EFFECT OF SUBTOXIC EXPOSURE OF OLIGOOXYETHYLENE PRODUCTS ON THE METABOLISM OF PROSTAGLANDINS

Vyshnytska Iryna Anatolyivna,
MSc, PhD of Biochemistry,
Professor of the Medical Biochemistry and Genetics Department,
James School of Medicine, HRDS Inc.,
Anguilla, Great Britain
ORCID: https://orcid.org/0000-0003-3880-201X
Sana Anwar,
MD,
Lugansk State Medical University,
Rivne, Ukraine
Svyrydovska Viktoriia Volodymyrivna,
MD5 student,
Saint James School of Medicine, HRDS Inc.,
Anguilla, Great Britain

The extremely wide range of physiological effects make prostaglandins vital for both normal physiological processes and the body's response to injury or illness [1]. The study of the metabolism of prostaglandins under the oligoethers «Polyols» exposure is a live issue since the oligooxyethylene products have a variety of applications due to their unique properties. They are used as surfactants in detergents and cleaning products; are useful in agriculture for soil improvement; are used in drug delivery systems and as components in medical devices; they are also used in the formulation of various cosmetic products, such as lotions and creams [2].

The aim of the work was to study the content of prostaglandins in the serum of rats, which were subjected to toxification in the subacute experiment with polyethers of the brands L-3003-2-60 and L-3503-2-70.

Materials and methods. The rats were orally exposed to oligo-feeding at the rate of 1/10, 1/100 and 1/1000 of DL_{50} doses for 45 days. The radioimmunological method was used to determine the following indicators using appropriate diagnostic test systems: prostaglandins of group E (PGE, PGE_1, PGE_2) and of group F ($PGF_{2\alpha}$ and 6-keto-$PGF_{1\alpha}$) in the rats liver at the end of subacute toxification.

Results and discussion. «Polyols» in 1/10 and 1/100 of DL_{50} are able to influence metabolic processes in biological membranes, stimulating the activity of phospholipase A_2. This enzyme mobilizes arachidonic acid for the synthesis of PGE, PGE_1 and PGE_2 (Table 1). An increase in the concentration of $PGF_{1\alpha}$ and a decrease in the level of $PGF_{2\alpha}$ (Table 2) indicate a significant strain in the protective-adaptive mechanisms and support for the homeostatic function of the body under animal toxicity conditions 1/10 and 1/100 of DL_{50}.

Table 1

Effect of "Polyols" on the PGsE content in blood serum during long-term subtoxic exposure in a subacute experiment

Experimental groups of rats	Dose, DL_{50}	Indicators, M±m		
		PGE (nmol/ml)	PGE_1 (pg/ml)	PGE_2 (pg/ml)
Control	–	246,8±15,3	2174,5±36,7	1572,6±22,8
L-3003-2-60	1/10	815,6±33,2*	4843,7±51,4*	3265,4±29,5*
	1/100	687,5±29,4*	3987,4±35,6*	2874,3±31,7*
	1/1000	262,7±18,7	2235,2±41,3	1586,3±24,3
L-3503-2-70	1/10	794,3±28,6*	4697,6±43,8*	3183,8±27,9*
	1/100	674,8±32,5*	3869,7±44,5*	2763,7±31,5*
	1/1000	258,3±16,3	2156,8±33,4	1595,7±26,7

Note: in Tables 1–2 * – the difference is probable ($p < 0.05$) with control.

Table 2

Effect of «Polyols» on the PGsF content in blood serum during long-term subtoxic exposure in a subacute experiment

Experimental groups of rats	Dose, DL_{50}	Indicators, M±m	
		$PGF_{2\alpha}$ (pg/ml)	6-keto-$PGF_{1\alpha}$ (pg/ml)
Control	–	18,43±1,67	6,15±0,54
L-3003-2-60	1/10	7,68±0,52*	18,23±1,68*
	1/100	13,56±1,13*	14,76±1,27*
	1/1000	19,66±1,45	7,18±0,63
L-3503-2-70	1/10	8,56±0,72*	17,68±1,44*
	1/100	14,85±1,37*	13,52±1,22*
	1/1000	20,16±1,43	6,79±0,57

It is known that the arachidonic acid, which is a precursor to the synthesis of PGs is present in phospholipids of all cell membranes. Therefore, the results of the study (Table 1) indicate that «Polyols» in 1/10 and 1/100 DL_{50} are able to affect metabolic processes in biological membranes, stimulating the activity of phospholipase A_2. This enzyme mobilizes arachidonic acid for the synthesis of PGE, PGE_1 and PGE_2. At the same time, these xenobiotics activate the second stage of synthesis of PGs by the enzyme cyclooxygenase at these doses [3, 4]. Taking into account the autocrine and paracrine effects of PGs on metabolic processes, numerous disorders of structural and metabolic processes in the cardiovascular, respiratory, digestive and genitourinary systems and internal organs should be expected because of over activity of PGs. And in some cases, they affect organs and tissues remotely, like the classical hormones do [4].

