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Odd-numbered Carbon Atom Fatty Acids:

Metabolic and Nutritional Aspects

by

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INTRODUCTION

It is known that the quality of the fats contained in foodstuffs influences the type of fats deposited in the animal organism. This occurs to a greater extent in the lower animals, while rising on the zoological scale, a close correspondence between deposited fats and those contained in the diet cannot always be demonstrated. This correspondence generally becomes more obvious when an unusual type of fats is administered. The time necessary to modify the constitution of the deposit fats is in relation to the quantity of the fat administered and differs in the various organs and tissues in proportion to the turnover velocity (1).

Besides the nature of the deposit fats, diet can influence that of the structure lipids amongst which, and particularly important, are the lipids of the cellular membranes (2).

What are not known however are the proportions between chemical

composition, understood as nature and proportions of the different molecular species, and function of the structures. In fact, while in some cases, as in the circulating erythrocytes, the composition of the phospholipids can be altered by the diet without influencing function (3, 4), in others it has been seen that the permeability of the membranes varies with the variation of their composition in fatty acids (5).

From this it is obvious that, when unusual fatty acids, such as those with odd-numbered carbon atoms, are used for food purposes, problems and perplexities arise through the possibility that these fatty acids may turn up again in deposit lipids or structure lipids with eventual possible alterations at the level of functions.

ORIGIN AND DISTRIBUTION IN NATURE (IN THE NATURAL STATE).

The odd-numbered fatty acids although they cannot be considered physiological compounds, are found in nature both in lipids of plant and animal origin (6). The presence of odd-numbered fatty acids in natural fats was established for the first time by Jantzen and Witgert (7) who identified minimum traces of n-nonanoic, n-undecanoic and n-triundecanoic acids in coconut oil.

Subsequently some odd-numbered fatty acids were found in mutton fat (8) and in butter (9, 10). More recently, analyses of the acid composition of fatty substances of samples of powdered milk on sale on the market (11) and butter (12) have revealed the presence in them of different odd-numbered fatty acids both linear and branched.

Schlenk in a recent survey (13) reports the percentages (sic) of total odd-numbered fatty acids present in different natural sources (table 1). As may be seen from the table, while generally the percentages (sic) of total odd-numbered fatty acids do not exceed 5%, in some cases, above all in the species of marine origin, considerably higher values are reached.

Table No. 1 -- Distribution of natural odd-numbered fatty acids (in nature)

Source	% odd-numbered fatty acids
<u>Bacterium anitratus</u>	2.5
<u>Aerobacter aerogenes</u>	3.8
<u>Escherichia dispar 4169</u>	11.5
<u>Chlorella pyrenoidosa</u>	1.3
<u>Euglena gracilis</u>	33.4
Olive Oil	<0.4
Chicken (deposit fat)	0.4-1.5
Cow's milk	2.4-4.9
Rat liver	0.5-2.9
Human fat	1.1
Human erythrocytes	0.8
Cod liver	2.4
Herring	0.9
Oyster	2.3
Flounder	1.0
Tuna	4.2
Trout	2.6
Grey Mullet	19.1-20.4

The data contained in this table were taken from Schlenk (13). Thus in the Euglena gracilis these represent 33%, in the Mullet 20%, and in the Lugworm (Arenicola marina) 16% of the total fatty acids. Higher percentages compared with the higher organisms are found in the microorganisms in which the synthesis of the fatty acids does not seem to be so rigidly directed towards the even-numbered series. It is to this cause that the author thinks that it is possible to trace back the major quantity of odd-numbered fatty acids found in animals of marine origin which, either directly or indirectly, feed on microorganisms. This hypothesis, however, does not

explain, as the same author stresses, the reason for the high percentages of odd-numbered fatty acids in some species of fish like the mullet, rather than in others which also live in the same environment and have similar feeding habits. It seems, however, more probable that these high concentrations of odd-numbered fatty acids, may be attributed to fortuitous circumstances, such as high quantities of precursors present in the diet, rather than to a special type of metabolism (14). Thus for example, the presence of high quantities of propionic acid, originating from the splitting of dimethylpropiothetine, contained in appreciable quantities in a marine alga, with the formation of acrylic acid from which, through biological reduction propionic acid is formed, (15), has been speculated upon in the diet of some fish.

