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INFLUENCE OF CONSUMPTION OF HIGH OLEIC SUNFLOWER OIL ON THE BIOSYNTHESIS OF FATTY ACIDS IN THE LIVER OF RATS

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Abstract

Background. To determine the effect of consumption of high-oleic sunflower oil on the content and biosynthesis of energy and polyunsaturated (PUFA) fatty acids in rat liver lipids.

Methods. Rats received a semi-synthetic fat-free diet in which 5 % or 15 % starch was replaced with high oleic sunflower oil. One group of rats received a diet with 5 % regular (high linoleic) sunflower oil. The duration of feeding was 30 days. Liver lipids were divided into three fractions: neutral lipids, phospholipids and free fatty acids, in which the fatty acid composition was determined by gas chromatography. The "activity" of fatty acid synthase, palmitic acid elongase, and stearyl-CoA desaturase (SCD18) was determined by the ratio of fatty acid content.

Results. It was found that the largest amount (60-80 %) of fatty acids in liver lipids are energy ($C_{16:0}$ + $C_{16:1}$ + $C_{18:0}$ + $C_{18:1}$). PUFA account for 10-30% of all fatty acids, and they are

also found in the liver lipids of rats fed a free-fat diet (FFD). Fatty diets reduce the "activity" of synthase, but increase the "activity" of elongase and desaturase. A diet with high linoleic sunflower oil reduces the content of ω-3 PUFA in lipids, while a diet with high oleic sunflower oil increases it dose-dependently. Fatty diets containing high oleic sunflower oil dose-dependently reduce the "activity" of palmitic acid desaturase (SCD16). Consumption of high linoleic sunflower oil sharply increases the ratio of ω-6/ω-3 PUFA in liver lipids, while diets with high oleic oil reduce it dose-dependently.

Keywords: liver lipids; fatty acids; ω-3 PUFA; oleic acid; fatty acid biosynthesis.

Introduction

All fatty acids in the animal body can be divided into 2 large groups. The 1st group is energy fatty acids (EFA), which are part of triglycerides and cholesterol esters and provide mitochondria with an energy substrate for the formation of ATP. The main energy fatty acid in the animal body is oleic ($C_{18:1}$, ω-9) [1-4]. The 2nd group is structural-regulatory fatty acids (SRFA), which are part of phospholipids, glycolipids, sphingomyelins. Structural regulatory fatty acids include polyunsaturated fatty acids (PUFA), which differ not only in the size of the carbon chain (C_{18}, C_{20}, C_{22}), but also in the number of double bonds (2, 3, 4, 5, 6), as well as their location(ω-6 or ω-3) [1, 2, 5]. Physiologically active substances (prostaglandins, leukotrienes, thromboxanes) with pro-inflammatory properties are formed from ω-6 PUFA (mainly arachidonic) under the influence of oxygenase enzymes [6]. Physiologically active substances (resolvins, protectins, maresins) with anti-inflammatory and reparative properties are formed from ω-3 PUFA under the influence of oxygenases [7].

It has been established that all these fatty acids, both EFA and SRFA, are synthesized in the body from non-lipid precursors (carbohydrates, proteins, organic acids, and alcohol). Moreover, the main site for the formation of EFA is the liver, and as for SRFA, it is possible that their biosynthesis is carried out by endogenous bacteria [8].

Despite the presence of endogenous biosynthesis of fatty acids in the animal organism, it still consumes fats and other lipids with food, often in very significant quantities.

Undoubtedly, exogenous fatty acids can affect the nature of endogenous fatty acid biosynthesis, which can lead to metabolic disorders and the development of various pathological conditions [9, 20-22].

The aim of this work was to determine the effect of high oleic sunflower oil (HOSO) on the content and biosynthesis of fatty acids in rat liver lipids in comparison with conventional high linoleic sunflower oil (HLSO).

Materials and research methods

The experiments were carried out on 24 Wistar white rats (male, 5 months old, body weight 225-235 g), divided into four equal groups: The groups received fat diets containing 5 % conventional sunflower (high linoleic) oil (HLSO), 5 % high oleic sunflower oil (HOSO) and 15 % HOSO, respectively. The composition of the diets is presented in table 1. Unrefined sunflower oil was used, the fatty acid composition of which is presented in table 2.

