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THE ROLE AND IMPORTANCE OF LIPIDS AND PHOSPHOLIPIDS IN HUMAN MITOCHONDRIA

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ANNOTATION: This article examines the problem of prolonging life while maintaining a healthy body condition. It is worth noting that prolonging life is of great importance to humans, and the main goal of many studies is to solve this problem.

The path to solving this problem can be long and difficult. One of the models for this issue is calorie-restricted nutrition. This model is used by many researchers, in their work some aspects of the problem of prolonging life have been identified.

KEYWORDS: Lipid, molecule, fatty acids, hormone, phosphatidylcholine, acetylphosphatides.

INTRODUCTION: More than 90% of the lipids in biological membranes are phospholipids, and the remaining 10% are cholesterol, mono-, di- and triglycerides, free fatty acids, cholesterol esters, and methyl esters of fatty acids. Phospholipids are divided into glycerophospholipids (phosphatidylcholine, phosphatidic acid, acetylphosphatides or plasmalogens, lysophospholipids and polyglycerophosphatides), sphingomyelins, and phosphatidylinositols. All natural glycerophosphatides are derivatives of 1-α-glycerophosphoric acid. Bases (choline, ethanolamine, serine) are attached to the phosphoric acid residue, which is a must-have in phospholipids. Fatty acids are attached to the α and β hydroxyls of glycerol by complex ester bonds. Glycerophospholipids, which have lost one molecule of fatty acid from their composition, are

called lysophospholipids. Sphingomyelin contains the unsaturated amino alcohol sphingosine in its composition. Phosphatidylinositol contains, in addition to glycerol, the 6-atom cyclic alcohol inositol. Phospholipids differ not only from each other in the above, but also in the homogeneity of fatty acids. Phospholipidic acid is the main precursor in the synthesis of phosphoglycerides. Lysophosphatidylcholine has been studied the most among other lysophospholipids. It has been proven in many literatures that phospholipids play an important role in various biological and physiological-biochemical processes. The most important role is played by especially acidic phospholipids (phosphatidylserine, phosphatidylinositol and phosphatidic acid) and lysophospholipids, since they have high biological activity [Racker E, 1976]. Minor phospholipids are characterized by high polarity and the ability to selectively bind and transport various ions. These properties determine their biological activities [Bidon E et all., 1980;].

Many membrane-bound enzymes or polyenzyme systems cannot exhibit their catalytic activity without phospholipids. As a result of lipid delipidation, the activity of lipid-dependent enzymes of various organelles, including mitochondria, is lost, and their activity can be restored with the help of externally introduced (exogenous) phospholipids. It was found that the effectiveness of different phospholipids is not the same. In addition, each phospholipid that is part of biological membranes performs a specific function that is important for life. In addition, it has been found that phospholipids of the same type, but obtained from different sources, exhibit different activities in delipidated enzyme systems. For example, the maximum activity of oligomycin-sensitive ATP synthase is observed when phosphatidylserine, cardiolipin, phosphatidylcholine and phosphatidylethanolamine are added from mitochondrial phospholipids.

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Phosphatidylcholine and phosphatidylethanolamine have been shown to play a role in maintaining high levels of enzyme activity in mitochondrial membrane vesicles. The addition of cardiolipin, along with other phospholipids, further enhances enzyme activity.

However, artificial phosphoglycerides containing saturated fatty acids are considered inhibitors of enzymes [Yu.S. Tarakhovsky, et al., 2013; Racker E., 1976]. Phosphatidylcholine is necessary for high activity of cytochrome oxidase and β-oxybutyrate dehydrogenase. It is assumed that the interaction of cytochrome c with cytochrome oxidase, and cytochrome b with succinate dehydrogenase is mediated by phospholipids. It has been shown that there are several cytochrome c-binding sites in the mitochondrial membrane. They bind not only cytochrome c and other cytochromes, but also phospholipids. Phosphatidylethanolamine and phosphatidylserine are the main components of cytochrome oxidase. Cardiolipin, which plays an important role in the process of oxidative phosphorylation, is of great importance in maintaining the structure of mitochondrial enzyme systems in a certain norm [Almatov, 1990]. In our opinion, cardiolipin, which is necessary for the implementation of the catalytic functions of enzymes, probably plays a decisive role in the implementation of electron transfer processes [Almatov, 1993]. Thus, analyzing the results obtained, it should be noted that enzymes and polyenzyme systems located in the mitochondrial membrane lose their catalytic activity as a result of membrane delipidization, but their activity can be restored by adding phospholipids.

