SYMPOSIUM: MEDIUM CHAIN TRIGLYCERIDES

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Nutritional Properties of Medium-Chain Triglycerides[1]

HANS KAUNITZ and RUTH ELLEN JOHNSON, Department of Pathology, College of Physicians and Surgeons, Columbia University, New York, New York

Abstract

The biological effects of MCT (medium-chain triglycerides) differed from those of conventional fats, and certain of these suggested examination of the fatty acid composition and triglyceride structure of the adipose tissues and other organs of rats which were fed medium- or long-chain triglyceride mixtures with two levels of linoleic acid. Fatty acid compositions and TG patterns varied with the tissue, with the dietary fat, and with the level of linoleate in the diet. Increasing the latter resulted in the deposition of more linoleate at the expense of oleate and in the deposition of more of the dietary fatty acids. The percentage of completely saturated triglycerides (S_3), in adipose tissue with the higher linoleate supplement in the rats fed MCT, decreased in those fed LCT and was unchanged in the controls fed a fat-free diet. The increased deposition of the dietary fatty acids was more pronounced in the S_3 band.

Introduction

NUTRITIONAL EXPERIMENTS with saturated fatty acids of medium-chain length (C 6–10) and with triglycerides composed of these acids have been carried out by many investigators. This paper will summarize some of the results of such investigations.

Most clinical studies have so far involved the peculiarities of medium-chain triglycerides (MCT) with regard to hydrolysis, absorption, and transport. MCT hydrolyze more easily than triglycerides of longer-chain length. Temperatures as low as 350F may lead to some hydrolysis, which must be taken into consideration when and if MCT are to be incorporated into any cooked foods. Playoust and Isselbacher (1) have demonstrated a) that the intestinal mucosa contains an enzyme which splits MCT but has little activity in hydrolyzing tripalmitin and b) that MCT can be absorbed into the mucosa as triglycerides. Earlier investigators had shown that medium-chain fatty acids enter the portal blood as free fatty acids rather than the lymphatics (2) and are more rapidly metabolized than other fats (3). Large amounts of C 6–10 acids are not deposited in the fat depots. These observations have suggested the clinical use of MCT in steatorrhea and other malabsorption syndromes. This subject has been covered by other reviewers (4).

Only one point may deserve some discussion. In studies of Kritchevsky and Tepper (5) it was noted that the addition of 5% of the fatty acids constituting MCT or fatty acids from other fats led to an increased incidence of cholesterol-induced plaques in rabbits compared with diets containing only MCT or the other fats. The fact that MCT are fed as triglycerides is of importance, and more studies of the biological effects of MCT compared with their constituent fatty acids are necessary.

A second area of investigation has been the influence of dietary MCT on several aspects of lipid metabolism. It was observed by Kaunitz et al. (6) that the serum cholesterol levels of rats fed a cholesterol-free diet containing MCT were significantly lower than those of rats fed the same diet containing lard. This was true of freely eating animals and for those on a restricted food-intake. Later it was noted that rats fed MCT had lower liver cholesterol levels than did rats fed long-chain saturated triglycerides, LCT, (C 12–18 acids), or a low-fat diet (7). This hypocholesterolemic effect was also seen in rats in which high serum cholesterol levels had been induced by the induction of experimental nephrosis (8). It has also been observed in man (9) and in dogs (10). In chickens, feeding of MCT led to lower liver cholesterol levels than did LCT but to higher serum cholesterol levels (11).

In examinations of liver slices from rats pre-fed with MCT, Kritchevsky and Tepper found that they synthesized somewhat more cholesterol from an acetate substrate than did livers from rats pre-fed corn oil; at the same time they had a much higher rate of fatty acid synthesis (12). This may be related to

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the observation from Kinsell's laboratory that the feeding of MCT was associated with high serum glyceride levels in two of the three patients given this fat. There was no effect on serum cholesterol levels in these three patients (13). Furman et al. observed that MCT were effective in reducing hyperglyceridemia in patients with fat-induced hyperlipemia but had no effect in patients with hyperlipemia which has accentuated by the intake of high carbohydrate levels (14). Earlier Ahrens and Spritz had observed that MCT were less effective in the treatment of carbohydrate-induced hyperlipemia (15).

Although studies of MCT absorption and its effect on lipid metabolism have so far received most attention, several other observations have also been made. In one long-term study, rats fed a purified diet containing 20% of MCT had a survival rate after two years as high if not higher than did rats fed lard (14/18 vs. 10/19 of the controls fed lard) (6). Further work with other species would be desirable if MCT are to be used extensively for human beings. In this connection it may be of interest that two women, who are now more than 60 years old, have been consuming MCT as their main dietary fat for more than 10 years with no ill effects.

