

Research Article

Endogenous Intoxication of Oligoether in Experimental

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Abstract

The study of the effect of oligoether L-1601 on the level of dopamine, adrenalin, norepinephrine, DOPA, tryptophan, serotonin, cAMP, cGMP was conducted. Studies have shown a different orientation of the substance to the adrenergic, dopaminergic and serotonergic systems. In the experiment 20 white rats (N = 20) were used. In each group, both in the experimental and in the control, there were 10 animals (n = 10). The cycle of cyclic nucleotides in the blood plasma and in the organs of the biliary strains was visibly radiated by the immunologic method with reactants of company Amersham International (Great Britain). The observed increases in the level of cAMP in the blood plasma and a decrease in the level of cGMP in the plasma indicate activation of adaptive mechanisms aimed at providing the homeostatic function of the organism under subacute toxication with the xenobiotic.

Keywords: Biogenic Mediators; Oligoether; White Rats

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Introduction

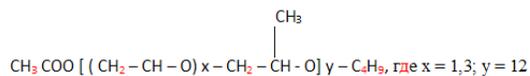
The aggravated environmental problem of the present, due to the sharp limitation of water supply of settlements, which was due to increased pollution of water ecosystems by industrial waste water, which adversely affects the health of the population. The solution of this issue requires an in-depth study of the molecular structural and metabolic mechanisms underlying the formation of pathological states, the disturbance of homeostasis when exposed to the body of xenobiotics. Neurotransmitters (cyclic 3'5'-adenosine monophosphate - cAMP and cyclic 3'5'-guanosine monophosphate - cGMP) belongs to the great importance in maintaining of homeostasis. Known close association of exchange of cAMP with biogenic amines - norepinephrine, adrenaline, dopamine, serotonin, GABA, glutamic acid and phosphorylation [1]. In this regard, the great interest is the study of the activity of neurotransmitters and secondary messengers under the influence of the oli-

goethers on the organism in order to substantiate their mechanism of biological action [2-4]. After all, evaluation of the indicators of the system of biogenic amines provides a basis for understanding the pathogenesis of the development of clinical manifestations of intoxication [5-8]. The purpose of the study was to study the influence of oligoethers in a subacute toxicological experiment on the metabolism of biogenic amines and cyclic nucleotides in the context of their oral administration to warm-blooded animals.

Objects and Methods of Research

The subject of the study was endogenous intoxication of the body of warm-blooded animals under the influence of chemicals. The research program included subacute experiments on mature white rats weighing 180-200 grams, which for 45 days were orally exposed to xenobiotics in small doses of 1/100 LD₅₀. The substance in the form of an aqueous solution was administered to the experimental animal (N=20, n=10) orally, using a metal probe, in the morning before feeding the animals. In each group, both in the experimental and in the control, there were 10 animals. In the experiment, 20 white rats were used in compliance with the main rules of GLP (1981), the rules for laboratory animals (1977), the Council of Europe Convention for the Protection of Animals, the

European Convention for the Protection of Vertebrates, which are used for experimental and other scientific purposes “(Strasbourg, 1986), EEC Directive № 609 (1986) and Order of the Ministry of Health of Ukraine № 281 of 01.11.2000” On Measures for the Further Improvement of Organizational Standards of Work with the Use of Experimental Animals”, “General Ethical Principles of the Ex” approved by the First National Congress on Bioethics, Kyiv, 2001, the Law of Ukraine” On the Protection of Animals against Cruel Treatment” of February 21, 2006, № 3477 - 1U, which is confirmed by the conclusion of the Commission on Bioethics. As a research object, the oligoether of the molecular mass of MM was used 1600, which had accordingly the product name oligoestr brand: L-1601, with regulated physico-chemical properties. “LaProl 1601 - 2 - 50” P “(L - 1601” P “) - acetyls of polyoxypropylene oxyethylene glycol monobutyl ether, transparent viscous liquid, well soluble in water and organic solvents, molecular weight 1600; Specific gravity, g / cm³ 1,04; functionality 1; the content of hydroxyl groups (%), not more than 1,0 - 1,2; acid number, mg KOH / g, not more than 0,1; PH (methanol: water 70: 30) 6.5 - 8.0; Hepler viscosity at 25°C (mPa · C) 160 - 230; flash temperature 210°C.