Other possible origins of the odd-numbered fatty acids are the α -oxidation of the even-numbered fatty acids, as has been found in the brain (16) and in some plants and bacteria (17, 18) and the methyloxidation of hydrocarbons in some microorganisms (19) (Fig. 1).

Normal or branched-chain odd-numbered fatty acids have been found both in the saturated and in the unsaturated series. For the latter it must be pointed out that the nature and the position of the double bonds of the molecule are very similar to those of the corresponding even-numbered series. In fact it is a matter of double cis bonds, often in the same position as the corresponding even-numbered, higher homologue, as in the case of 9-17: 1 and 9-18: 1; 6, 9, 12-17: 3 and 6, 9, 12-18: 3; 5, 8, 11, 14-19; 4 and 5, 8, 11, 14-20; 4. Therefore many unsaturated odd-numbered fatty acids may be grouped, with reference to the terminal methyl group, in the families ω 8, ω 5, ω 2, just as for the corresponding even-numbered series there are the families ω 9, ω 6, ω 3, whose most important components are, respectively, oleic, linoleic and linolenic acids (13). Thus also unsaturated and elongated odd-numbered fatty acids are found in animals fed

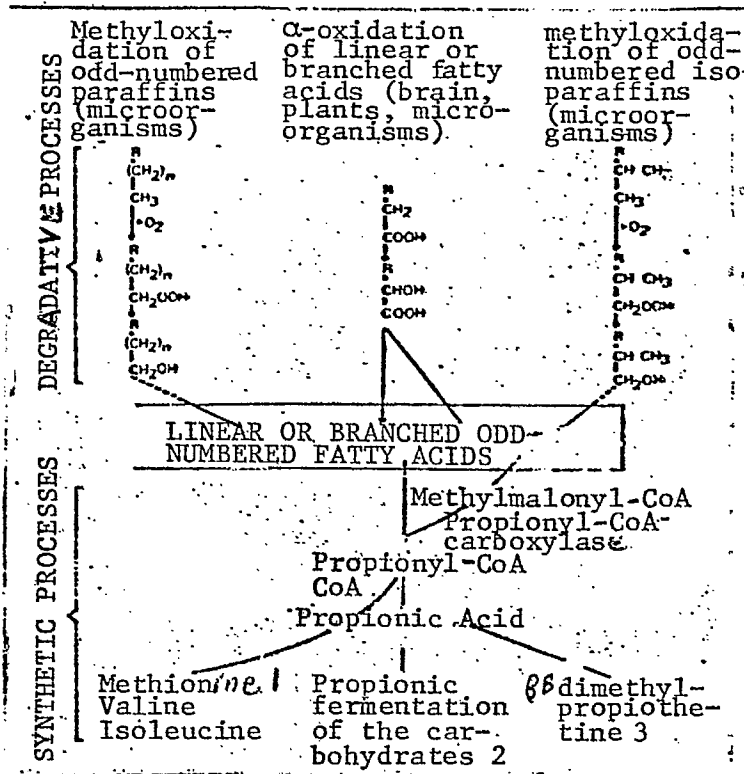
with lower, odd-numbered homologues in the case of the 9-17: 1 ω 8 and 5, 8, 11-19: 3 ω 8 acids found in the liver lipids of rats fed with saturated odd-numbered fatty acids similarly to what occurs in the even-numbered series (20).

These similarities in structure and metabolism have led us to consider the existence of metabolic pathways for the odd-numbered fatty acids similar to those existing for the even-numbered ones as regards chain elongation and desaturation mechanisms.

Starting from this observation, Schlenk speculated and then experimentally demonstrated the possibility that unsaturated odd-numbered fatty acids behave like essential fatty acids (21).

Particularly high quantities of odd-numbered fatty acids are present in the lipids of the microbial biomasses obtained by growing strains of yeast on hydrocarbons derived from petroleum. Various studies indicate that the type of fatty acids is influenced by the hydrocarbon composition of the substrate (22, 23, 24).

Thus Mishina et al. (22), by determining the composition in fatty acids of the yeast lipids of the genus *Candida* (*Candida lipolytica* and *Candida tropicalis*) grown on mixtures of even-and odd-numbered hydrocarbons and on individual 11, 13, 15 and 17 carbon atom hydrocarbons in comparison with substrates of glucose or even-numbered (carbon atoms) alkanes, found that the percentages of odd-numbered fatty acids increase while the corresponding ones of the substrate increase (Table 2).



