.05 when compared with impact of LS.

At the same time, it should be emphasized that such changes had a statistically significant discrepancy with the dynamics of loss of passive-protective reaction by the control group of rats only in 30 minutes after application of LS.

When using LSF in the conditions of CTC poisoning, both changes similar to those detected on the background of the action of LS and significantly different from them were observed (Table 2).

In amnesized rats, sunflower L caused changes close to those established with the use of LS, with the recovery of CRPA on day 1 in 11.1%, and on day 7 and 14 on average in 47%-53%, this (in recent cases) significantly exceeded the initial and the indicators established under the influence of an electric current. In contrast to LS, LP of CRPA with the use of LSF decreased slightly.

#### CONCLUSIONS

Determination of the effect of soy L and sunflower L on the state of cognitive processes in rats showed:

1. There are no significant differences between them. L, obtained from both plants, in conditions of

CTC intoxication prevents the suppression of mobility, research and unconditional reflex activity and improves the reproduction of CRPA.

2. At the same time, LSF, in contrast to LS, shows a greater ability to reduce anxiety in animals, i.e. demonstrates antidepressant and higher nootropic activity.

3. LS showed a more significant anti-amnesic effect.

Conflict of interest. The authors declare no conflict of interest.

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