Table 1. The composition of diets for rats [15]

Components	Content , %			
	1 FFD	2 HLSO, 5 %	3 HOSO, 5 %	4 HOSO, 15 %
Corn starch	64	59	59	49
Soybean meal defatted	20	20	20	20
Ovalbumin	6	6	6	6
Sucrose	5	5	5	5
Mineral mixture	4	4	4	4
Vitamin mixture	1	1	1	1
High linoleic sunflower oil (HLSO)	0	5	0	0
High oleic sunflower oil (HOSO)	0	0	5	15

FFD – free fat diet.

Table 2. Fatty acid composition of used oils (%)

Fat acid	Short formula	High linoleic sunflower oil	High oleic sunflower oil
Myristic	$C_{14:0}$	0,12	0,06
Palmitic	$C_{16:0}$	6,53	4,15
Palmitooleic	$C_{16:1}$	0,12	0,13
Stearic	$C_{18:0}$	2,86	2,75
Oleic	$C_{18:1}$	30,29	84,57
Linoleic	$C_{18:2}$, ω-6	57,12	6,16
α-linolenic	$C_{18:3}$, ω-3	0,08	0,21
Arachidonic	$C_{20:4}$, ω-6	0	0
Eicosapentaenoic	$C_{20:5}$, ω-3	0	0
Docosapentaenoic	$C_{22:5}$, ω-3	0	0
Docosahexaenoic	$C_{22:6}$, ω-3	0	0

The duration of feeding was 30 days. After euthanasia of the animals under thiopental anesthesia, the liver was isolated and lipids were extracted from it according to the Dole method [10]. Lipids were divided into 3 fractions: neutral lipids (triglycerides + cholesterol esters, NL), phospholipids (PL), and free fatty acids (FFA) [11]. The lipid fractions of

individual rats of each group were pooled and used to determine the fatty acid composition by gas chromatography [12].

The "activity" of fatty acid synthase was determined by the total content of palmitic and palmitooleic acids. The "activity" of the palmitic acid elongase enzyme was determined by the formula $A=(C_{18:0}+C_{18:1})/(C_{16:0}–C_{16:1})$ [13]. The activity of the stearyl-CoA desaturase (SCD) enzyme was determined by the $C_{18:1}/C_{18:0}$ ratio (SCD18) and by the $C_{16:1}/C_{16:0}$ ratio (SCD16) [14].

Results and discussion

Table 3 presents the results of determining the composition of fatty acids in the fraction of neutral lipids in the liver of rats receiving fat-free and fatty diets. All fatty acids are divided into 3 groups: energy, which make up the majority (63-83 %), PUFA (10-30 %) and other fatty acids (short-medium-chain, long-chain saturated or monounsaturated C_{20} and more), the total number of which was 5-9 %.

Table 3. Influence of fatty diets on the content (%) of energy (EFA) and polyunsaturated (PUFA) fatty acids in the neutral lipid fraction of rat liver

Fat acid (FA)	FFD	Fat diets		
		HLSO, 5 %	HOSO, 5 %	HOSO, 15 %
A. EFA				
Palmitic ($C_{16:0}$)	29,49	21,62	20,66	16,88
Palmitooleic ($C_{16:1}$)	10,54	6,08	4,61	2,29
Stearic ($C_{18:0}$)	2,68	1,69	1,31	2,69
Oleic ($C_{18:1}$)	37,95	33,37	54,10	61,22
Total EFA	80,66	62,76	80,68	83,08
B. PUFA				
Linoleic ($C_{18:2}$, ω-6)	7,31	27,29	11,27	8,86
α- linolenic ($C_{18:3}$, ω-3)	0,34	0,23	0,31	0,90
Arachidonic ($C_{20:4}$, ω-6)	1,77	2,69	1,32	0,99
Eicosapentaenoic ($C_{20:5}$, ω-3)	0,08	0,01	0,02	0,23
Docosapentaenoic ($C_{22:5}$, ω-3)	0,11	0,09	0,12	0,25
Docosahexaenoic ($C_{22:6}$, ω-3)	0,19	0,13	0,27	0,63
Total PUFA	9,80	30,44	13,31	11,86
B.Other FA	10,54	6,80	6,01	5,06

From the presented data, it can be seen that the total number of EFA is reduced by 22.2 % only with the consumption of high-linoleic sunflower oil. Consumption of high oleic sunflower oil, although it reduces the content of palmitic and palmitooleic acids, however, significantly increases the content of oleic acid.

