



New Day in Medicine
Новый День в Медицине

NDM



TIBBIYOTDA YANGI KUN

Ilmiy referativ, marifiy-ma'naviy jurnal



AVICENNA-MED.UZ



ISSN 2181-712X.
EiSSN 2181-2187

11 (49) 2022

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**ТИББИЁТДА ЯНГИ КУН
НОВЫЙ ДЕНЬ В МЕДИЦИНЕ
NEW DAY IN MEDICINE**

Илмий-рефератив, маънавий-маърифий журнал

Научно-реферативный,

духовно-просветительский журнал

УЧРЕДИТЕЛИ:

**БУХАРСКИЙ ГОСУДАРСТВЕННЫЙ
МЕДИЦИНСКИЙ ИНСТИТУТ
ООО «ТИББИЁТДА ЯНГИ КУН»**

Национальный медицинский
исследовательский центр хирургии имени
А.В. Вишневского является генеральным
научно-практическим
консультантом редакции

Журнал был включен в список журнальных
изданий, рецензируемых Высшей
Аттестационной Комиссией
Республики Узбекистан
(Протокол № 201/03 от 30.12.2013 г.)

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11 (49)

2022

ноябрь



Received: 09.10.2022

Accepted: 20.10.2022

Published: 10.11.2022

UDC 616.36-006-06-092-078]577.175.823:577.112.387.088.6

COMPARATIVE ASSESSMENT OF THE RESPIRATION AND OXIDATIVE PHOSPHORYLATION INTENSITY IN THE EXPERIMENT

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✓ *Resume*

The work is devoted to the study of the intensity of cellular respiration and metabolism in toxic liver damage by chemical factors. In chronic poisoning with the pesticide Fozalon, the intensity of respiration and oxidative phosphorylation with the use of the liver pyruvate substrate decreased in all leads and terms of poisoning. The state of the ADP/0 ratio decreased to 87.7; 80.7; 83.4%. So, the intensity of respiration and oxidative phosphorylation with the addition of pyruvate substrate in liver mitochondria in chronic poisoning with Fosalon was suppressed. The specific biochemical mechanisms of the toxic effect of a separate representative of organophosphorus pesticides – Fosalon and, in general, the entire group of these compounds still remain unclear.

However, we have experimentally studied the main patterns of the development of biochemical disorders in the body of experimental animals under the influence of Fosalon, their orientation, depth and sequence give additional valuable information to the hands of hygienists, toxicologists, researchers, clinicians, which can be used to select early indicators of intoxication – sensitive diagnostic tests, means of prevention and treatment of these intoxications. By analyzing the obtained the author drew the appropriate conclusions from the results.

Key words: experiment, toxicology, biologically active substances, phyto preparations, phosphorylation, liver, toxic lesion.

СРАВНИТЕЛЬНАЯ ОЦЕНКА ДЫХАНИЯ И ИНТЕНСИВНОСТИ ОКИСЛИТЕЛЬНОГО ФОСФОРИЛИРОВАНИЯ В ЭКСПЕРИМЕНТЕ

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✓ *Резюме*

Работа посвящена изучению интенсивности клеточного дыхания и метаболизма при токсическом поражении печени, вызванном химическими факторами. При хроническом отравлении пестицидом Фозалон интенсивность дыхания и окислительного фосфорилирования с использованием пируватного субстрата печени снижалась во всех отведениях и сроках отравления. Состояние отношения АДФ/О снизилось до 87,7; 80,7; 83,4%. Так, интенсивность дыхания и окислительного фосфорилирования с добавлением пируватного субстрата в митохондриях печени при хроническом отравлении фосалоном угнеталась. Конкретные биохимические механизмы токсического действия отдельного представителя фосфорорганических пестицидов - фосалона и в целом всей группы этих соединений до сих пор остаются невыясненными. Однако экспериментально изученные нами основные закономерности развития биохимических нарушений в организме подопытных животных под влиянием фосалона, их направленность, глубина и последовательность дают дополнительную ценную информацию в руки гигиенистов, токсикологов, исследователей, клиницистов, которые могут быть использованы для выбора ранних признаков интоксикации – чувствительных диагностических тестов, средств профилактики и лечения этих интоксикаций. Анализируя полученные результаты, автор сделал соответствующие выводы.

Ключевые слова: эксперимент, токсикология, биологически активные вещества, фитопрепараты, фосфорилирование, печень, токсическое поражение.