He is present in the molecule of an oligoether of a hydrophilic group and of hydrophobic radicals provides them with special surface-active properties. The calculation of intermediate-dose doses (LD₅₀) was performed according to the Deimah, Kerber, and Bernese method. Cumulative oligoethers were studied by the Lim method. Doses were chosen in such a way as to determine the lethal effect in the range of lethal doses LD₀-LD₁₀₀. Animal observations were carried out within 15 days. Recorded the time of death of animals and the total amount of the administered substance. The evaluation of the results was based on the average effective time of animal death. Dead animals and animals that survived were subject to further macroscopic and microscopic examination. Based on the parameters of acute toxicity, the substance belongs to moderate and low toxic substances (3.4 hazard class), which do not possess cumulative properties. The mediated dose of LD₅₀ for white rats was set at a level of 5.17 g / kg body weight, and a cumulative coefficient of 7.13, for L-1601 -2-50 «P». The choice of the study group of xenobiotics was based on the lack of information in the scientific literature on mechanisms of damage to oligoesters, large volume of their production and wide contact with the population, as well as the absence of a prognostic assessment of the potential hazard of oligoesters for humans and the environment.

This substance is widely used in various sectors of the national economy for the production of polyurethanes, enamels, varnishes, foam, epoxy resins, artificial leather, brake, hydraulic and cooling liquids. On the basis of toxicity parameters, it refers to moderate and low-toxic compounds (grade 3-4 of hazard), which

does not possess cumulative and skin-irritating properties. The content of cyclic nucleotides in blood plasma and organs of white rats was determined by immune method using Amersham International (United Kingdom) reagents. The method is based on the competitive relationship between the trasylere and the non-radioactive antigen in reaction with antibodies. The determination of radioactivity was carried out using a rare scintillation counter SBS-2 according to a generally accepted methodology. The activity of the adenylate cyclase system was evaluated in preparations of membranes by liver microsomes and synaptosis of the brain of white rats according to the generally accepted method of cAMP RIA KIT (Czech Republic). The activity of adenylate cyclase was determined by the level of cyclic adenosine monophosphate (cAMP).

Results

The results of the study showed that the chemical compound at a dose of 1/100 LD₅₀ disturbs the exchange of nutrient amines and cyclic nucleotides.

In the study, we found the most significant differences with oligoether control at a dose of 1/100 LD₅₀. We have studied some aspects of the metabolism of biogenic amines and their precursors as well as the activity of intracellular cGMP and cAMP mediators under conditions of a subacute experiment on white rats in the case of oligoether exposure of 1/100 LD₅₀. The content of adrenaline, norepinephrine, DOPA, dopamine, tryptophan, serotonin in the liver and the brain was studied. Oligoether L-1601 at a dose of 1/100 LD₅₀ lowered the DOPA level and increased the level of norepinephrine in the brain. In the liver, L-1601 reduced the content of DOPA, dopamine, norepinephrine and adrenaline (Table 1).

Indicators		Control	L-1601 (1/100 LD50)	The differences
B	DOPA	2,02±0,12	1,84±0,28	p >0,05
R				
A				
I	Dopamine	3,45±0,54	4,06±0,53	p >0,05
	Norepinephrine	0,77±0,22	2,61±0,67	p <0,05
N	Adrenalin	1,110±0,002	0,12±0,07	p >0,05
L	DOPA	4,01±0,31	3,40±0,11	p <0,05
I				
V				
E	Dopamine	1,76±0,19	1,08±0,26	p <0,05
	Norepinephrine	0,81±0,10	0,76±0,25	p >0,05
R	Adrenalin	0,15±0,02	0,08±0,02	p <0,05

Table 1: Influence of oligoethers on biogenic monoamines in the subacute experiment.

The influence of substances on the concentration of precursors of biogenic monoamines revealed that L-1601 1/100 LD₅₀ did not affect the accumulation of tryptophan in the brain, but reduced its content in the liver (Table 2).

Indicators		Control	L-1601 (1/100 LD50)	The differences
B	Tryptophan	5,95±0,89	5,68±0,91	p >0,05
R				
A				
I	Serotonin	2,68±0,70	5,85±0,55	p <0,05
N				
L	Tryptophan	14,00±2,53	8,98±2,22	p <0,05
I				
V				
E	Serotonin	3,03±0,76	8,99±1,46	p <0,05
R				

Table 2: The content of serotonin and tryptophan in white rats under the influence of oligoesters (µg / g tissue).

The level of serotonin in the experiment increased both in the liver and in the brain. Taking into account the influence of oligoethers on biogenic mediators (adrenaline, noradrenaline, serotonin, DOPA, dopamine, tryptophan), there is a reason to expect changes in the state of intracellular mediators (cAMP and cGMP). At the next stage of the study, the effect on the system of the cyclic nucleotides of the internal organs and blood plasma under the conditions of oral effect of L-1601, at a dose of 1/100 LD₅₀ was studied.