In contrast to EFA, the content of PUFA increases sharply (almost 3 times) in neutral lipids of the liver of rats treated with HLSO.

The content of other fatty acids in the consumption of fatty diets is reduced by 1.5-2 times.

Table 4 presents the results of determining the fatty acid composition of phospholipids in the liver of rats treated with FFD and fatty diets. It should be noted that EFA spredominate in the phospholipid fraction (63-72 %). The share of PUFA accounts for 20-30 %, and most of all PUFA are in the phospholipid fraction in rats fed a diet with 5 % of HOSO. The share of other fatty acids in the phospholipid fraction accounts for 5-8.5 %, and in rats fed fatty diets, the content of these acids is lower than in rats fed with FFD.

Table 4. The effect of fat diets on the content (%) of energy (EFA) and polyunsaturated (PUFA) fatty acids in the fraction of rat liver phospholipids

Fat acid (FA)	FFD	Fat diets		
		HLSO, 5 %	HOSO, 5 %	HOSO, 15 %
A. EFA				
Palmitic ($C_{16:0}$)	27,05	24,70	21,35	18,08
Palmitooleic ($C_{16:1}$)	4,43	2,98	1,98	1,55
Stearic ($C_{18:0}$)	25,32	22,14	19,70	19,65
Oleic ($C_{18:1}$)	14,95	16,07	19,75	32,37
Total EFA	71,75	65,89	62,78	71,65
B. PUFA				
Linoleic ($C_{18:2}$, ω-6)	7,33	14,00	10,79	8,22
α- linolenic ($C_{18:3}$, ω-3)	0,08	0,01	0,06	0,34
Arachidonic ($C_{20:4}$, ω-6)	10,17	11,96	15,48	9,56
Eicosapentaenoic ($C_{20:5}$, ω-3)	0,23	0,01	0,10	0,42
Docosapentaenoic ($C_{22:5}$, ω-3)	0,21	0,09	0,41	0,46
Docosahexaenoic ($C_{22:6}$, ω-3)	1,66	0,13	3,24	3,99
Total PUFA	19,68	26,19	30,08	22,99
B.Other FA	8,57	7,92	7,14	5,36

Table 5 presents the results of determining the content of fatty acids in the FFA fraction of rat liver lipids. In this fraction, the share of EFA is 65-67 %, and the share of PUFA is 25-37 %, and most of all in rats treated with HLSO. In the FFA fraction, other fatty acids make up 7-11 %, and in rats fed fatty diets, the content of these acids is lower than in rats on FFD.

On fig. 1 shows the "activity" of the fatty acid synthase enzyme, more precisely, palmitic acid, which we evaluated by the total content of palmitic and palmitooleic acids. As can be seen from these data, the highest "activity" of synthase is observed in rats treated with

FFD and according to the results of the study of the NL fraction. The consumption of fatty diets dose-dependently reduces the "activity" of synthase according to the results of the study of all fractions of liver lipids.

Table 5. The effect of fat diets on the content (%) of energy (EFA) and polyunsaturated (PUFA) fatty acids in the free fatty acid fraction of rat liver

Fat acid (FA)	FFA	Fat acid		
		HLSO, 5 %	HOSO, 5 %	HOSO, 15 %
A. EFA				
Palmitic ($C_{16:0}$)	22,63	17,89	17,10	15,71
Palmitooleic ($C_{16:1}$)	5,85	4,92	3,25	1,91
Stearic ($C_{18:0}$)	12,72	7,49	9,31	11,25
Oleic ($C_{18:1}$)	19,05	24,40	31,85	37,90
Total EFA	60,25	54,70	61,51	66,77
B. PUFA				
Linoleic ($C_{18:2}$, ω-6)	8,19	21,44	11,94	9,40
α- linolenic ($C_{18:3}$, ω-3)	0,12	0,15	0,19	0,88
Arachidonic ($C_{20:4}$, ω-6)	16,47	14,52	15,65	9,06
Eicosapentaenoic ($C_{20:5}$, ω-3)	0,52	0,04	0,31	1,17
Docosapentaenoic ($C_{22:5}$, ω-3)	0,60	0,26	0,57	0,84
Docosahexaenoic ($C_{22:6}$, ω-3)	2,83	1,19	2,28	4,03
Total PUFA	28,73	37,60	30,34	25,38
B.Other FA	11,02	7,70	8,15	7,85