1 = in the higher organisms

2 = in the intestine and above all in rumen

3 = in some algae

Fig. 1. Possible pathways of origin of odd-numbered fatty acids in nature.

Table No. 2. Percentage of odd-numbered fatty acids in the cellular lipids of strains of *Candida* grown on different substrates.

Substrate	<i>Candida lipolytica</i>	<i>Candida tropicalis</i>
	% odd-numbered fatty acids	% odd-numbered fatty acids
Glucose	2.9	6.6
C ₁₂	0.9	3.3
C ₁₄	1.0	2.1
C ₁₆	1.6	1.1
C ₁₈	3.4	0.3
Mixture(*)	13.8	46.9
C ₁₁	9.6	40.1
C ₁₃	60.0	67.1
C ₁₅	80.9	73.5
C ₁₇	85.4	83.9

(*)Mixture = $\left\{ \begin{array}{l} C_{11} 23.9\% \\ C_{13} 46.8\% \\ C_{15} 26.3\% \\ C_{17} 3.0\% \end{array} \right.$

The data contained in this table have been taken from Mishina et al. (22).

Among the odd-numbered fatty acids those present to the greatest extent, in each case, are those at 17 C and among these, above all, C_{17:1} followed then by C_{17:0}; furthermore the percentage of C₁₇ increases considerably with the increase in length of the carbon chain of the substrate, demonstrating in this way that the "intact incorporation mechanism", that is to say, the accumulation of fatty acids of the same length as the substrate molecule, is predominant.

However the elongation mechanisms of the chain and of synthesis ex novo starting from a precursor with a lesser number of carbon atoms are also working, as the same authors demonstrate, with studies on the composition in fatty acids during the course of fermentation (22).

Similar results are reported by Pelechova et al. (23) who by studying the composition in fatty acids of the lipids of 6 strains of yeast grown on a mixture of paraffins containing from C₁₁ to C₂₃ hydrocarbons, found similar profiles in all the strains studied, with high percentages of C_{17:1}. This indicates that the nature of the cellular fatty acids is independent of the type of yeast used and, to the contrary, reflects that of the substrate. On the other hand by adding n-hexadecane to deparaffinized fuel oil, the percentage of total odd-numbered fatty acids present in the lipids of lipolytic Candida grown on this substrate, diminishes considerably, whilst that of the even-numbered fatty acids increases in parallel (24.)

METABOLIC ASPECTS

It has been demonstrated experimentally that the odd-numbered fatty acids which are found in animal organisms can be either of exogenous or endogenous nature. This results from the fact that these compounds, once having entered into circulation either in the liberated state or as part of the molecules of neutral or complex lipids, are deposited directly into

the adipose tissue as triglycerides or catabolized in the liver where through β -oxidative scission they give rise to molecules of acetic and propionic acid. The propionic acid, which therefore represents the final metabolite characteristic of odd-numbered fatty acids, can however derive also from the catabolism of other molecules, like certain amino-acids, or by intestinal bacterial fermentations. In particular, in the case of ruminants, the presence in the rumen of propionic bacteria, determines the formation of considerable quantities of this acid. Since the propionic acid, formed in any case, constitutes the biosynthetic precursor of the odd-numbered fatty acids, as has been fully confirmed with experiments in vitro on the mammary gland of oxen (25), on pigeon liver (26), on the adipose tissue of the rat (27), in the rat brains (28) and in vivo on the mouse (29), this explains why odd-numbered fatty acids can be found in the tissues and organs of animals which most definitely have not been fed with these compounds,

As regards man, Gompertz found an accumulation of odd-numbered fatty acids in the liver lipids of a child who died of propionic acidemia (30), an illness caused by the lack at birth of the enzyme propionylCoA carboxylase which catalyzes the conversion of propionylCoA to methylmalonylCoA (31). In particular it is the saturated and monounsaturated C_{17} which is found for the most part in the different lipid fractions analyzed, representing in total respectively 3% and 2% approximately of the total fatty acids, while $C_{15:0}$ (?) represents approximately 1%. Furthermore it is important to point out that the odd-numbered fatty acids are present not only in the triglycerides and among the free fatty acids, but also, even though in lesser proportion, in the phospholipids.