TAJRIBDA NASAF OLIISH VA OKSIDATIV FOSFORILLANISH INTENSIVLIGINI QIYOSIY BAHOLASH

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Farg'ona tibbiyot instituti sog'liqni saqlash

✓ Rezyume

Ish kimyoviy omillar ta'sirida jigarining toksik shikastlanishida hujayrali nafas olish va metabolizm intensivligini o'rganishga bag'ishlangan. Fozalon pestitsid bilan surunkali zaharlanishda jigar piruvat substratidan foydalanish bilan nafas olish va oksidlovchi fosforlanish intensivligi zaharlanishning barcha belgilari va muddatlarida pasaydi. ADP/0 nisbati holati 87,7 ga kamaydi; 80,7; 83,4%. Shunday qilib, Fosalon bilan surunkali zaharlanishda jigar mitoxondriyalarida piruvat substrat qo'shilishi bilan nafas olish va oksidlovchi fosforillanish intensivligi bostiriladi. Organofosforli pestitsidlarning alohida vakili - Fosalon va umuman, ushbu birikmalarning butun guruhining toksik ta'sirining o'ziga xos biokimyoviy mexanizmlari hali ham noaniq bo'lib qolmoqda.

Biroq, biz eksperimental ravishda Fosalon ta'sirida tajriba hayvonlari organizmida biokimyoviy buzilishlar rivojlanishining asosiy qonuniyatlarini o'rganib chiqdik, ularning yo'nalishi, chuqurligi va ketma-ketligi gigienistlar, toksikologlar, tadqiqotchilar, klinisyenlar qo'llariga qo'shimcha qimmatli ma'lumotlar beradi. intoksikatsiyaning dastlabki ko'rsatkichlarini tanlashda foydalanish mumkin - sezgir diagnostik testlar, ushbu intoksikatsiyalarning oldini olish va davolash vositalari Olinganlarni tahlil qilish orqali muallif natijalardan tegishli xulosalar chiqardi.

Kalit so'zlar: eksperiment, toksikologiya, biologik faol moddalar, fitopreparatlar, fosforlanish, jigar, toksik lezyon.

Relevance

Environmental medicine studies and evaluates the effects of environmental factors both in individuals and in populations or its various subgroups. Each examined person considered as a unique individual, exposed to very specific environmental conditions and requiring, accordingly, individual prophylaxis and/or therapy. Environmental medicine is an integral part of preventive and clinical medicine. It uses the methods of epidemiological analysis, clinical, immunological, genetic and molecular research methods, the results of in-depth studies of the state of the environment, quality of life parameters to establish the specific role of certain environmental factors in the etiology of diseases [1,2,3,11,12,13,15,16]. It is well known that, generalizing the group of chemicals that have a harmful toxic effect on the human body, it is customary to refer to a special group, to the group of pesticides, that is, to chemically diverse structures used to control weeds and plant pests. Along with the term pesticides, the concept of agricultural pesticides used to refer to the above-mentioned compounds. At the same time, depending on the purpose, pesticides divided into several groups, among which the most important in terms of the breadth of use in practice are insecticides used to kill insects. [1,6,9,15,16]. The active substance of toxic pesticides used to destroy plant pests and weeds has a harmful effect on the health of agricultural workers. In addition, there are also fungicides used to combat pathogens of fungal, bacterial and viral plant diseases, substances used to kill ticks, zoocides that destroy rodents, and others [4,5,6,7,8,9,10,11,14].

Morphological and hygienic assessment of the changes in the body under experimental conditions and development of preventive measures is one of the urgent problems of today

The purpose of the study. Comparative assessment of the intensity of oxidative phosphorylation in the experiment on the background and without the use of biologically active substances to assess the effectiveness of preventive measures against the toxic effect of chemical factors on the liver.

Material and methods

As experimental animals were used white male rats with an initial weight of 150-220 g, which were in standard conditions and on ordinary laboratory feed throughout the experiments. 2 series of experiments were conducted using 138 rats. The studies were carried out in comparative terms with the

reproduction of models of toxic liver damage: with the use of medicines (BAS, herbal remedies). The intensity of oxidative phosphorylation was studied in dynamics in all groups of the experiment. The phosphorylation efficiency (ADP/O ratio) was calculated by the Hour-Vilgis: the respiration rate of the tissue was expressed in micromoles of oxygen per minute (mkAO₂/min).