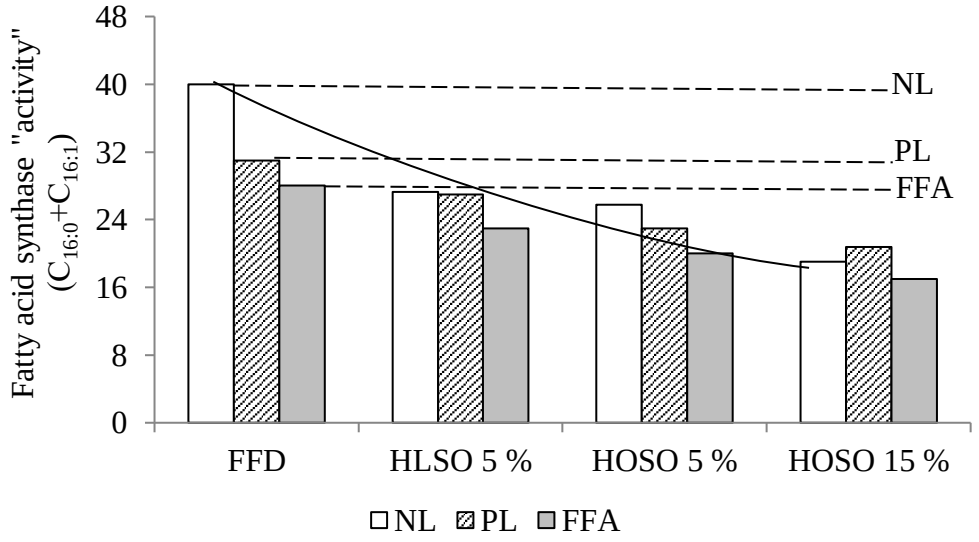

Fig. 1. Effect of fat difets on fatty acid synthase “activity”

(FFD – fat-free diet, HLSO – high-linoleic sunflower oil, HOSO – high oleic sunflower oil; NL – neutral lipids, PL – phospholipids, FFA – free fatty acids)

On fig. 2 shows the "activity" of the palmitic acid elongase enzyme, which we determined by the formula $(C_{18:0} + C_{18:1})/(C_{16:0}–C_{16:1})$, which also takes into account the content of stearic and palmitic acid metabolites. It can be seen that the "activity" of elongase increases in a dose-dependent manner with the consumption of fatty diets, and most clearly according to the results of the study of the fractions of NL and FFA.

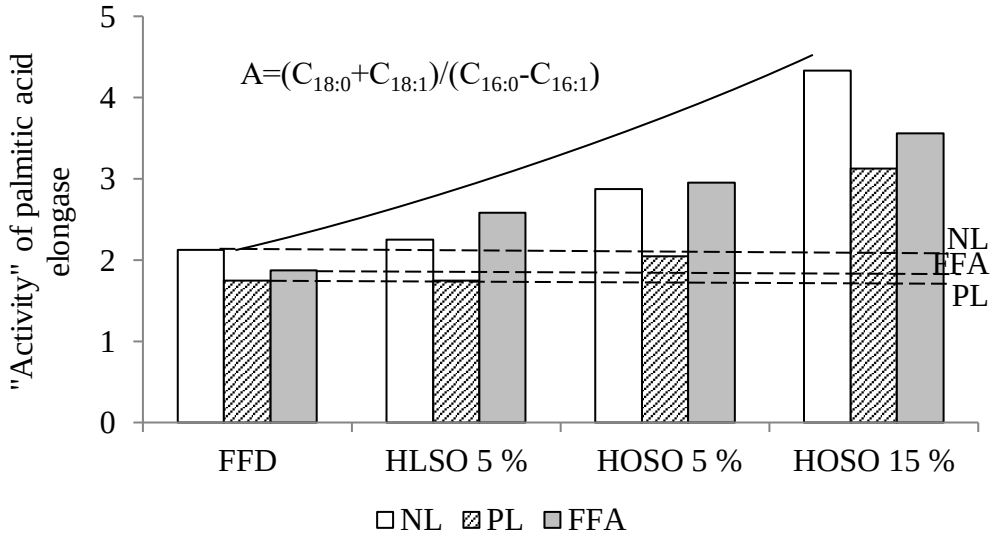

Fig. 2. Influence of fat diets on the "activity" of palmitic acid elongase in rat liver lipids (FFD, HLSO, HOSO, NL, PL, FFA – see Fig. 1)

On fig. 3 shows the "activity" of the enzyme stearic acid desaturase (SCD18) in fatty diets. The highest "activity" of this enzyme is determined in the NL fraction, and the lowest, in the PL fraction. All high-fat diets increase SCD18 "activity", especially diets with HOSO.