Kishimoto (32) also found an accumulation of normal- and branched-chain odd-numbered fatty acids in the nervous tissue of a child who died of methylmalonic aciduria, an illness which can be caused by the lack of

the enzyme methylmalonylCoAmutase or by the inability to use vitamin B₁₂ by converting it into the coenzyme desoxyadenosyl B₁₂ of methylmalonylCoAmutase.

Recent experiments conducted on hogs kept on a diet lacking in fats for 5 months have shown an increase of saturated and unsaturated C₁₇, C₁₉ and C₂₁ odd-numbered fatty acids in the triglycerides and hepatic phospholipids as compared with hogs kept on a diet without fats for one month and with animals fed normally (33). Since 5 months of a lipid diet are considered a sufficient time for the appearance of fatty acids of endogenous origin only, the capacity of the organism to synthesize odd-numbered fatty acids from endogenous precursors is thus clearly demonstrated.

In line with these results there seem to be reported by Molnar (34) who finds odd-numbered fatty acids from C₁₃ to C₂₁ (C₁₃, C₁₅, C_{15.1}, C_{17.1}, C₂₁) in the lipids of the heart, kidneys and lungs of hogs in decreasing quantities with the progress of the development phase of the fetus (Table 3).

Table No. 3-- Percentage of total odd-numbered fatty acids in the lipids of the heart, lungs and kidneys of hogs in the fetal and post-natal periods.

Period	Heart	Lungs	Kidneys
Fetuses 45 days . . .	8.3	11.3	7.3
Fetuses 60 days . . .	7.4	8.0	8.1
Fetuses 70 days . . .	8.5	8.7	8.1
Fetuses 90 days . . .	6.4	7.8	8.0
Birth 1 day . . .	2.3	2.1	1.4
Birth 14 days . . .	1.0	1.5	1.3

The 15 C odd-numbered fatty acids, saturated and mono-unsaturated, represent approximately 15% of the total odd-numbered fatty acids.

In fact even if the explanation of such behaviour is not supplied, the endogenous synthesis capacity of these fatty acids starting from a precursor which could be propionic acid seems to be confirmed. This could

accumulate in the first phases of life through the lack of the enzymes which catalyze the conversion of propionic acid to succinic acid; but this hypothesis remains to be demonstrated. Other biochemical alternatives for propionic acid are certainly possible. It is, in fact, known that besides the pathway of biosynthesis of the odd-numbered fatty acids and that of oxidation via (by way of) methylmalonylCoA \rightarrow succinylCoA \rightarrow Kreb's cycle, the propionic acid can take other metabolic pathways, like that of gluconeogenesis. What is not yet known is the regulation of these different metabolic lines. That \checkmark propionic acid is gluconeogenic has been demonstrated by Deuel (35) who, by administering tripropionine to rats, found quantities of glycogen higher than those found by administering equivalent quantities of triacetin and tributyrin. On the other hand, Van Itallie (36), in animals (fasting for 24 hours previously) fed for 4-6 weeks with triundecanoic and which therefore had 26-40% of C_{11} in the adipose tissue found that hepatic glycogen diminishes much less rapidly as compared with controls fed normally. In the hours following fasting the hepatic glycogen increased both in the controls and in the test animals, but the level always remained higher in the group fed with odd-numbered fatty acids. The neogenesis of glucose from propionic acid could, according to Deuel (37), be the cause of the diminished ketogenesis observed in animals fed with odd-numbered fatty acids, especially those with a short chain. For this reason some authors, some years ago, had recommended the use of odd-numbered fatty acids for diabetics (38, 39).

However, recently Guisard et al. (40) always found in the plasma of dogs which had been given (by infusion) triglycerides containing even- or odd-numbered medium chain fatty acids, acetoacetate and β -hydroxybutyrate, even though the levels may be slightly lower in the case of the odd-numbered fatty acids. This, on the other hand is in keeping with the fact that during β -oxidation the fatty acids supply next to propionylCoA

different acetylCoA molecules as well.

As regards the turnover velocity of the odd-numbered fatty acids, studies conducted on the adipose tissue of the rat indicate for example for C_{11} an average lifetime of approximately 12 days and a more or less complete disappearance in approximately one month (41).

