

## BIOLOGY

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### THE EFFECT OF ASIAN COBRA VENOM ON THE CONTENT OF RAT HEART AND LIVER MITOCHONDRIAL PHOSPHOLIPIDS AND THE PROTECTIVE EFFECT OF BENZONAL

#### Abstract

Administration of a cobra venom to rats resulted in decrease of heart and liver mitochondrial cardiolipins (1.88 and 1.29 times), phosphatidylethanolamines (1.56 and 1.42 times) and phosphatidic acid (1.14 and 1.29 times), whereas the content of phosphatidylcholins increased by 1.42 and 1.51-fold, respectively. The content of phosphatidylinositol increased by 3.09 times in liver mitochondria and decreased by 1.28 times in heart mitochondrial phosphatidylserine content impaired after the venom administration but even exceeded it. Benzonal also minimized changes in mitochondrial phospholipid induced by the cobra venom, and also reduced liver and heart phosphatidic acid content by 1.36 and 1.7 times.

**Keywords:** rats, liver, heart, mitochondria, phospholipids, snake venom, Central Asian cobra *Naja naja oxianci* Echwald, benzonal

#### Introduction

It is known, that at a poisoning with toxic of the Central Asian cobra *naja naja oxina* Echwald are disturbed frame and functions of elements and tissue, mid most radical changes are noted in mitochondrions [1,2]. Recently we had been displayed, that initiating in an organism of animals of Benzonalum against operation of toxic of the Central Asian cobra result in increase of longevity of animals [3,4]. The stability improvement of animals to action of toxic of a cobra depends on period of initiating of Benzonalum. The earlier after toxic influx the specimen is inducted, the aftereffects of operation of toxic are less expressed and life of animals is more sequel. After initiating of

Benzonalum against operation of toxic a cobra velocity of an oxygen uptake is moderated in comparison with control animals. It means, that Benzonalum regulates breathing function of an organism, creates a favorable conditions for job at an oxygen starvation. Thus carbohydrate metabolism arguments in blood are normalised. The modest intensification of a glycolysis, with saving of datum level. of animal starch in tissue is watched.

Simultaneously in comparison with indexes of control animals against repeatability of a contents of a lactate the rising tendency of level of glucose and a pyruvate is noted. Presence of Benzonalum at a brain tissue notifies glycolysis magnification in this connection practically it does not watch increasing of level of a lactate and pyruvate level recession. Take into consideration, the learning of action of toxic of a cobra on phospholipide metabolism of membranes of mitochondrions of various elements and tissue is of interest.

It is known, that the trial function of biological membranes consists in provision of structural organization of cells and endocellular organoids, and also maintenance of a persistence of physico-chemical performances of cytosol. Phospholipides of membranes are organized a hydrophobic "liquid" lower die to which one function squirrels can be bundled and play the relevant role in regulation of properties of membranes [5,6].

In true job we have been aimed to trace regularities in quantitative changes of various fractions of phospholipides in membranes of mitochondrions of a liver and heart of rats after a poisoning of animals with toxic of the Central Asian cobra without and with application of Benzonalum .

### Procedure

Experiments are conducted on the white rats-males with mass of 120-130 g maintained on a standard nutrient budget in the conditions of a vivarium. Animals have been divided on 3 groups on 16 animals in each. In the first and second groups of animals, toxic of the Central Asian cobra *naja naja oxina* Echwald an animal was inducted inside-is muscular in a dose of weight by of 160 mkg/kg. Through 2 minutes animals of second group injected Benzonalum in edition - 50 mg/kg of weight. A normal saline solution received 3 group of rats. Animals decapitated through 15 minutes after injecting toxic of a cobra. Toxic of the Central Asian cobra gained from Institute of zoology of AN RUZ. Samples of toxic of a collection of 2001 g, exsiccated in an exsiccator over calcium chloride were used.

Escape of mitochondrions from a heart and liver tissue spent on earlier presented procedure [7]. Protein determined on Louri [8].

Phospholipides of mitochondrions extracted on method of Keits [9]. Fos-folipides structure of mitochondrions was analysed with a method of a two-dimensional thin-layer chromatography [10].

**Results and their arguing**

Results of probes have been displayed the significant decrease of a contents of cardiolipins (in 1,88 times) and phosphatidylethanolamins (in 1,56 times) in mitochondrions of a liver after injection in an organism of an animal of toxic of cobra (tab. 1). Contents of increasing of phosphatidilcholines (in 1,42 times), phosphatidilinosits (in 3,09 times) and minute decrease of fraction of phosphatidilserins (in 1,09 times) and phosphatidin acids (in 1,15 times) is thus detected. Observable fluctuations, apparently, are a direct consequence of hydrolytical action of phospholipase A<sub>2</sub> of toxic of a cobra [11] and breaking of euzymatic reactions of methylation, a decarboxylation, exchange of the base and transalkiliration, being in a liver tissue. It is possible to admit, that at a poisoning with toxic of a cobra, phospholipase A<sub>2</sub> of toxic is hydrolyzed a cardiolipin and phosphatidiletanolamin first of all.

