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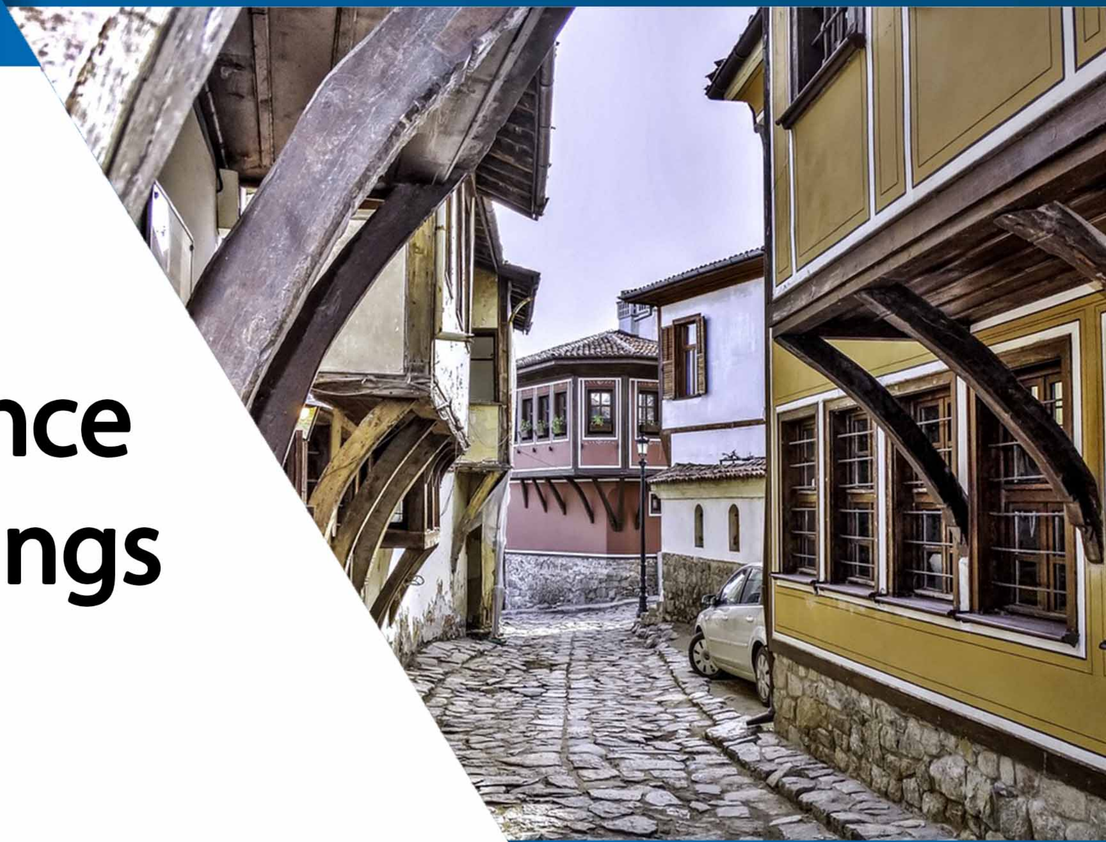

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# TRENDS IN THE DEVELOPMENT OF SCIENCE AS THE MAIN WAY TO REPLACE OLD TECHNOLOGIES

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# THE ROLE OF HIGHER FATTY ACIDS IN CELL MEMBRANES

**Valentyna Slipchuk**
Doctor of Sciences in Pedagogy, Professor,
Professor of the Department of Medical Biochemistry and Molecular Biology

**Diana Hapon**
Student of medical faculty №1,
specialty 222 "Medicine",
Bogomolets National Medical University,
Kyiv, Ukraine,

The study of the role of higher fatty acids in cell membranes is a topical issue in medicine, biochemistry, physiology, immunology, etc. Polyunsaturated higher fatty acids perform extremely important functions in the human body, namely:

- plastic - they are a substrate for the formation of the body's own fats, cell membranes, tissue hormones (prostaglandins), nerve fiber sheaths, connective tissue, and phospholipids;
- regulatory - provide cell membrane functions, promote growth and development of the body, are closely related to the metabolism of B1 and B6, stimulate immune functions of the body, promote the excretion of excess cholesterol, prevent the formation of gallstones, increase elasticity and reduce blood vessel permeability;
- energy.

All polyunsaturated higher fatty acids are also integral components of membrane phospholipids [1].

Glycerophospholipids, the main class of natural membrane phospholipids, contain a saturated fatty acid at position 1 and an unsaturated fatty acid at position 2 of glycerol. Unlike saturated fatty acids, unsaturated fatty acids have a nonlinear chain due to the presence of one or more carbon-carbon double bonds. As a result, saturated fatty acids can pack tightly, while unsaturated fatty acids prevent such tight packing and form more flexible aggregates. This phenomenon has a major impact on the flexibility of phospholipid membranes. The unsaturation index (UI) is an important parameter for describing the flexibility of a biological membrane. An increased UI means greater membrane flexibility, and a decreased UI implies greater membrane stiffness. Arachidonic acid is one of the key fatty acids and an increase in its percentage in the phospholipid tails improves membrane flexibility due to its four double bonds [2].