But the return to normal of the plasmatic levels of triglycerides and free fatty acids for C_9 as compared with C_8 and C_{10} is slower, thus indicating the ability of the organism to eliminate triglycerides and even-numbered fatty acids more readily than odd-numbered fatty acids.

Sloveva et al. (42) in rats which had been fed with a protein-vitamin complex composed of yeast cells grown on hydrocarbons, found after one month's feeding with standard diet again similar odd-numbered fatty acid levels as compared with the controls.

Finally, it must be pointed out that somewhat high quantities of normal- and branched-chain odd-numbered fatty acids (up to 20% of the total fatty acids) are found again in the fecal lipids of the rat (43). This phenomenon is ascribed, at least partly, to preferential synthesis of C_{15} and C_{17} in the caecum, as demonstrated by the incorporation experiments with marked precursors conducted on the caecal content. On the other hand an increase in the proportion of fecal odd-numbered fatty acids may occur following feeding with these compounds, because it has been seen that their absorption velocity is considerably lower than that of the corresponding even-numbered fatty acids (44, 45).

NUTRITIONAL ASPECTS

The first research on the nutritive value of odd-numbered fatty acids present in the synthetic fats obtained through oxidation of the paraffins, date back to the period of the Second World War (46), when, in Germany, triglycerides containing synthetic fatty acids from C_{10} to C_{18} were prepared

industrially. These synthetic triglycerides contained even-and odd-numbered fatty acids, generally saturated, as well as a certain quantity of branched (-chain) fatty acids, dicarboxyl acids, lactones, etc.

The various teams of researchers which, almost simultaneously, carried out studies on animals and man, agreed in pronouncing themselves in favour of the introduction into human and animal feeding of synthetic triglycerides which, if appropriately purified and free from branched (-chain) fatty acids, were perfectly assimilated in the dose of 50 g pro-die (47).

The main data which emerged had shown that:

- a) The odd-or even-numbered fatty acids lower than C_{12} do not accumulate in the organism nor are they found in urine, thus indicating that they are oxidized. The same thing happens for the fatty acids higher than C_{18} ;
- b) The deposit or tissue fats contain essentially fatty acids between C_{12} and C_{18} , even-and odd-numbered;
- c) Both even-and odd-numbered fatty acids can be desaturated in high quantity.

Even if one does not wish to doubt the reliability of this research, it is necessary, however, as Deuel reports, to bear in mind that during that period results contrasting with those presented were not published.

On the other hand, more recent experiments carried out on rats fed with synthetic fats containing even-and odd-numbered fatty acids, have shown a reduction in growth, protein and lipid efficiency of the odd-numbered synthetic fats, as compared with mixtures of even-and odd-numbered (fats) (48). Saxena et al. (49) also found reduced growth and ketonuria in rats fed for 13 weeks from the time of weaning with diets containing 19.3% of even-and odd-numbered medium-chain fatty acids as compared with another

two groups which received diets in which food fats were composed of even-numbered medium-chain fatty acids or of sunflower oil. Since the diets were isoenergetic and consumption equal, the differences, according to the authors, are to be attributed to an incomplete oxidation of the odd-numbered chain fatty acids which stops at the propionic acid molecule, as well as to loss of energy through the formation of ketone bodies.

In correlation with an excess of propionic acid which originates from the fermentation of the cereals in the rumen (50) and which, as has already been stated, seems to be the main precursor of the small quantities of odd-numbered fatty acids normally present in the animal organism, it has been observed that the adipose tissue of animals fed with diets containing 90% of barley, was soft and of unusual composition because it contained high quantities of both linear and branched odd-numbered fatty acids. The latter, above all on account of their lower fusion point could have been responsible for the unusual look of the adipose tissue. Garton et al. (51) have confirmed the presence of linear and branched odd-numbered fatty acids and diminution of long-chain even-numbered saturated fatty acids in the subcutaneous adipose tissue of lambs fed for 20 weeks with diets containing a high quantity of barley or propionic acid. The authors advanced the possibility that if excessive quantities of propionate compared with those which can normally be metabolized were present in the organisms, the carboxylation product, methyl-malonate, could compete with (contend against) the malonate in the synthesis of the fatty acids, giving rise to branched fatty acids just as had been shown by Cardinale with experiments in vitro (52). In subsequent research (53) the authors confirmed that the methyl-malonate can substitute the malonate at each stage of elongation of the chain of the synthesized fatty acids starting from the acetate or from the propionate.