In earlier work it was observed that rats fed MCT had body weights similar to those of rats fed a low-fat (high-carbohydrate) diet; they were lighter than those fed lard and had smaller epididymal fat pads, an indication of reduced neutral fat deposition. Caloric requirements for weight maintenance were higher in rats fed MCT than in those fed lard (16). These observations suggested that MCT might be useful to obese patients. Such studies were carried out on a group of patients not confined to the hospital. Although strictly controlled conditions were not possible, the fact that these patients, who had had little success with other diets, had weight losses on a restricted diet containing MCT as the dietary fat, suggested further studies.

The effects of dietary MCT on several pathological states have been compared with those of LCT or various naturally occurring fats. Among rats fed a vitamin E-deficient diet, those fed MCT had significantly less severe testicular damage than did those fed LCT. In chickens, on the other hand, the presence of MCT in a vitamin E-deficient diet enhanced the occurrence of exudative diathesis compared with no fat or oleic acid (17).

When experimental nephrosis was induced in rats by means of a rabbit antirat kidney serum, the renal lesions were less severe in those fed MCT than in those fed LCT (8). In another study the toxic effect of feeding a fraction of oxidized cottonseed oil could be modified by the simultaneous feeding of fresh fat. Liquid fats, especially MCT, reduced the toxicity whereas hard fats, such as LCT and beef fat, aggravated the toxic effects (18). In studies of Kritchevsky and Tepper (5) it was found that aortic lesions induced in rabbits by the feding of large amounts of cholesterol were less severe when MCT or corn oil was fed but, once the disease had been established, feeding of MCT exacerbated the lesions to a greater extent than did corn oil.

The interrelationship of triglyceride chain-length and the linoleic acid (LA) content of the diet was first examined in studies of body weight, organ weight, and lactation performance (7). It was found that rats fed LCT had higher LA requirements than did those fed MCT. In a comparison of weight gains in groups of weanling male rats which were fed marginal amounts of LA (0.1–0.5% of the diet) it was found that the group fed LCT required approximately four times as much LA as did those fed MCT (19).

TABLE I

Fatty Acid Composition (% of Fatty Acids) of Triglycerides from Epididymal Fat of Rats Fed Diets Containing no Fat, 20% of MCT, or 20% of LCT and Supplemented with 0.1 or 2% of Linoleic Acid (LA)

Fatty acid	Low-Fat Diet + 0.1% LA	Low-Fat Diet + 2% LA	20% MCT Diet + 0.1% LA	20% MCT Diet + 2% LA	20% LCT Diet + 0.1% LA	20% LCT Diet + 2% LA
8:0	....	....	.9	1.8	....	....
10:0	....	.1	1.2	7.4	.1	.1
12:0	.1	.2	1.2	2.1	.8	.6
14:0	2.1	2.3	3.6	3.6	2.6	2.3
16:0	30.7	29.8	35.8	31.1	29.6	25.8
16:1	15.6	12.8	11.9	7.1	9.1	6.1
18:0	4.3	3.6	5.5	5.4	10.0	12.2
18:1	44.0	33.6	37.3	22.9	41.0	30.3
18:2	2.0	16.2	1.5	16.2	6.2	21.6

In later studies, fatty acid analyses of epididymal fat were carried out on rats which were fed no fat, a sample of MCT containing 8% C 6, 78% C 8, and 14% C 10, or a sample of LCT containing 45% C 12, 25% C 14, 8% C 16, and 16% C 18. All diets were fed with and without LA for three-and-a-half months. Among the rats given no LA, the fatty acid compositions of the epididymal fat pads were similar in those fed the fat-free and MCT diets except for the occurrence of small amounts of C 6–10 in the latter group. The fat pads of those fed LCT contained about 30% C 12 and C 14. Addition of 2% LA to the fat-free diet did not alter the fatty acid composition of the fat pads except for the deposition of approximately 20% of LA at the expense of oleate. Supplementation of MCT with LA was associated with increased deposition of C 6–10 acids as well as linoleate, all at the expense of palmitoleate and oleate. Inclusion of 2% LA in the LCT diet resulted in higher levels of C 12, 14, 18 and linoleate (20). These data showed the regulatory action of LA on the adipose tissues.

Experimental Section

In a recent continuation of these studies, triglycerides (TG) from epididymal fat and heart were analyzed for their fatty acid compositions and for their structural patterns. In this study, weanling male rats were fed purified diets containing no fat, MCT, or LCT, each supplemented with 0.1 or 2% of LA. The MCT used in this experiment consisted of 61% C 8, 32% C 10, 2% C 12, and 5% of longer acids; the LCT contained 37% C 16, 55% C 18, 5% C 18:1, and 3% of other acids. Both TG mixtures were randomized. The rats were sacrificed after eight weeks on the diets, and the tissues from each group were