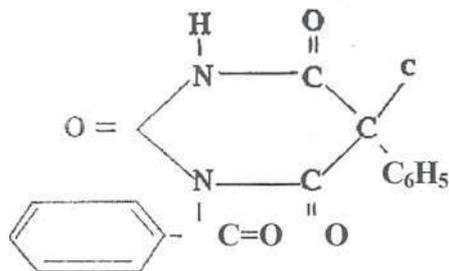
Table 1

Change of a contents of phospholipides of mitochondrions of a liver of rats at action of toxic of a cobra and Benzonaum protective effect (in % from a common contents of phosphotides. M±m, 11=6-8)

| <i>Phospolipides</i>                              | <i>Intact animals</i> | <i>Animals poisoning of toxic of cobra</i> |                    |
|---|-----------------------|--|--------------------|
|   |                       | <i>Bensonalum</i>                          | <i>Control</i>     |
| <i>Phosphotidilcholine</i>                        | 48,30±0,68            | 62,60±0,53<br>***                          | 68,50±0,42<br>**** |
| <i>Phosphotidiletanoiamin</i>                     | 22,30±0,64            | 13,90±1,53*                                | 9,90±0,19**        |
| <i>Cardiolipin</i>                                | 6,87±0,23             | 1,67±0,13<br>****                          | 0,85±0,65<br>****  |
| <i>Phosphadilserine</i>                           | 4,83±0,22             | 5,73±0,16**                                | 4,40±0,08*         |
| <i>Phosphatidilinosit</i>                         | 2,43±0,49             | 6,10±0,14*<br>**                           | 7,50±0,11*<br>**   |
| <i>Phosphatide acid</i>                           | 6,23±0,61             | 3,97±1,28*<br>**                           | 5,33±0,25*         |
| <i>Not identified phosphotides</i>                | 9,04±1,31             | 6,03±0,37**                                | 3,52±0,67 ****     |
| <i>Phosphotidilcholine/Phosphatidiletanolamin</i> | 2,16                  | 4,50                                       | 6,92               |
| <i>Neutral phosphotides(NFL)</i>                  | 48,30±0,68            | 62,00±0,53<br>***                          | 68,50±0,42*<br>**  |
| <i>Acid phosphotides(KFL)</i>                     | 35,79±1,96            | 29,70±3,11                                 | 27,13±10,63*       |
| <i>Coefficient NFL/KFL</i>                        | 1,35                  | 2,10                                       | 2,52               |

Remarks: Here and in table 2 the confidence coefficient is marked out by a stars: \*p < 0.05, \*\* p < 0.02, \*\*\* p < 0.01, \*\*\*\* p < 0.001.

Toxic of a cobra, in our opinion, accelerates synthesis of phosphatidilinosite in a liver tissue. In a number of works it is displayed [12], that in animal tissues phosphatidilinosite and phosphatidilserin are formed in a course of transferase reactions. Exchanging of the bases with phosphatidilcholine or phosphatidiletanolamine is a single method of formation of phosphatidilserine and phosphatidilinosite for animals [12,13].



Decrease of contents of phosphatide acids in mitochondrions of liver under the influence of toxic of a cobra is connected, on the one hand, with action of toxic of phospholipase A<sub>2</sub>, and with other - with weakening of its synthesis. It is known, that in mitochondrions, and in the outward membrane, the phosphatide acid is synthesised, one of central metabolites of phosphalipide exchanging [14].

After injecting of Benzonalum on phone of action of toxic of a cobra the contents of phospholipides not only is refunded in norm, but also a little is exceeded (in 1,19 times). The contents of phospholipides acids after Benzonalum application is decreased. Despite similarity of character of fluctuations of a contents of other fractions of phospholipides in mitochondrions of a liver of experimental untreat animal and treated of Benzonalum, the percent of a diverting of their contents from norm under the influence of toxic of a cobra at treatment are appeared minimum.

The ratio phosphatidilcholin/phosphatidiletanolamine, playing the relevant role in saving of integrity of membranous frames, at a poisoning with toxic of a cobra is increasing in 3,2 times. Benzonalum injecting in an organism of poisoning animals is resulted to cutting-down of a coefficient to 2,08 times.

At a poisoning of animals with toxic of a cobra in mitochondrions of heart the contents of phosphatidilcholine and phosphatidilserine raises in 1,51 and 1,28 times accordingly from level of rate (tab. 2). Thus contents of a cardiolipin, phosphatidiletanolamine, phosphatidilinosite and phosphatide acids are decreased in 1,82, 1,42, 1,28 and 1,29 times accordingly. After ingesting of Benzonalum against action of toxic of a cobra level of phosphatidilserine is even more increased (in 1,98 times), and the contents of phosphatidilinosite is exceeded rate in 1,95 times. Unlike the indicated phospholipides, magnification

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of decrease of fraction of phosphatide acids in (1,70 times) is simultaneously watched. At one-type character of fluctuations in a contents of phosphatidilcholine, phosphatidiletanolamine and a cardiolipin in mitochondrions of heart of not treated and treated rats with Benzonalum, the percent of a diverting of their contents from rate at treatment appears minimum. The determined differences in character of fluctuations of a contents of phosphatidilserine and phosphatidilinosite in mitochondrions, probably, are bundled to an attack of a tissue of heart and a liver toxic of a cobra. It does not noted, at the same time, appreciable fluctuations in a contents of phosphatidilcholine, phosphatidiletanolamine and a cardiolipin in membranes of mitochondrions of heart and a liver under the influence toxic of a cobra.

