INFLUENCE OF LEAD ACETATE ON LIPID PEROXIDATION IN THE PROCESS OF LIVER MITOCHONDRIAL MEMBRANE AND ITS CORRECTION WITH DHQ-11 CONJUGAT

Ernazarov Z.M[1].,
Pozilov M.K[2].,
Toshmatova Sh.R[3].,
Jurakulov Sh.N[4].
[1]Institute of Biophysics and Biochemistry under the National University of Uzbekistan, Tashkent city.
[2]National University of Uzbekistan named after M.Ulugbek
[3]Kokand State Pedagogical Institute named after Mukimi
[4]Institute of Chemistry of Plant Substances named after Academic S. Yu. Yunusov.

Abstract

In recent years, the development of industrial enterprises has led to an increase in the amount of heavy metals in the soil. The excess of heavy metal compounds, which are considered as adverse environmental factors, in the environment beyond the permissible standards, can lead to the development of various pathological conditions not only in the digestive system, but also in the whole organism. One such heavy metal is lead, which is almost ubiquitous. The widespread use of lead in industrial, domestic, agricultural and modern technological processes has led to its worldwide distribution. More than 50% of lead emissions are released into the environment due to cars running on gasoline [2]. When a person breathes, up to 50% of inorganic lead is absorbed into the blood through the lungs. Adults absorb 15% of lead in food, and children up to 50% through the gastrointestinal tract. The half-life of lead in blood is about 1 month, and in bones it is 20-30 years [9]. Lead affects both male and female reproductive organs. It can cause loss of libido and fertility in men, and menstrual disorders and spontaneous abortion in women [6]. Data on the direct carcinogenicity of lead are insufficient, but according to available data, it may cause lung, stomach cancer and gliomas [7].

The evidence of hepatocarcinogenic effect of Pb^{2+} in toxicological studies conducted on animals became the basis for new studies to study the toxicology of Pb^{2+} from a biochemical and molecular point of view. Under the influence of lead, the amount of hemoglobin in the blood, the activity of superoxide dismutase and catalase enzymes significantly decreased. The amount of reactive oxygen species (ROS) and thiobarbituric acid in the blood increased significantly [1]. Mitochondria located in the cell are targets for Pb^{2+}. In pathological conditions, the inhibition of mitochondrial respiratory chain complexes leads to an increase in the amount of ROS in mitochondria. Recent studies have shown that Pb^{2+}-induced increase in ROS generation in mitochondria is one of the toxicological mechanisms that can cause oxidative stress in cells. In addition, Pb^{2+} destabilizes intracellular calcium homeostasis [10].

Studies have shown that when liver mitochondria are exposed to Pb^{2+}, mitochondrial respiratory complexes inhibit enzyme activity and complex III is the main source of Pb^{2+}-induced ROS formation, increasing LPO and ATF consumption. In addition, as a result of Pb^{2+} effect on mitochondria, mitochondrial megachannel (mPTP) permeability increased, membrane potential decreased, cytochrome C was released [4].

Mitochondria placed in the cell are targets for heavy metals. Among them, Pb^{2+} ions have a negative impact on the functional system of mitochondria[5]. Under the influence of heavy metals, there is a violation of electron transport in the mitochondrial respiratory chain and an increase in the amount of ROS. Damage to the mitochondrial membrane caused by heavy metals can be repaired with plant substances. However, the effect of the DHQ-11 conjugate [8] based on the flavonoid dihydroquercetin separated from the Siberian cedar and the isoquinoline alkaloid F-18 on LPO induced by Pb^{2+}, Fe^{2+} and ADP in the liver mitochondrial membrane has not been investigated *in vitro*.

Objective: To determine the effect of DHQ-11 conjugate on rat liver mitochondrial membrane LPO.

Research methods. Experiments were carried out on 180-200 g purebred white male rats. Mitochondria were isolated from rat liver by differential centrifugation. Liver mitochondrial membrane LPO level was defined by polarographic method. Oxygen consumption was measured using a Mitocell S 200 microrespirometry system based on a Clark type oxygen electrode (Strathkelvin Instruments, Scotland). The incubation medium for mitochondrial membrane LPO detection was as follows: 175 mM KCl, 10 mM Tris-HCl, and 3 mkM rotenone, pH 7,4.

Results. In the experiment, oxygen consumption during membrane lipid peroxidation induced by ADP/Fe^{2+} and lead acetate in rat liver mitochondria was characterized by two-phase kinetics. At the same time, the stages of the lag-phase and rapid oxygen consumption are distinguished carefully. In our experiment, oxygen consumption by mitochondria was 4,38 mkg, 4,22 mkg, 3,65 mkg for 5 minutes under the influence of the DHQ-11 conjugate on the LPO process of the mitochondrial membrane of the liver at concentrations of 3, 5, 10, 20, and 30 mkM. 1,98 mkg, 1,39 mkg. atomic O_2/min. was defined that it turned out.

Based on the results obtained, a conclusion can be drawn; a concentration of 30 mkM of the DHQ-11 conjugate had a strong inhibitory effect on the lipid peroxidation of the mitochondrial membrane.

References

1. Flora S., Saxena G.P., Gautama P., Kaur P., Gill K. D. Response of lead-induced oxidative stress and alterations in biogenic amines in different rat brain regions to combined administration of DMSA and MiADMSA // Chemico-Biological Interactions. – 2007. – V.170, - P. 209–220
2. Jarup L. Hazards of heavy metal contamination // Brit. Med. Bull. – 2003. – V.68, - P. 167-182.
3. Kashiwada Y. et al. Anti-HIV benzylisoquinoline alkaloids and flavonoids from the leaves of Nelumbo nucifera, and structure–activity correlations with related alkaloids // Bioorganic & medicinal chemistry. – 2005. – V. 13, № 2. – P. 443-448.
4. Long M., Liu J., Dong J.X., Zhao J., Jiang F., Xiao Q. Toxicity of Pb2+ to rat liver mitochondria induced by oxidative stress and mitochondrial permeability transition // Toxicol. Res. – 2017. – V. 6, № 6. – P. 822-830
5. Peterson G.L. Simplification of the protein analysis method by Lowry et al. what is more widely applicable // Analytical biochemistry. – 1977. – V.83, № 2. – P. 346-356.
6. Sadeghniat K., Aminian O. , Chavoshi F. ,Bahaedini L. S. , Soltani Sh. and Najarkolaei F. R. Relationship between blood lead level and male reproductive hormones in male lead exposed workers of a battery factory: A cross-sectional study // Iran J. Reprod Med. – 2013. – V. 11, №8. – P. 673–676.
7. Steenland K., Boffetta P. Lead and cancer in humans: where are we now? // Am. J. Ind. Med. – 2000. – V. 38. – P. 295-299.
8. Uz IAP 06757. 28.02.2022 г. Азаматов А. А., Режепов Ж., Рахманова Х. А., Журакулов Ш. Н., Виноградова В. И. Средство, проявляющее антиаритмическую и местно-анестизирующую активность // Патент Узбекистан 2022.
9. WHO. Lead. Environmental Health Criteria, Geneva: World Health Organization. – 2020. - V.165.
10. Yang X. Y., Wang B., Zeng H. Q., Cai C. Q., Hu Q. S., Cai S. X., Meng X. J., Zou F. Role of the mitochondrial Ca^{2+} uniporter in Pb^{2+}-induced oxidative stress in human neuroblastoma cells // Brain Res. – 2014. – V.1575. – P. 12-21.