In recent years much interest has been directed towards the study

of the interaction between odd-numbered fatty acids and metabolism of the essential fatty acids, as well as towards the study of the probable essential functions attributed to the structures of some odd-numbered fatty acids (20, 54).

Mohrhauer and Holman (20) have studied the influence of individual even- and odd-numbered saturated fatty acids on the metabolism of linoleic acid. The variations in the metabolism of linoleic acid have been shown by following the concentrations of arachidonic and eicosatrienoic acids in rat's liver lipids; by adding trivalerin and triundecanoin separately (one by one) to a basic diet without fat but containing 0.5% of the energy of linoleic acid, responses were obtained which were different from those observed when a triglyceride composed of even-numbered carbon atom fatty acids was added. In particular higher levels of arachidonic acid and lower concentrations of eicosatrienoic acid were found and thus lower triene/tetraene ratios in the animals which were given trivalerin and triundecanoin. Since the weight growth of these animals were decidedly lower than that of the animals which were given triglycerides with even-numbered fatty acids, according to the authors, the diminution of the triene/tetraene ratio is to be interpreted as a lesser utilization necessity of the reserves of essential fatty acids through the synthesis of new cellular structures. Furthermore the considerable increase in the liver of the saturated and unsaturated long chain odd-numbered fatty acids subsequent to the administration of trivalerin and triundecanoin, has led the authors to think that probably some of the odd-numbered chain unsaturated fatty acids could have substituted the 20:3 ω 9 whose level appeared considerably reduced in some structures. The presence of 17:1 and 19:3 in the lecithins probably in β position, in the above-mentioned experimental conditions, would seem to confirm this theory.

The importance that a similar possibility could occur in the animal

organism appears in all clarity because, synthesis and incorporation of unusual fatty acids in the lipid structures such as the biological membranes, could determine marked alterations in the functioning of these (55). For example in Refsum's disease, an hereditary disease lipid metabolism, it has been pointed out that a high percentage of fatty acids are substituted by an unusual branched fatty acid (tetramethylhexadecanoic acid or phytanic acid) and the theory has been advanced that the serious neurological disturbances observed may, in some way, be associated with the accumulation in the tissues and the presence in the lipid structures of this acid (56). In the case of feeding with odd-numbered fatty acids, since it has been proven that the hematoencephalic barrier is permeable to lipid molecules (57) and that therefore the type of brain lipids is influenced by the diet lipids (58, 59), the possibility of some sort of alteration at the level of the central nervous system consequent to a variation in the chemical composition of the existing lipid structures could be considered. It should furthermore be noted that in the brain cerebrosides, under normal conditions, small quantities of odd-numbered fatty acids (above all alpha-hydroxy C_{23}) are present and that these increase with age (60). These odd-numbered fatty acids could result either from synthesis starting from propionate (but to a modest extent apparently), as postulated by Harya and Radin (28), or else from degradation processes. This latter mechanism gives rise to odd-numbered fatty acids by operating an α -oxidation as demonstrated by Mead et al. (16, 61) and by Davies et al. (62). What the biological significance of this particular metabolic system in the brain could be is not clear: according to Mead the degradation of a carbon could serve to shorten the very long chains of fatty acids present in the brain in such a way that they would be more assailable by the usual metabolic oxidation systems.

Since odd-numbered fatty acids seem to accumulate with age, it could be thought that this phenomenon is linked to ageing processes and myelin breakdown.

The nutritional effects of feeding with odd-numbered fatty acids described so far are related above all to artificially produced lipids and in general to those containing short- or medium-chain fatty acids.

There is little literature regarding experiments on the effects of feeding with the lipid fraction of biomasses grown on hydrocarbons which, as stated above, contain high quantities of odd-numbered fatty acids, above all to 17 C.

Studies of this kind have been carried out in the Soviet Union on two preparations of biomasses composed of yeasts grown on hydrocarbons containing respectively in the lipid fraction 21% and 5.3% of odd-numbered fatty acids (63, 64, 65). It has been seen that by substituting 100% of diet proteins with these preparations, there is, in the rat a fatty infiltration of the liver after two weeks' treatment, while no effect is encountered by substituting 25% of the proteins (64). Thus also by feeding rats with a diet whose protein quota is composed 100% by biomasses one finds an increase in cholesterol levels in the liver, while the substitution of 25% of proteins in the diet with microbial proteins does not cause any variation in the cholesterol levels in the liver, in the serum and in the aorta.