Table 2

Exchange of contents of phospholipides of mitochondrions of heart of rats at poisoning of toxic of a cobra and Benzonalum protective effect (in % from a common contents of phospholipides.  $M \pm m$ ,  $n=6-8$ )

| <i>Phosphotides</i>                                 | <i>Intact animals</i> | <i>The animals poisoning with toxic of a cobra</i> |                       |
|---|-----------------------|--|-----------------------|
|   |                       | <i>Benzonalum</i>                                  | <i>Monitoring</i>     |
| <i>Phosphotidilcholin</i>                           | <i>36,00+0,41</i>     | <i>41,00+0,71**</i>                                | <i>54,30+0,37****</i> |
| <i>Phosphotidiletanolamin</i>                       | <i>20,30+0,32</i>     | <i>17,20+1,72*</i>                                 | <i>11,70+0,48****</i> |
| <i>Cardiolipin</i>                                  | <i>8,72+0,27</i>      | <i>6,82+1,23*</i>                                  | <i>1,56+0,60****</i>  |
| <i>Phosphatidilserin</i>                            | <i>2,71+0,27</i>      | <i>5,38+0,28****</i>                               | <i>3,46+0,91*</i>     |
| <i>Phosphatidilinosit</i>                           | <i>3,81+0,36</i>      | <i>7,41+0,11****</i>                               | <i>2,75+0,57*</i>     |
| <i>Phosphatide acid</i>                             | <i>7,00+0,28</i>      | <i>2,09+0,29****</i>                               | <i>5,00+0,32**</i>    |
| <i>Not identified phospholipides</i>                | <i>21,46+1,97</i>     | <i>20,10+2,33</i>                                  | <i>21,23+2,03</i>     |
| <i>Phosphotidilcholine/ phosphatidiletanolamine</i> | <i>1,78</i>           | <i>2,36</i>  | <i>4,64</i>           |
| <i>Neutral phosphotides (NFL)</i>                   | <i>36,00+0,41</i>     | <i>41,00+0,71**</i>                                | <i>54,30+0,37****</i> |
| <i>Acid phosphotides (KFL)</i>                      | <i>33,82+1,23</i>     | <i>32,08+2,40</i>                                  | <i>22,91+2,28**</i>   |
| <i>Coefficient NFL/KFL</i>                          | <i>1,06</i>           | <i>1,27</i>  | <i>2,37</i>           |

At a poisoning of animals with toxic of a cobra in heart mitochondrions fluctuations in the ratio a

phosphatidilcholine/phosphatidiletanolamine are detected. So, if in lack of Benzonalum this coefficient is increased in 2,6 times, in the presence of it - only in 1,32 times.

Analysing the gained effects, it is possible to conclude, that at poisoning with toxic of a cobra breaking of frame of mitochondrions of a liver and heart [1,2] is escorted by fluctuations in ratio of phospholipides. Namely there is a decrease of a contents of cardiolipins and phosphatidiletanolamines and is increasing of phosphatidilcholines. Watched at a poisoning with toxic of a cobra of fluctuation of phospholipids structure of membranes of mitochondrions can be stipulated violation of make up of phospholipides component of membranes, collapse of phospholipides under the influence of phospholipase A<sub>2</sub> of toxic of a cobra.

The gained effects indicate productivity of Benzonalum at a poisoning with toxic of a cobra. Benzonalum contributes in maintenance in mitochondrions of a liver and heart of a fixed level of neutral and acid phosphotides as structurally and functionly various grades of the phosphotides indispensable for saving of physico-chemical properties of operating membranes. Preventing of possible oscillations in a qualitative and quantitative contents of phosphotides in biological systems is one of the chief conditions of provision of their normal physiological status.

Thus, against developing of morphological and metabolic breakings in mitochondrions of a liver and heart of animals at a poisoning with their toxic of a cobra occur breakings of quantitative ratio between separate structural joints. The presented fluctuations concern to various phosphotides in membranes of mitochondrions that are important for understanding of the gear of evolution of the multiple metabolic breakings stipulated by dysfunctions of a number membranes connected phospholipids depend ferment systems and synthesis of ATF. Description progress, characteristic for poisoning with toxic of a cobra, are relevant for a performance measurement of treatment by Benzonalum. According to the gained effects, Benzonalum action on developing of deflection in ratio of phospholipides in membranes of mitochondrions of elements of animals is well-marked. Benzonalum application in certain extent bolsters level of neutral and acid phospholipides within rate and prevents with developing of appreciable breakings in their ratio.

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