The significant elevation of PGs production can disrupt intracellular metabolism by affecting the activity of membrane-bound enzymes. This disruption can alter the balance of cyclic nucleotides like cAMP and cGMP, which are crucial for various cellular signaling pathways. Additionally, PGs can influence the levels of cofactors and coenzymes, which are essential for numerous biochemical reactions within cells [5]. Considering the main biological effects of PGsE, one can expect the development of inflammatory processes, dilation of bronchial smooth muscles, uterine contractions, suppression of gastric secretion, hypotensive effect – vasodilation, activation of sodium excretion and clearance of free water, inhibition of platelet aggregation, activation of

lipolysis, modulation of the effects of antidiuretic hormone on water transport, and increased peristalsis of the gastrointestinal tract, among others. All these effects can occur under the influence of «Polyols» at 1/10 and 1/100 DL_{50} during prolonged subtoxic exposure in subacute experiments. It is necessary to note that elevated levels of PGE_1 and PGE_2 often indicate the development of oncological diseases [4].

Studies of the effect of oligoethers on serum PGsF showed a decrease in $PGF_{2\alpha}$ concentrations and an increase in 6-keto-$PGF_{1\alpha}$ (prostacyclin) under 1/10 and 1/100 DL_{50} (Table 2).

Thus, «Polyols» L-3003-2-60 reduced the concentration of $PGF_{2\alpha}$ by 58.33 % and 26.42 %, and L-3503-2-70 – by 53.55 % and 19.42 % respectively, in the groups of animals toxicized with 1/10 and 1/100 DL_{50}. The level of prostacyclin in blood serum had the opposite dynamics: L-3003-2-60 increased the content of 6-keto-$PGF_{1\alpha}$ by 196.42 % and 140 %, and L-3503-2-70 – by 187.48 % and 119.84 %, respectively, under the influence of xenobiotics in 1/10 and 1/100 DL_{50} (Table 2).

The posted research indicates that the effects of PGsF in most cases are the opposite of those that occur under the influence of PGsE. They are characterized by vasoconstriction of blood vessels, bronchi, contractions of the uterus, gastrointestinal tract, modulation of the adenylate and guanylate cyclase mediator system, antilipolysis, etc. [4]. An increase in the concentration of $PGF_{1\alpha}$ and a decrease in the level of $PGF_{2\alpha}$ indicate a significant tension of protective and adaptive mechanisms and the maintenance of the homeostatic function of the organism under conditions of toxicification of animals 1/10 and 1/100 DL_{50}.

Conclusions. The results of the study show that «Polyols» in 1/10 and 1/100 of DL_{50} are capable of disrupting the structural and metabolic activity of biological membranes by affecting the activity of phospholipase A_2, cyclooxygenase, phospholipid metabolism and arachidonic acid. Under such conditions, it is necessary to expect numerous damages and dysfunctions of all organs and systems of the body, the functions of which are based on membrane pathology. In 1/1000 of DL_{50} «Polyols» do not affect the metabolism of prostaglandins.

References.

1. Utiger R. D. Prostaglandin. Encyclopedia Britannica. 2024, July 2. URL: https://www.britannica.com/science/prostaglandin.

2. Owoseni O. Surfactants - Fundamental Concepts and Emerging Perspectives. *IntechOpen*. 2024. doi: 10.5772/intechopen.105270

3. Muhalska Y. B., Muhalska Y. B., Gonsky J. I. State of antioxidant system at toxical damage by heavy metals and organophosphorus compounds. Achievements of clinical and experimental medicine: materials of the final scientific-practical conference. Ternopil, 2012. 246 p.

4. Ricciotti E., FitzGerald G. A. Prostaglandins and inflammation. *Arterioscler Thromb Vasc Biol*. 2011. Vol. 31 (5). P. 986–1000. doi: 10.1161/ATVBAHA.110.207449

5. Jang Y., Kim M., Hwang S. W. Molecular mechanisms underlying the actions of arachidonic acid-derived prostaglandins on peripheral nociception. *J Neuroinflammation*. 2020. Vol. 17. P. 30. doi: https://doi.org/10.1186/s12974-020-1703-1