Levachev when studying the effects of the administration of these two preparations on the composition in fatty acids of the blood, liver, heart, skeletal muscles and adipose tissue in the rat, found the presence of odd-numbered fatty acids $C_{15:0}$, $C_{17:0}$, $C_{17:1}$, $C_{19:0}$, in all the organs and tissues studied. Furthermore, while the substitution of the diet proteins with the compound which is less rich in odd-numbered fatty acids,

does not cause any variations in the level of linolenic and arachidonic acids, the substitution of 100% or of 25% in the case in which the product with a higher content of odd-numbered fatty acids is used, determines a reduction of linolenic acid and an increase of the arachidonic acid in all the tissues studied.

CONCLUSIONS

From the series of research works reported in the literature it appears that there exist in the organism mechanisms which are able to synthesize odd-numbered fatty acids; however, under normal conditions, synthesis is always modest, while an increase of this is generally associated with alteration of metabolism processes or of deterioration of normal physiological processes.

Even though some works would seem to indicate the existence of negative effects on growth following feeding with some synthetic triglycerides containing odd-numbered fatty acids (20, 48, 49) and the possibility that these fatty acids are also incorporated in the complex lipids, such as for example those present in biological membranes (48, 55), there is a lack of indepth studies on the relationships between lipid composition of the actual membranes and their functions.

Studies conducted with synthetic liposomes containing phospholipids with different fatty acids and which have the same osmotic behaviour as natural erythrocytes, have shown that permeability to glycerol varies with the variation of the fatty acids chain and specifically increases with the diminution of the length of the chain and with the degree of unsaturation (2, 55).

The great number of molecular species with often different physical properties in the membrane lipids (it is calculated that in the membranes of the erythrocytes approximately 200 different lipid molecules are present) makes it difficult to pinpoint their functional significance.

It is nevertheless interesting to note that when neurological manifestations associated with poor absorption or unsuccessful utilization of vitamin B₁₂ or with alterations at the level of some enzyme systems appear, as for example those responsible for the conversion of methylmalonylCoA to succinylCoA or of phytanic acid to pristanic acid, the presence of odd-numbered and even-numbered branched fatty acids has been evidenced in the nervous tissue (32, 56, 66). No conclusive proof yet exists to establish whether the neurological disturbances are determined by the accumulation in the nervous tissue or in the membrane lipids of these odd- or even-numbered branched fatty acids, or if their presence must be considered independent and of no pathogenetic importance.

Finally it must be considered that the odd-numbered fatty acids introduced with the diet could influence, besides the deposit and structural fats, the circulating fats as well. These molecules could thus have different chemical-physical properties, as results from the experiments of Van Deenen (2) in which it is seen that synthetic lecithin and lysolecithin display different lytic activities with respect to the erythrocytes of oxen depending on the composition in fatty acids. In particular the lysolecithins have shown an increasing hemolytic activity with the increase of the length of the chain up to C₁₈ only then to diminish, while the synthetic lecithins have shown maximum activity with medium-chain (C₉, C₁₀, C₁₁) fatty acids.

Studies in this field are just beginning and a reply to these uncertainties will come only from specific studies in this regard.

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SUMMARY

ODD-NUMBERED FATTY ACIDS: METABOLIC AND NUTRITIONAL ASPECTS

Odd-numbered fatty acids are present in natural sources of animal or vegetable origin. Their concentration is generally not higher than 5% of the total fatty acids. In some cases, however, like in the mullet or *Euglena gracilis*, the value reaches 20% of the total fatty acids. Higher concentrations, up to 80%, have been found in some hydrocarbon-grown microorganisms.

In the animal organisms metabolic pathways for the synthesis or degradation of the odd-numbered fatty acids are present, but the adaptive capacity and the regulation of the different pathways are not known.

The consequences of feeding animals or human beings on these unusual fatty acids in large amount are uncertain, because the composition of the fat depots, of the lipid structures and the circulating lipids can be affected, possibly influencing the membrane functions and, particularly the nervous system functions.

The literature sighted shows the scarcity of specific studies in this field and indicates the need for further and more detailed researches.