MATERIALS AND METHODS: In recent years, much attention has been paid to lysophosphatidylcholine. According to the data obtained so far, the amount of lysophosphatidylcholine in tissues does not exceed 5 mol.% compared to total phospholipids. However, the amount of lysophosphatidylcholine in human and animal blood plasma reaches up to 20% compared to total phospholipids, and this phospholipid is in a complex state with albumin and other proteins.

Lysophosphatidylcholine is a substance belonging to the second group of mediators formed as a result of the activation of hormone-sensitive cytosolic phospholipase A2. The molecular weight of cytosolic phospholipase A2 is 6 times greater than that of secretory phospholipase A, and its activation requires a much smaller amount of calcium than that of calcium, which activates secretory phospholipase A. Cytosolic phospholipase A2 is activated by hormones and agonists through a specific G-protein receptor. This process occurs as a result of growth factors and an increase in intracellular calcium [Prokazova N.V. et al., 1998]. In this case, the enzyme is translocated from the cytoplasm to the membrane, resulting in the formation of three types of second messengers: arachidonic acid, a precursor of prostaglandin synthesis, non-esterified fatty acids, and lysophosphatidylcholine. Lysophosphatidylcholine is actively transported to the cell membrane by lipoproteins in association with the cell. Lysophosphatidylcholine, which is transported to the membrane, is converted to phosphatidylcholine by the cell's metabolic machinery [Jun Dong, Xiaoming Cai, et. al 2010].

In recent years, lipids have been considered the most important biological effectors, regulators and mediators involved in almost all the most important physiological processes in the body (immune response, neuronal information transmission, regulation of vascular and muscle tone, homeostasis, inflammation, etc.), as well as in biochemical reactions in animal and human cells [Dyatlovitskaya E.V., Bezuglov V.V., 1998]. As secondary messengers, they transmit various external signals into the cell, and are also intercellular mediators [Kim D.U., Koh T. et al., 1999]. In carrying out their functional effects, lipids perform several different functions [Lenaz G., 1979]:

1. Lipids are binding surfaces for proteins, and as such they can modulate enzymatic activity.

2. Lipids are essential for the separation of two aqueous compartments for processes such as vectorial transport of ions, such as calcium transport, and oxidative phosphorylation. The “lipid” ring around the protein is essential for this role.

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3. Lipids can provide a hydrophobic environment or binding interface. They are important for enzymes involved in lipid metabolism and enzymes that enter the membrane; they are also important for the solubility of lipid-soluble cofactors such as coenzyme Q in mitochondria.

4. Lipids are essential for the formation of membranes from dissociated subunits; the release of lipids causes dislocations in the subunits of membrane-bound multiprotein complexes.

5. Finally, lipids can act as modulators of membrane-bound enzymes, inducing the conformation of catalytic proteins or initiating conformational changes that are critical for the course of the catalytic cycle. This role has been demonstrated by data obtained from conformational studies of model proteins and serum lipoproteins, as well as membrane proteins.

RESULTS: Recently, a comprehensive study of many pathological processes has revealed that structural and functional changes in membranes are primarily associated with changes in the lipid composition, their state and mutual relationships. The manifestation and duration of membrane-damaging processes in the body determine the clinical severity and course of many diseases. Membrane destruction as a pathological phenomenon is associated with the participation of lipids and their lysoforms in the processes of lipid peroxidation, which leads to changes in lipid-protein bonds, the stability of enzyme complexes, their functional activity, damage to other macromolecules in the membrane, nucleic acids, and disruption of cellular metabolism [Zelinsky B.A., Vlasenko M.V., 1990].

As for mitochondria, such changes are characteristic primarily of the functionally active proteins of the inner membranes of mitochondria, oxidative phosphorylation, membrane-bound phospholipases and lipid peroxidation processes [Almatov K.T. 1990, 1993].