Result and discussion

In chronic poisoning with the pesticide Fosalon, the intensity of respiration and oxidative phosphorylation with the use of the liver pyruvate substrate decreased in all leads and terms of poisoning. At the same time, the oxidation rate in an environment with an oxidation substrate decreased to 73.4 on the 30th, 60th and 90th days of poisoning, respectively; 73.6 and 69.8%, the rate of oxidation with the addition of ADP – decreased to 77.5-71.9% and the rate of respiration after phosphorylation at the V₄ position and amounted to 20.1±0.75 microns/0 on 30-80 days with the control of 27.73±1.29 mmol 2, the rate of respiration with the addition of DNF (inhibitor) decreased during all study periods (DNF), the changes amounted to 103.2-113.4%. The state of the ADP/O ratio decreased to 87.7; 80.7; 83.4% on the 30th, 60th and 90th days of priming. So, the intensity of respiration and oxidative phosphorylation with the addition of pyruvate substrate in the liver mitochondria in chronic poisoning with Fosalon is suppressed.

Table 1 shows the effect of the pesticide Fosalone at a dose of 1/20 LD₅₀ on the rate of respiration and oxidative phosphorylation of succinic acid substrate (succinate) in liver mitochondria.

Table 1
The state of respiration and oxidative phosphorylation of the succinic acid substrate during poisoning with Fosalon

Research days	Stat. indicators	V ₂ (mkAO ₂)	V ₃ (mkAO ₂)	V ₄ (mkAO ₂)	DK	ADP/O
Control	Msr±m %	20,18±0,55	30,62±1,09	23,97±1,09	1,34±0,10	2,07±0,07
Experience 30 day	Msr ±m %	17,28±0,79* 85,6%	26,58±1,19** 86,9%	20,17±0,95 84,1%	1,33±0,09 99,2%	1,82±0,08* 87,9%
Experience 60 day	Msr ±m %	17,42±0,80 86,3%	27,27±1,12* 89,1%	19,83±1,23* 82,7%	1,47±0,14 109,7%	1,74±0,08* 84%
Experience 90 day	Msr ±m %	17,13±0,83* 84,9%	26,18±0,98* 85,5%	18,02±0,73** 75,2%	1,47±0,11 109,7%	1,20±0,10** 57,9%

Note: confidence in relation to control: *-p<0.05; **-p<0.01; ***-p<0.001

At the same time, in animals of the control groups in positions V₂ was 20.18±0.55 mkAO₂, V₃ – 30.62±1.39, V₄ – 23.97±1.09 kAO₂, and respiratory control, respectively, ADP/O was at the level of 1.34±0.10 and 2.07±0.07. When succinic acid was used in poisoned animals in position V₂, it decreased to 85.6, 86.3 and 89.9% during all periods of the experiments. In the V₃ and V₄ positions, it also decreased to 85.5-86.9% and 75.2-84.1%, the DC changes were disproportionate. ADF/O indicators decreased 57.9-87.9% at all times. Consequently, the use of succinate substrate, the intensity of respiration and redox processes in the liver is inhibited by Fosalon poisoning. When using citric acid substrate in liver mitochondria, the intensity of oxidative phosphorylation and respiration decreases, as with the use of substrates (Table 2).

At the same time, respiration and phosphorylation indicators in the V₂, V₃ and V₄ positions in the control group animals decrease at all times.

The oxidation rate with the oxidation substrate of the control group was 22.7±0.74 mkAO₂, V₃ – 33.3±0.92.

Table 2.

The state of respiration and oxidative phosphorylation of citric acid substrate in case of Fosalon poisoning

Research days	Stat. indicators	V ₂ (mkAO ₂)	V ₃ (mkAO ₂)	V ₄ (mkAO ₂)	DK	ADP/O
Control	Msr ±m %	22,7±0,74	33,33±0,92	26,50±1,35	1,24±0,09	1,89±0,06
Experience 30 day	Msr ±m %	18,18±0,74** 80,1%	28,95±0,69** 86,9%	22,13±0,96* 83,5%	1,31±0,05 105,6%	1,49±0,10 78,8%
Experience 60 day	Msr ±m %	18,02±0,89*** 79,4%	27,38±0,90*** 82,1%	19,07±0,72** 71,9%	1,43±0,09 115,3%	1,52±0,08 80,4%
Experience 90 day	Msr ±m %	18,33±0,95** 80,7%	27,73±0,88** 83,2%	18,70±0,89** 70,6%	1,51±0,09 121,8%	1,48±0,08 78,3%

Note: confidence in relation to control: *-p<0.05; **-p<0.01; ***-p<0.001

In the experimental groups with chronic poisoning with the pesticide Fosalon, in terms of citric acid oxidation in the liver, the intensity in positions V₂, V₃ and V₄ at all times (30, 60, 90 days) decreased in relation to the control from 80.1 to 86.9 and 70.6%. The respiratory control index increased to 105.6 and 121.8%, and the state of the ADP/O ratio decreased from 68.8-80.4%. So, the application of citric acid substrate to the intensity of respiration and oxidative phosphorylation in the liver mitochondria is inhibited.