On fig. 4 shows the "activity" of palmitic acid desaturase (SCD16), which is an order of magnitude lower than the "activity" of SCD18. From the presented data, it can be seen that, in contrast to SCD18, the "activity" of SCD16 decreases in a dose-dependent manner with the consumption of fatty diets, and most clearly according to the results of the study of the NL fraction.

On fig. 5 shows the content of ω-6 PUFA (more precisely, the sum of $C_{18:2}$ and $C_{20:4}$) in rat liver lipid fractions. The highest content of ω-6 PUFA is observed in the FFA fraction, and the lowest in the NL fraction. When HLSO is consumed, the content of ω-6 PUFA increases in all fractions, but is especially strong in the NL fraction. Consumption of diets with HOSO increased the content of ω-6 PUFA in the PL fractions of liver lipids in rats fed a diet with 5 % HOSO.

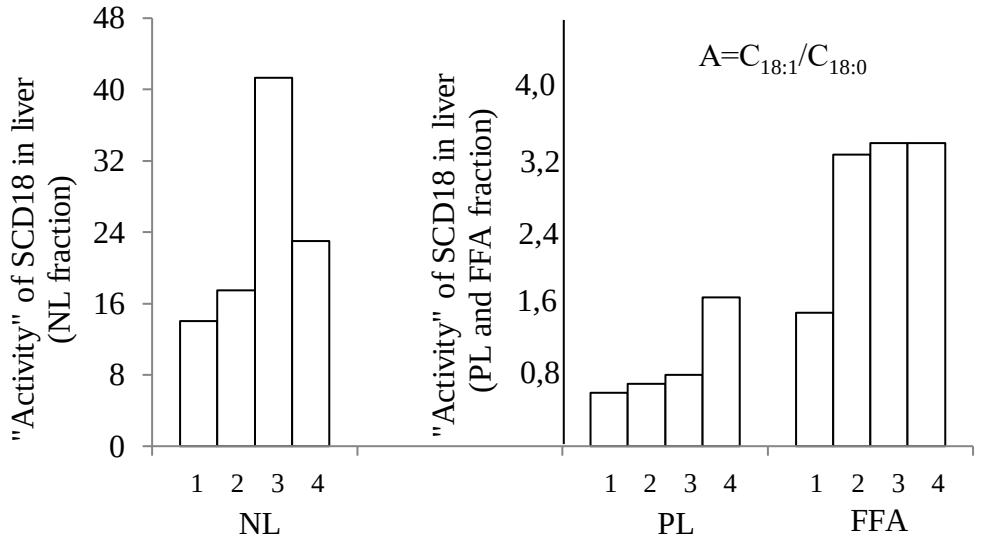

Fig. 3. The influence of fat nutrition on the "activity" of stearic acid desaturase SCD18 in rat liver lipids (1 – FFD, 2 – 5 % HLSO, 3 – 5 % HOSO, 4 – 15 % HOSO)

