Influence of Liposomal Form of Polyunsaturated Fatty Acids on the Lipid Profile of Blood Serum in Animals with Experimental Hyperlipidemia

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ABSTRACT

This work is dedicated to the influence of a combination of polyunsaturated fatty acids and antioxidant vitamins (A and E) on the lipid profile of blood serum of rats. It presents the data of biochemical studies of blood serum of experimental animals in twin models of hyperlipidemia. The results of these studies indicate that the use of liposomal substances with natural polyunsaturated fatty acids and vitamin E leads to a positive correction of the serum lipid profile in experimental rats.

INTRODUCTION

An interest in polyunsaturated fatty acids (PUFAs) arose in the 30s of the last century. Biochemical mechanisms of action of each individual PUFAs in the human body were discovered relatively not long ago: less than 40 years ago [1]. It has been found that these acids having a large number of carbon atoms and multiple double bonds play an important role in the living organism. According to the liquid-mosaic model the fluidity of biomembranes is caused by the respective distribution of PUFAs residues between molecules of different phospholipids. As a part of the membrane lipids PUFAs play a transport role: they transfer fat-soluble vitamins A, D, E, K, and are able to modulate the physiological activity of the latter.

An effect of ω-3 PUFAs on the blood lipid profile is well known. In the works of Harris et al., it was found that the intake of ω-3 PUFAs leads to a decrease in triglycerides (TG), which is accompanied by increased levels of low density lipoprotein cholesterol (LDL-C), mainly due to slightly atherogenic low-weight fractions, and increased levels of high density lipoprotein cholesterol (HDL-C) [2, 3]. The U.S. Food and Drug Administration has approved the use of ω-3 PUFAs as a drug that reduces the concentration of triglycerides in the blood of patients with severe hypertriglycerideridemia [4].

The lack of essential fatty acids is accompanied by a number of systemic diseases: diabetes mellitus, tumors, multiple sclerosis, Crohn's disease, Raynaud's syndrome, myocardial infarction, etc. [5]. According to modern concepts, these pathological conditions are caused by disorders of fat metabolism, structure and functioning of biological membranes [6, 7].

Numerous studies have shown a positive effect of PUFAs of both vegetable and marine origin on the status of various components of the cardiovascular system. It was found that people who receive food enriched with ω-3 acids are less prone to coronary heart disease and have less blood clotting, which is associated with decreased platelet aggregation, lowering of blood pressure, decreased triacylglycerol and cholesterol circulation [8-11].

Determining that PUFAs are able to reduce the risk of cardiovascular disease was followed by the creation of supplements containing PUFAs and enrichment of foods by the latter. The idea of using any substance normally consumed with food as a therapeutic agent reflects new trends in pharmacology. This idea consists in the gradual switch from the search for chemical compounds that are inhibitors of any specific biochemical processes to the search for "physiological" regulators and modulators of complex biochemical systems [3, 9, 12].

Essential PUFAs whether structural components of biological membranes, intracellular messengers or directly bioprecursors of eicosanoids play an important role in development, regulating and eliminating of many pathological conditions. Therefore, searching for new raw material sources of these compounds and developing...
technologies of effective substances derived from these sources is a point of particular interest. The high content of fatty acids, especially PUFAs, suggests searching for transport forms and ways to stabilize the oxidation processes that would increase the overall efficiency and bioavailability of biologically active substances.

**Aim** of our studies was to evaluate the lipid-lowering properties of liposomes prepared from the fat of the Baikal seal.

**Methods:**

The investigations were carried out on Wistar male rats weighing 220-280 g delivered from the Research Institute of Biophysics vivarium of the Federal Stat Budgetary Educational Institution of Higher Professional Education "Angarsk State Technical Academy". Animals were placed in individual cages. All animals were fed according to a standard diet.

The experiments were performed in compliance with all rules and recommendations of the European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes (Strasbourg, 1986).

Marine mammals are a known source of PUFAs. In particular, the fatty acid content in the fat of the ringed seal (*Phoca hispida*) living in the Kara Sea is equal to 94.78 g/100 g of total lipids (17 fatty acid named according to the chain length from 14 to 22 carbon atoms). The content of unsaturated fatty acids exceeds the content of the saturated ones by 4.3 times, while the amount of PUFAs is 31.81 g/100 g, with ω-3 fatty acids being in the amount of up to 26.55% of all PUFAs [13].

The fat of Baikal seal (*Phoca sibirica*) also has a high content of PUFAs. Fatty acid composition of the seal fat has a various composition. Investigations revealed 60 fatty acids containing from 8 to 22 carbon atoms. Of these, saturated acids constitute 17-19%, monounsaturated acids - 59-60% (mainly oleic acid - 31%), polyunsaturated acids - 22-23% (including diene acids – 6.1-7.0%; triene acids - 0.2-0.3%; tetraene acids - 3.9-4.1%; pentaenoate acids - 4.6-5.0%; and hexaenoic acids – 6.2-7.0%) [14].

Thus, fats of various seals are a valuable source of polyunsaturated fatty acids.

Our work used liposomes prepared from phospholipids from the liver of Baikalian seals enriched with seal fat, vitamin E [15] and A.

Hyperlipemia in rats was induced by a force program using a single intraperitoneal injection of Tween-80 at the dose of 250 mg per 100 g body weight in 1 ml of distilled water.