The composition of membrane phospholipids is regulated by three systems:

1) biosynthesis,

2) peroxidation and

3) enzymatic hydrolysis (transacylation and transalkylation of phospholipids).

The lipid biosynthesis system carries out regulation at a slow pace - de novo synthesis of phospholipids in the endoplasmic reticulum occurs at a low rate and is transported to other membranes with the help of transport proteins. Relatively “fast” regulation of phospholipid composition in response to external influences is carried out by the phospholipase system (phospholipase A2, lysophospholipase A1 and A2, phospholipase S and phospholipase D), as well as the free radical system of lipid peroxidation, and there is apparently a certain connection between the two mechanisms. All these systems are universal, they are found in almost all membrane types and play an important role in transport, energy, signal transduction processes, including in various pathological conditions. In general, to date, a large amount of information has been accumulated about the bioeffector functions of lipids in the cell and in the organism as a whole.

For example, there is a large amount of information about the participation of representatives of the phosphoinositide cycle - diacylglycerols, inositol phosphate, inositol-1,4,5-triphosphate, phosphatidic acids as second messengers in signaling processes, which stimulate some forms of protein kinase S, mobilize calcium ions from intracellular depots [Frank W., Munnik T. et al., 2000]. 1-O-alkyl-2-acetylphosphatidylcholine (platelet aggregation factor) is a powerful bioeffector that controls many biological processes in the blood.

Recently, much information has appeared about the regulatory function of lysophosphatidylcholine, which was previously considered only as an endogenous detergent. It was found that at low concentrations (1-10 μM) lysophosphatidylcholine stimulates the activity of protein kinase S, enhances cell proliferation, stimulates the differentiation of lymphoid cells, etc. [Prokazova N.V., Zvezdina N.D., Korotaeva A.A., 1998]. It was found that lysophosphatidylcholine and free fatty acids increase the activity of some forms of protein kinases induced by diacylglycerols [Dyatlovitskaya E.V., Bezuglov V.V., 1998]. Lipids, and especially phospholipids, play a very important role in determining the functional state and structural structure of biological membranes. These properties of phospholipids are determined

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by the formation of a hydrophobic matrix in the membrane, which in turn plays an important role in the functional state of the cell or its organelles [Boldyrev A.A., 1990; Almatov K.T., 1990].

Changes in the amount of phospholipids in mitochondrial membranes lead to structural and functional changes in the membrane. As a result, changes are observed in the passage of ions through the membrane, the activity of receptors, oxidative phosphorylation, and the activities of various enzymes located there.

The results obtained when correcting changes in phosphatidylcholine, phosphatidylethanolamine and their lysoforms under the conditions of peroxidation of lipids in mitochondria with haplogenin-7-glycoside are presented in Table 1.

Phosphatidylcholine is included in the “neutral phospholipids” and forms the basis of biological membranes, but has a weak metabolic activity compared to acidic phospholipids [Gribanov G.A., 1979]. Monoacyl, diacyl and plasmogenic forms of phosphatidylcholine are found in biological membranes. Lysophospholipids differ from phospholipids of the diacyl type by the absence of one fatty acid in the first or second case. One of such compounds is lysophosphatidylcholine. Lysophosphatidylcholine is a product of the metabolism of phosphatidylcholine, the main phospholipid of all eukaryotic and many prokaryotes. Lysophosphatidylcholine is formed as a result of the hydrolytic action of various lysoform phospholipases A2 on phosphatidylcholine, as well as the transfer of a fatty acid residue from phosphatidylcholine to cholesterol by lecithin-cholesterol-acyltransferase. The amount of lysophosphatidylcholine is only 5% of the total phospholipids in tissues. In the blood plasma of humans and animals, it is 20% of the total phospholipids, where it is complexed with albumin and other proteins [Prokozova N.V., Zvezdina N.D., Korotaeva A.A., 1998]. In recent years, it has been shown that lysophosphatidylcholine can induce or enhance cell proliferation, stimulate lymphoid cell adhesion and differentiation, monocyte chemotaxis, modulate the contractile ability of muscle tissue, platelet aggregation, etc. [Prokozova N.V., Zvezdina N.D., Korotaeva A.A., 1998]. Therefore, interest in lysophosphatidylcholine is currently increasing among scientists.

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