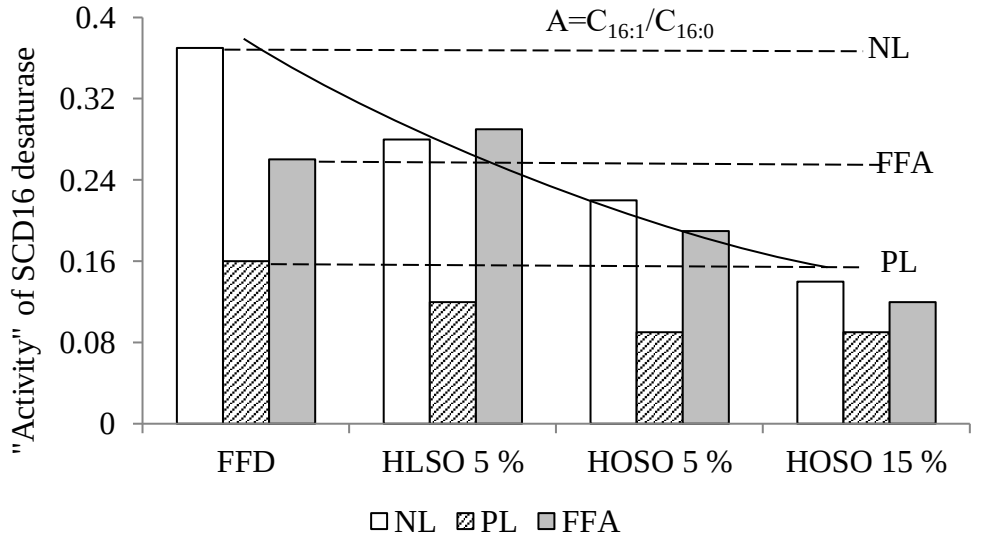

Fig. 4. Influence of fat diets on the "activity" of SCD16 desaturase in rat liver lipids (FFD, HLSO, HOSO, NL, PL, FFA – see Fig. 1)

On fig. 6 shows the content of ω-3 PUFA ($C_{18:3}$, $C_{20:5}$, $C_{22:5}$ and $C_{22:0}$) in rat liver lipids. It is seen that the highest content of ω-3 PUFA is observed in the FFA fraction, and the lowest in the NL fraction. Consumption of HLSO sharply reduces the content of ω-3 PUFA in all lipid fractions, but most strongly in the PL fraction. Consumption of HOSO not only does not reduce the content of ω-3 PUFA, but even significantly and dose-dependently increases

their content in the fractions of PL and FFA, moreover, when consuming a diet with 5 % HOSO, 1.8 times, and when consuming a diet with 15 % HOSO 2,5 times.

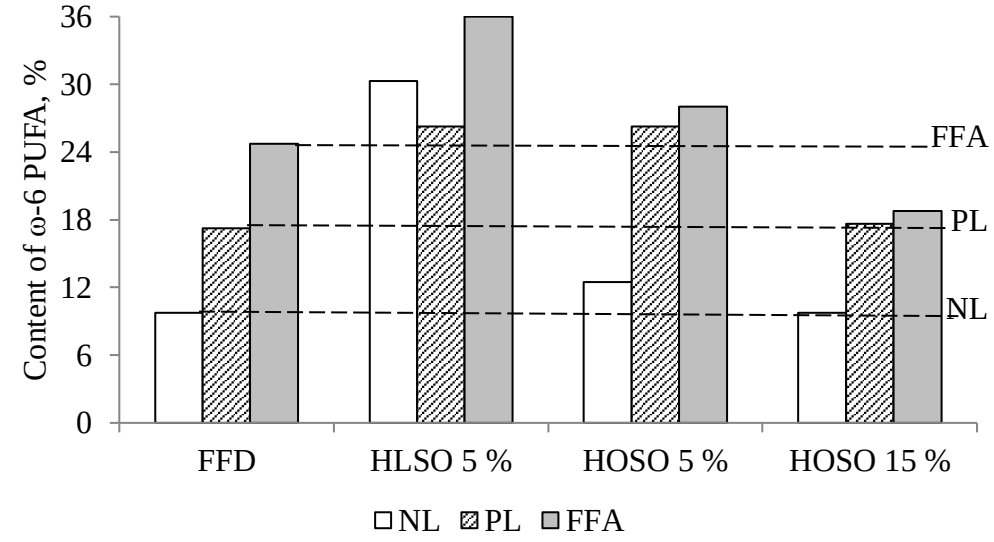

Fig. 5. Effect of fat diets on the content of ω-6 PUFA in rat liver lipids (FFD, HLSO, HOSO, NL, PL, FFA – see Fig. 1)