Similar changes were observed in the rate of respiration and oxidative phosphorylation of oxalic-acetic acid (OAA) substrate in the liver during chronic poisoning with Fosalon (Table 3.).

At the same time, in position V₂, at all times (30, 60 and 90 days), the indicators decreased in relation to the control to 71.7-81.8%. In leads, V₃ – up to 75.4-78.9%, and V₄ – also decreased during all periods of the study. With the addition of homogenate, the cessation of the process of dinitrophenylhydrazine respiratory control changes were within the limits of physiological fluctuations. The ratio of adenosine phosphate (ADP) and oxygen decreased to 77.0-82.8%.

Table 3

The state of oxidative phosphorylation of oxaloacetic acid substrate in Fosalon poisoning

Research days	Stat. indicators	V ₂ (mkAO ₂)	V ₃ (mkAO ₂)	V ₄ (mkAO ₂)	DK	ADP/O
Control	Msr ±m %	19,5±0,74	26,9±0,89	20,82±1,06	1,29±0,06	1,74±0,04
Experience 30 day	Msr ±m %	14,0±1,23* 71,7%	20,28±0,90** 75,4%	17,48±0,82 83,9%	1,16±0,05 89,9%	1,44±0,08* 82,8%
Experience 60 day	Msr ±m %	15,95±1,06* 81,8%	21,23±1,31* 78,9%	15,72±0,69* 75,5%	1,36±0,09 105,4%	1,44±0,05 82,8%
Experience 90 day	Msr ±m %	14,73±1,04* 75,5%	19,72±0,81 73,0%	16,6±0,83* 79,7%	1,19±0,04 92,2%	1,34±0,04** 77,0%

Note: confidence in relation to control: *-p<0.05; **-p<0.01; ***-p<0.001

So, the data obtained indicate that the intensity of tissue respiration and oxidative phosphorylation of succinate, pyruvate, citric and oxalic-acetic acid substrates metabolized through the tricarboxylic acid cycle in liver mitochondria under the influence of the pesticide Fosalon was observed inhibition of processes.

Thus, when exposed to a pesticide of the FOS – Fosalon group in the liver and blood of experimental animals, an increase in pyruvic acid and a decrease in the amount of glycogen in the studied biological media are observed. These phenomena indicate the stimulation of glycolysis and some inhibition of the



tricarboxylic acid cycle. The highest rate of anaerobic breakdown of carbohydrates and inhibition of their further utilization in liver tissue. Changes in the activity of redox enzymes - GDH, MDH, SDH and LDH, the intensity of respiration and oxidative phosphorylation in liver mitochondria were also revealed.

The specific biochemical mechanisms of the toxic effect of a separate representative of organophosphorus pesticides – Fosalon and, in general, the entire group of these compounds remain unclear. However, we have experimentally studied the main patterns of the development of biochemical disorders in the body of experimental animals under the influence of Fosalon, their orientation, depth and sequence give additional valuable information to the hands of hygienists, toxicologists, researchers, clinicians, which can be used to select early indicators of intoxication – sensitive diagnostic tests, means of prevention and treatment of these intoxications.

Thus, with chronic pesticide poisoning, there was a decrease in the synthesis or breakdown of total protein and an increase in nitrogen and pigment metabolism in the blood serum, which indicates a violation of the functional state of the liver. With chronic poisoning with the pesticide Fosalon, there is a decrease in the level of glycogen and the activity of mitochondrial enzymes – glutamate, succinate, malate dehydrogenase and an increase in lactate dehydrogenase in liver tissue. The intensity of tissue respiration and oxidative phosphorylation of succinate, pyruvate, citric and oxaloacetic acid substrates metabolized through the tricarboxylic acid cycle in the liver mitochondria under the influence of the pesticide Fosalon, inhibition of processes is observed.

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Entered 15.10.2022