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Study of Antioxidant and Membrane Resistant Peculiarities of a New Cyan Containing Lactone in Membranes of Hepatocytes with Sarcoma-45

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Abstract

The antioxidant and membrane resistant peculiarities of a new derivative (2-cyan-3,4,4-trymethil-2-buten-4 -olyd) of cyan containing unsaturated lactones have been studied in membranes of hepatocytes with Sarcoma-45 [1].

The results of our previous research [1, 2, 3] showed significant changes of phospholipid exchange in hepatocytes of microsomal membranes at experimental animals vaccinated with Sarcoma-45 tumor strain. It is manifested in significant changes of quantitative and qualitative contents of membrane phospholipids separate fractions, increase of cytotoxic LPCs, PIs and PAs levels, significant decrease of PCs and SPs contents, statistically significant changes of PL/PL ratio, peroxidation ratio intensity, dramatic increase of PLA2 activity, quantitative and qualitative changes of adenyl nucleotides, as well as disorders of ATPase system activity [3-5, 6, 7].

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Introduction

The antioxidant and membrane resistant peculiarities of a new derivative (2-cyan-3,4,4-trymethil-2-buten-4-olyd - CTBO) of cyan containing unsaturated lactones have been studied in membranes of hepatocytes with Sarcoma-45 [1].

The results of our previous research [1, 2, 3] showed significant changes of phospholipid (PL) exchange in hepatocytes of microsomal membranes at experimental animals vaccinated with Sarcoma-45 tumor strain. It is manifested in significant changes of quantitative and qualitative contents of membrane phospholipids separate fractions, increase of cytotoxic lysophospholipids (LPCs), phosphatidylinositol (PI) and phosphatidic acid (PA) levels, significant decrease of phosphatitylcholines (PC) and sphingomyeline (SP) contents, statistically significant changes of PL/PL ratio, peroxidation ratio intensity, dramatic increase of phospholipase A_2 (PLA_2) activity, quantitative and qualitative changes of adenyl nucleotides, as well as disorders of adenosine triphosphatase (ATPase) system activity [3, 4, 5, 6, 7].

Relative changes in activity and levels of antioxidant and pro-oxidant metalloprotein (taken from rats' liver) at Sarcoma- 45 and after the application of cyan containing lactone (compared to controller (100%)). Table 1

This disease is addressed by certain changes of the level of metalloproteins with antioxidant and pro-oxidant activation, which is manifested by inhibition of antioxidant system, particularly by decrease of total superoxide dismutase (SOD) (Cu,Zn-SOD and Mn-SOD) and catalase activation, as well as increase of pro-oxidant metalloproteins level, particularly cytochrome b558 .

The intensity of Met-Hb and cytochrome b558 NADPH oxidase (Nox isoforms) complex formation in liver cell membranes are observed at Sarcoma-45.

The tumor growth decrease for 45% (in mass) is observed after using the studied new derivative of cyan containing unsaturated lactones.

The results of our previous research indicate

Table 1. The changes of Metalloprotein at Sarcoma- 45 after the application of cyan containing lactone

Metalloprotein	Sarcoma 45 n =8	Treatment n =8
Fractionation level of cytochrome b558 in liver cell membranes	+ 28,7 ± 4,1**	+ 16,1 ± 2,2*
NADPH-dependent generating O2- activity of cytochrome b558 in liver cell membranes in homogeneous phase	+24,8±2,3**	+ 11,3 ± 2,0*
NADPH-dependent generating O2- activity of cytochrome b558 in liver cell membranes in heterogeneous phase	+ 41,3± 3,3***	+ 34,8 ±4,9**
MetHb restorative activity of cytochrome b558 in liver cell membranes in homogeneous phase	- 35,7± 3,6**	- 10,3 ± 1,8*
MetHb restorative activity of cytochrome b558 in liver cell membranes in heterogeneous phase	- 51,4± 4,3***	- 20,2 ± 3,1**
Cytochrome C	-36,7± 4,1**	-24,9 ±3,0**
Cu,Zn- SOD Mn- SOD sum of fractions	-31,5± 2,1**	-18,4 ± 3,0*
Catalase	-22,9 ± 2,7**	-8,4 ± 0,8

* (P<0,05), ** (P<0,01), *** (P<0,001)

that use of a new derivative of the unsaturated lactones regulates the quantitative and qualitative structure of certain phospholipids in lipid bilayer of hepatocytes membranes, the intensity of lipid peroxidation, as well as the activity of phospholipase A_2 in experimental animals [3 ,4].

Researches conducted under these conditions connected with the investigation of changes in anti-(SOD, catalase) and pro-oxidant (cytochrome C, cytochrome b558) systems activation, as well as in quantitative changes of adenyl nucleotides (adenosine triphosphate-ATP, adenosine diphosphate-ADP, adenosine monophosphate-AMP) after CTBO application have showed that the studied compound is characterized by normalization of anti- and pro-oxidant metalloproteins certain activation. Under this condition it is observed some normalization of ATPase activation, as well as ATP, ADP, and AMP levels regulation [4].

Conclusion

It is proved that the studied compound inhibits the release of Nox isoforms which probably depends on the membrane-resistant peculiarities of it.

The results of our previous researches showed that after the application of the new derivative of the unsaturated lactone some regulation of the membrane phospholipid lipid bilayer exchange is observed, expressed by regulation of phospholipid peroxidation and decomposition processes and by regulation of adenine nucleotide levels [4]:

After CTBO application at Sarcoma-45 the inhibition of tumor growth, the regulation of as membrane PLs quantitative and qualitative contents, as well as of certain enzymes of membrane-dependent ATPasa system, pro- and antioxidant metalloproteins, and lipid peroxidation activity are the proofs for certain antitumor, antioxidant and membrane-regulated properties of the studied compound.

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