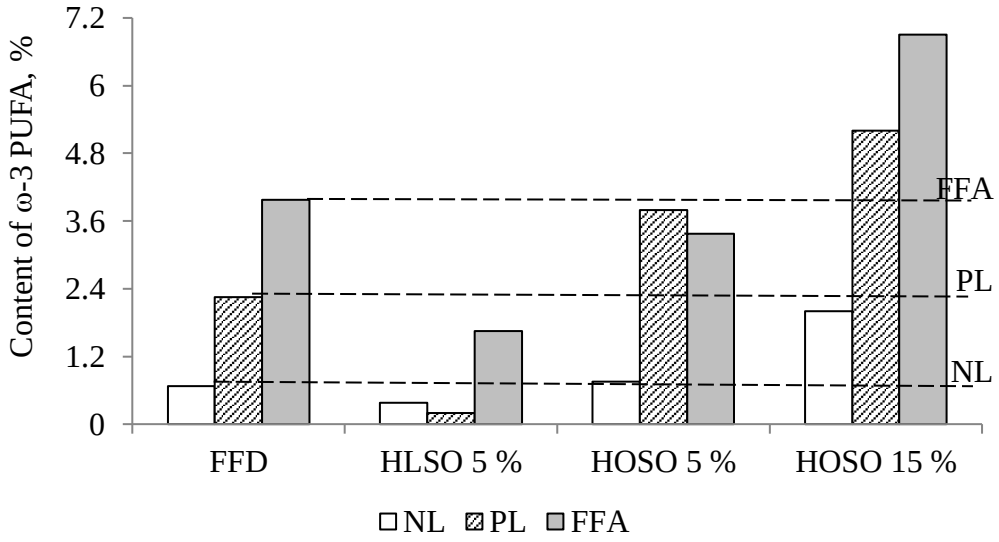

Fig. 6. Influence of fatty diets on the content of ω-3 PUFA in rat liver lipids (FFD, HLSO, HOSO, NL, PL, FFA – see Fig. 1)

On fig. 7 shows the ratio ω-6/ω-3 of PUFA, which was the highest in the NL fraction, and the lowest in the PL and FFA fractions. HLSO consumption dramatically increased the ω-6/ω-3 PUFA ratio in all lipid fractions, especially strongly in the PL fraction. Consumption of

a diet with 5 % HOSO had little effect on this ratio in all fractions, and consumption of a diet with 15 % HOSO significantly reduced it.

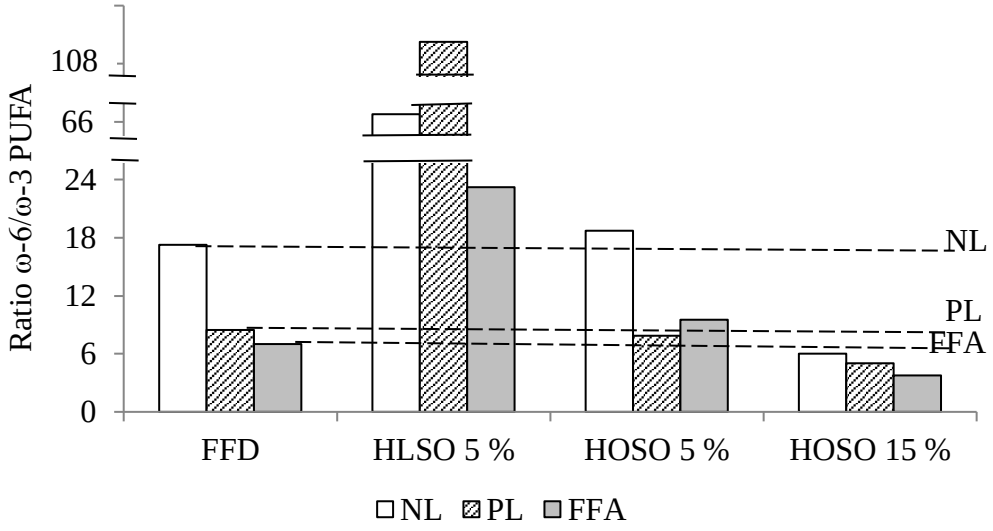

Fig. 7. Influence of fat diets on the ratio ω-6/ω-3 PUFA in rat liver lipids (FFD, HLSO, HOSO, NL, PL, FFA – see Fig. 1)

Thus, our studies have shown that in an animal organism receiving a fat-free diet, endogenous biosynthesis of fatty acids and lipids from non-fat substances, apparently, mainly from carbohydrates, is carried out.