Oligoethers in the study dose of 1/100 LD₅₀ lowered cAMP levels in the liver, kidneys, spleen; in the blood plasma of rats increased - cAMP and reduced - cGMP (Table 3). Reduced cAMP concentration in the organs, accompanied by an increase in its plasma content. The results of the experiments allow us to conclude about the structural and metabolic disturbances of mediator regulation of cellular units under the influence of oligoether.

Bodies	Control	L-1601	The differences
Content of cAMP in organs (nmol / g)			
Liver	170,12±12,01	106,32±13,75	p <0,05
Kidney	210,35±17,04	150,96±14,23	p <0,05
Spleen	188,24±14,85	161,53±29,84	p <0,05
The content of cAMP and cGMP in plasma (nmol / ml)			

cAMP	115,13±12,46	180,32±14,17	p <0,05
cGMP	9,10±0,86	6,90±0,98	p <0,05

Table 3: Content (total number per unit weight) of cAMP in organs and tissues and in blood plasma of white rats under the influence of oligo-ester (dose - 1/100 LD₅₀).

Discussion

The study compound at a dose of 1/100 LD₅₀ reduces the levels of biogenic amines (which have a close relationship with cAMP-norepinephrine, adrenaline, dopamine, serotonin in the liver and brain of rats compared to control. Oligoether-L-1601 has almost no effect on the level tryptophan in the rat brain, and in the liver these parameters were lower than the control (p <0,05). Consequently, the decrease in the concentration of cAMP in the organs was accompanied by an increase in their content in plasma blood of experimental rats. The results of experiments allow us to conclude about the structural and metabolic disorders of mediator regulation of intracellular structural and metabolic units under the influence of oligoether. Detection of violations in the neurotransmitter mechanism of cellular regulation of the metabolism, which can lead to the development of degenerative and destructive changes of intracellular structures under the influence of molybioferin 1/100 LD₅₀.

Considering from this point of view the obtained results, it can be concluded that the oligoether causes an increase in the content of cAMP in the blood plasma and leads to the development of inhibitory processes, which, apparently, are further exacerbated by a decrease in the concentration of cGMP as an excitatory factor in these conditions. The observed increases in the level of cAMP in the blood plasma and a decrease in the level of cGMP in the plasma indicate the activation of adaptive mechanisms aimed at providing the homeostatic function of the organism under conditions of subacute toxicity with the xenobiotic studied.

Conclusions

Thus, the study of the receptor apparatus of cellular structures plays an extremely important role in understanding the mechanisms of homeostasis and pathogenesis of various diseases and intoxications, in assessing the hormonal regulation of the function of the organism. The analysis of the results of the study shows disintegrated indicators from the level of neurotransmitters in the organs of experimental animals. Thus, a significant inhibitory effect of oligoether in a dose of 1/100 LD₅₀ on lactic AMP in organs was investigated compared to control, which is of great importance in maintaining homeostasis and its increase in plasma.

References

1. Zhukov VI, Popova LD, Zaytseva OV (2000) Simple and macrocyclic ethers: Scientific bases of protection of water bodies. Kharkov: Tornado 438.

2. Byshevsky ASH, Tersenov OA (1994) Biochemistry for the doctor. – Yekaterinburg 383.
3. Piruzyan LA, Koval VI (1974) The action of physiologically active compounds on biological membranes. - Moscow: Nauka 375.
4. Kats MM, Laretskaya EF (1986) Receptors of biogenic amines in the brain: Structural mechanisms of functioning and interaction with physiologically active substances // Itogi of science and technology. BLAME. Bioorganic chemistry 8: 226.
5. Rimarchuk GV (1999) Improvement of children in areas of environmental disadvantage. ML 11: 89-94.
6. Bagmutl Yu (2014) Action of oligoethers on the metabolism of biogenic amines and cyclic nucleotides Materials of the All-Ukrainian Educational-Scientific Conference with International Party "Achievements and Prospects for the Implementation of the Credit-Modular System of Organization Educational Process in Upper Medic (Pharmaceutical) Educational Institutions of Ukraine", dedicated to the 160th anniversary of the birth of I.Ya. Gorbachevsky (with a remote connection of the VM (F) NZ of Ukraine through videoconferencing), the city of Ternopil 577-578.
7. Bagmut Iyu (2014) Influence of oligoether cyclocarbonate P-803 and polyoxyethyleneoxypropylene glycol P-2501-2-50 butylalyl ether in subtoxic doses on the receptor apparatus and intracellular metabolism Scientific-theoretical and practical journal "Contemporary Scientific Journal". – Belgorod 31: 39 - 49.
8. Zhukov VI, Klimenko NA, Bagmut Iyu (2016) The role of regulatory mechanisms in the development of damage to the heart and brain. - Saarbrücken, Germany: Lambert Academic Publishing 120.