**Experimental animals were divided into 4 experimental groups:**

- **Group 1** - intact (animals fed standard diet and water);
- **Group 2** - control (animals fed standard diet and water and also were administrated single Tween-80 i.p. at the dose of 250 mg per 100 g body weight);
- **Group 3** - experimental (rats received liposomal suspension at the dose of 20 mg/kg of body weight vitamin E in a concentration of 1% by weight of the lipids in liposomes; group 3 animals were administrated the above-noted substance daily for 14 days preemptively before an exposure to the atherogenic agent);
- **Group 4** – test group (rats received liposomal suspension at the dose of 20 mg/kg body weight vitamin E in the same concentration as group 3 animals, and vitamin A in the dose of 0.2 mg/250 g of body weight; group 4 animals were administrated the above-noted substances daily for 14 days preemptively before an exposure to the atherogenic agent).

The degree of severity of dyslipidemic state in animals was estimated by the level of serum total cholesterol (TC), high density lipoprotein (HDL), low density lipoproteins (LDL), very low density lipoproteins (VLDL), triacylglycerols and atherogenic index (AI).

All biochemical analyzes were performed with standard reagents produced by "Abris+" and "Dias" companies using biochemical analyzer BS-400 (China).

Statistical processing of the results was carried out in MS Excel 6.0 using the t-distribution function. Results yielding a p-value of ≤0.05 were considered significant.

**Main part:**

Indicators of the serum lipid profile of experimental animals are presented in Figures 1-3.

As shown in Figure 1, the administration of Tween-80 caused an increase in the level of total cholesterol by 29.2% compared to intact animals, HDL levels decreased by 29.4% and LDL content increased by 150%, respectively. Atherogenic index increased by 152%. The data obtained characterizes the state of hyperlipidemia in animals from the control group, in which there is an increase in total cholesterol levels accompanied by an increase in pro-atherogenic LDL and decrease in antiatherogenic HDL levels, which leads to an increase in atherogenic index. Increased atherogenic index indicates a high likelihood of pathologic vascular changes and the development of cardiovascular diseases.
It is known that increased intake of polyunsaturated fatty acids considerably lowers the level of serum cholesterol [16].

Fig. 1: Indicators of lipid fractions and atherogenic index in the serum of intact animals and animals receiving Tween-80.

High PUFAs content in the fat indicates a high probability of ongoing oxidation processes. We used vitamins E and A in order to prevent the oxidation of fatty acids. It’s far known that vitamins E and A belong to the group of natural antioxidants. They protect the lipid structures of biological membranes from free radicals. It is known that the use of high dose of antioxidants is contraindicated. So for this reason a good combination of antioxidants is essential, as there may be a synergistic effect or an effect of inhibiting [17].

Group 3 animals received liposomal suspension with vitamin E at the concentration of 1% as compared to the lipid component.

Figure 2 shows the data on the assessment of serum lipid profile in animals receiving liposomal suspension enriched with vitamin E.

Fig. 2: Indicators of the level of lipid fractions and atherogenic index in the serum of animals treated with liposomal form of PUFAs enriched with vitamin E.

The figure shows that preventive administration of liposomes enriched with vitamin E resulted in the decrease in the total cholesterol level by 10.9% as compared to the control group. By the way there was an increase in the level of HDL, which amounted to 16.6%. There were reductions in the level of LDL, VLDL and atherogenic index by 21.2%, 16.6% and 31.5%, respectively.

The findings suggest a high efficiency of liposomal form of PUFAs. The preventive administration of PUFAs led to the reduction in atherogenic and the increase in antiatherogenic components of the serum as compared to the animals of the control group.

Group 4 animals received the liposomal suspension enriched with vitamins E and A in the dose of 0.2 mg/250 g of the rat weight.

Figure 3 shows the change of lipid fractions in the serum of experimental animals from the group 4 towards the same parameters in the control group.

Figure 3 shows that the rate of total cholesterol in the blood serum of the animals from the test group number 4 that received liposomal suspension enriched with vitamins A and E decreased by 10.3%, HDL cholesterol increased by 11.1%, while LDL cholesterol decreased by 30% as compared to the same indicators in the control group of animals, which in turn resulted in the decrease in the value of atherogenic index by 33.7%. The experimental data showed that hypolipidemic effect of the liposomal form of Vitamin A containing Vitamin E and PUFAs was at the same level as without addition of vitamin A. In both cases it was found that the decrease in the atherogenic index as compared to that in the control group of animals is associated with significant lowering of atherogenic cholesterol fractions (LDL).
Conclusion:
Experimental dyslipidemia reproduced in this study by intraperitoneal administration of Tween 80 is characterized by an increase in the level of serum total cholesterol of rats, mainly due to the considerable increase in the fraction of LDL and decrease in the fraction of HDL. All the experiments revealed that the use of vitamin E only in liposomes containing PUFAs in combination with vitamin A causes a pronounced antiatherogenic effect of liposomal suspensions associated with a detergent-induced hyperlipidemia. Reduced probability of the risk of atherosclerosis in the animals treated with liposome enriched with PUFAs and vitamins E and A is apparently caused by the decrease in cholesterol content of the atherogenic fractions.

REFERENCES