The main product of endogenous fatty acid biosynthesis is energy fatty acids, which are formed mainly in the liver under the action of the palmitic acid synthase enzyme. Further transformations of palmitic acid occur with the participation of the enzymes elongase and stearyl-CoA desaturase (SCD18) with the formation of oleic acid. The latter is the main energy substrate for muscle and connective tissues, coming to them from the liver as part of very low density lipoproteins (VLDL).

Along with the endogenous biosynthesis of EFA in animals, endogenous biosynthesis of PUFA of both ω-6 and ω-3 series occurs in a more favorable ratio (about 7).

A possible source of PUFA in the body can be endogenous bacteria, the content of which in the human large intestine exceeds 2 kg (which is more than the mass of the liver) [16]. It has been established that a number of bacteria, fungi, and yeasts are capable of synthesizing PUFA [17, 18].

In the animal body in somatic cells, the endogenous biosynthesis of PUFA is blocked, which served as the basis for considering PUFA, in particular, linoleic acid ($C_{18:2}$, ω-6), as an essential one, which has the properties of a vitamin (vitamin F) [19].

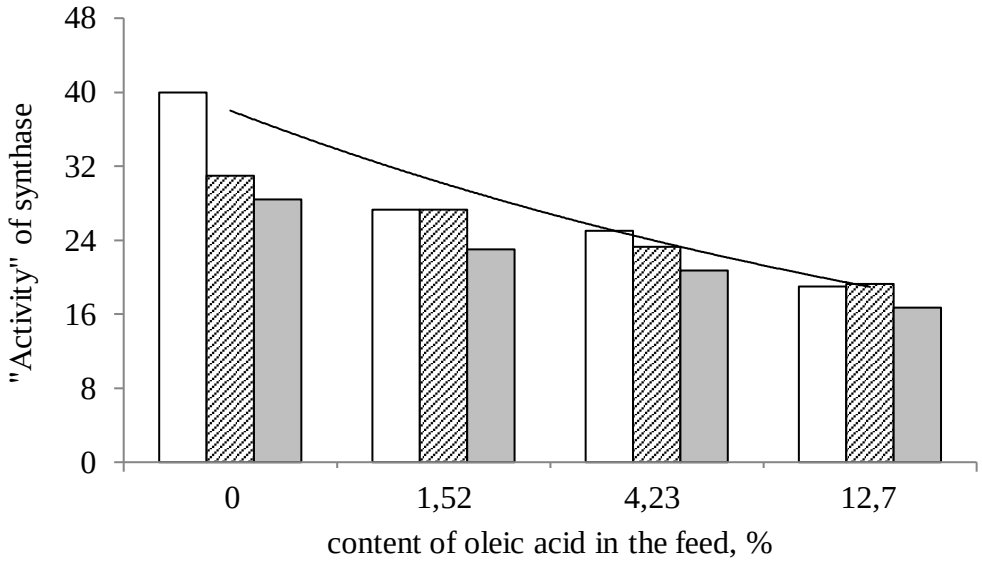

Fig. 8. Reduced "activity" of fatty acid synthase, depending on the content of oleic acid in the feed

Our studies have shown that one of the blockers of endogenous PUFA biosynthesis can be linoleic acid, the entry of which into the body as part of HLSO reduces the content of ω-3 PUFA in the composition of liver phospholipids by almost 10 times.

Our studies have shown that oleic acid, on the contrary, increases the synthesis of ω-3 PUFA in a dose-dependent manner. Since the endogenous biosynthesis of PUFA is carried out by the endogenous microbiota, it can be assumed that oleic acid stimulates the growth and increases the productivity of certain bacteria (or fungi) that produce these PUFA.

The results of our studies indicate the inhibitory effect of oleic acid on the "activity" of the key enzyme of endogenous biosynthesis of energy fatty acids - palmitic acid synthase in liver cells, as well as its inhibitory effect on palmitic acid desaturase (SCD16).

Conclusions

In the animal body, along with the main biosynthesis of energy fatty acids (mainly oleic), endogenous synthesis of PUFA also occurs, possibly due to the endogenous microbiota. Dietary fat intake reduces the endogenous biosynthesis of both energy fatty acids (possibly through retro-inhibition by oleic acid) and ω-3 PUFA (possibly due to suppression of the growth and productivity of the endogenous microbiota involved in their biosynthesis).

The activating effect of oleic acid on the endogenous biosynthesis of ω-3 PUFA was revealed.

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