The study of the effects of saturated and unsaturated higher fatty acids on biological and model (liposomal) membranes provides insight into the contribution of biophysical effects to the cytotoxicity observed with saturated higher fatty acids. *In vitro* experiments show that unsaturated higher fatty acids, such as oleic and linoleic, are less toxic and have less effect on membrane fluidity. To understand and evaluate the biophysical changes due to different higher fatty acids, the scientists performed computational analysis of model liposomes with palmitate, oleate, and linoleate. The results of their research showed that the chain of unsaturated higher fatty acids serves as a membrane stabilizer, preventing changes in membrane fluidity. Based on the Voronoi tessellation analysis, it was found that higher unsaturated fatty acids have structural properties that can reduce the ordering of lipids in model membranes. In addition, hydrogen bonding analysis indicated a more uniform level of membrane hydration in the presence of oleate and linoleate compared to palmitate. These observations, derived from computational studies, provide a possible mechanism by which higher unsaturated fatty acids minimize biophysical changes and protect cell membrane and structure. The scientists also conducted studies of liposome leakage, which showed that palmitic acid (the highest saturated fatty acid) causes greater destabilization of liposomes (more “leaky”) than oleic acid (the highest unsaturated fatty acid) [3].

Consumption of polyunsaturated higher fatty acids provides prevention of cancer and heart disease, as well as other benefits for maintaining human health. For example, the most influential ingredient in fish oil is the docosahexaenoic acid ω-3-PUFA (with 22 carbons and six double bonds), the longest and most unsaturated higher fatty acid commonly found in biological systems. In their research, the scientists focus on the molecular interactions between phospholipids containing docosahexaenoic acid ω-3-PUFA and cholesterol.

The concentration of docosahexaenoic acid (DHA) in neuronal membranes often approaches 50% of the total amount of higher fatty acids. The concentration of DHA in most human cells is low (usually $<5\%$ of the total number of acyl chains).

Numerous studies have shown that phospholipids containing DHA can have a very significant impact on membrane properties, including: increased membrane permeability, increased membrane synthesis and vesicle formation,
increase in phospholipid flip-flop (i.e., diffusion of membrane phospholipid molecules across the membrane), increase in in-plane membrane elasticity, and others. The reason for this is the extremely high degree of flexibility of the acyl chain, which is provided by polyunsaturation [4].

In one of the largest studies ever conducted, scientists have shown that the balance of ω-3 and ω-6 polyunsaturated fatty acids (PUFA) is the most important determinant of membrane composition in rats under “normal” conditions. Comparisons between mammalian species have shown that PUFA content in the brain is maintained with large changes in body weight, while PUFA content in the heart and skeletal muscle decreases with body size. In the human body, the PUFA content in brain membrane lipids is higher compared to other tissues (muscles, heart, liver, red blood cells), while in rats the opposite trend is observed [5].

Higher fatty acids affect the properties of the plasma membrane. Scientists at the Fukuda Laboratory have shown that membrane permeability is significantly affected by the composition of higher fatty acids in experiments using lipid vesicles or living cells. In order to stabilize the lipase activity of Rhizopus oryzae cells, the scientists investigated the effect of the composition of higher fatty acids in the cell membrane on the stability of the whole-cell biocatalyst. They found that cells that were enriched in oleic or linoleic acid (unsaturated higher fatty acids) showed higher initial methanolysis activity, and cells enriched in palmitic acid (saturated fatty acids) showed significantly higher enzymatic stability. The laboratory's researchers have shown that higher fatty acids increase the permeability and stiffness of the cell membrane, which ultimately leads to increased methanolysis activity and enzymatic stability. The researchers determined the optimal membrane composition by adding mixtures of oleic and palmitic acids to the culture medium in different ratios. The results of the experiment showed that the ratio of higher fatty acids, defined as the value of Rf [= oleic acid / (oleic acid + palmitic acid)] 0.67, led to both higher methanolysis activity and greater enzymatic stability [6].

The two essential higher fatty acids, α-linolenic acid and linoleic acid, and the higher unsaturated fatty acids synthesized from them, are critical for the development and maintenance of normal brain function. Deficiencies in these higher fatty acids have been shown to cause damage to neuronal development, cognitive and motor function. Using electrochemistry and imaging techniques, we studied the effect of two essential higher fatty acids on the dynamics of catecholamine release and vesicle content, as well as on the phospholipid composition of the cell membrane, in order to understand how they affect exocytosis and, as a result, neurotransmission at the level of a single cell. It was found that incubation with either of the two higher fatty acids reduces the size of secretory vesicles and allows for more double bonds to be incorporated into the cell membrane structure, resulting in greater membrane flexibility. Subsequently, this affects proteins that regulate the dynamics of exocytotic fusion and thus affects exocytosis. These studies indicate that two essential higher fatty acids affect membrane structure by acting on exocytosis and provide a potential treatment for diseases and disorders related to catecholamine signaling [7].

**Conclusions.** Thus, the saturated higher fatty acids that make up the phospholipids of membranes can be tightly packed, and the unsaturated higher fatty acids of phospholipids prevent such tight packing, increasing the membrane fluidity. The flexibility of a biological membrane is determined by the fatty acid unsaturation index UI, which increases with the amount of unsaturated higher fatty acids and provides greater membrane flexibility. Phospholipids containing the docosahexanoic acid ω-3-PUFA contribute to increased membrane permeability, increased membrane synthesis, vesicle formation, and increased membrane elasticity. In the human body, the content of polyunsaturated higher fatty acids in the lipids of the brain membranes is higher compared to other tissues (muscles, heart, liver, red blood cells).

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