TABLE II

Structural Patterns (% of Molecules) of Triglycerides from Epididymal Fat of Rats Fed Diets Containing no Fat, 20% of MCT, or 20% of LCT and Supplemented with 0.1 or 2% of Linoleic Acid (LA)

Triglyceride type	Low-Fat Diet + 0.1% LA	Low-Fat Diet + 2% LA	20% MCT Diet + 0.1% LA	20% MCT Diet + 2% LA	20% LCT Diet + 0.1% LA	20% LCT Diet + 2% LA
S_3	3.9	3.6	11.7	14.6	8.2	5.9
S_2O	24.1	13.1	32.6	20.8	28.5	16.0
SO_2	42.1	23.9	41.0	9.4	29.5	13.1
S_2L	2.2	6.8	1.0	20.0	5.0	15.4
SOL	5.1	18.7	3.2	14.1	10.1	21.6
O_3	21.4	14.4	10.3	10.7	16.2	8.1
SL_2	....	9.1	....	5.1	1.2	7.9
O_2L	1.2	10.4	....	5.0	1.3	9.5
OL_2	....	....	....	.2	....	2.5

TABLE III

Fatty Acid Compositions (% of acids) of Bands Containing Completely Saturated TG (S_3) After Separation of Epididymal Adipose Tissue and Heart TG on $AgNO_3$-Impregnated Silicic Acid

	Epididymal Adipose Tissue TG						Heart TG	
	Low-Fat Diet		20% MCT Diet		20% LCT Diet		20% MCT Diet	
Chain length	+ 0.1% LA	+ 2% LA	+ 0.1% LA	+ 2% LA	+ 0.1% LA	+ 2% LA	+ 0.1% LA	+ 2% LA
C 8	....	....	....	.3	....	....	....	....
10	....	.9	.9	11.0	....	....	2.6	3.2
12	....	1.1	2.5	4.9	2.0	1.6	1.9	2.5
14	7.1	7.4	9.2	8.9	7.2	5.7	7.5	7.6
16	81.5	79.4	74.2	63.8	68.6	61.2	73.0	71.4
18	11.4	11.1	13.2	9.9	22.2	30.5	15.0	14.2

pooled. Homogeneous portions of a tissue pool were cut on a freezing microtome and homogenized in a Tri-R homogenizer with a tube of 40-ml capacity and a motor-driven Teflon pestle in a dry-ice bath. Microscopic examination of the tissue particles suspended in the 2:1 chloroform:methanol reagent showed them to be uniformly of about 20–30 microns in diameter. TG were isolated from the total lipid extracts by preparative TLC.

Separation of structural types was carried out with silver nitrate TLC on 200 × 400 mm plates by using a sandwich technique. This method (21) separates TG more or less according to the unsaturation of the molecule, i.e., from the top down, successive bands consist predominantly of S_3, S_2O, SO_2, and S_2L, SOL and O_3, SL_2 and O_2L, OL_2, and L_3, where S indicates saturated, O indicates monoenoic, and L indicates dienoic acids. The individual bands were scraped off and eluted with pentane and 5% methanol in pentane. Their fatty acid compositions were analyzed in a Barber-Colman Model Gas Chromatograph with a hydrogen flame detector, a 6-ft. glass column, packed with 12% stabilized diethylene glycol succinate on Anakrom ABS 90–100 mesh at a temperature of 175C and with a nitrogen flow rate of 95 ml/min. Analysis of *beta*-monoglycerides were carried out by means of lipase hydrolysis, according to the method of Luddy et al. (22).

Results

At the time of sacrifice the average body weights and epididymal fat pad weights were as follows:

	Fat-Free		MCT		LCT	
	0.1% LA	2% LA	0.1% LA	2% LA	0.1% LA	2% LA
Body weight (grams)	257	282	271	288	208	220
Epididymal fat weight (grams)	2.82	2.75	2.68	2.23	1.13	1.07

LCT, composed mostly of palmitate and stearate, was not well tolerated by the rats, as evidenced by their low body weights and a mortality rate of about 50%.

In Table I are given the fatty acid compositions of the epididymal TG. As in earlier work, there was considerable similarity in the TG from the LA-deficient rats fed the fat-free and MCT diets; LA supplementation led to increased deposition of the dietary acids in the rats fed MCT and LCT.

In Table II are summarized the results of the silver nitrate chromatography. Among the rats fed the linoleate-low diets, S_2O and SO_2 were the main TG types. Increased dietary linoleate levels resulted in the expected increase in types containing L at the expense of S_2O and SO_2. However the effect of the higher linoleate level on the other structural types varied from group to group. The S_3 was unchanged in the rats fed the fat-free diet whereas it increased somewhat in those fed MCT and decreased in those fed LCT. Despite the over-all fall in the level of oleate and palmitoleate with linoleate supplementation, type O_3 did not decrease in the rats fed MCT as it did with the other diets. Analyses of perirenal adipose tissue TG gave nearly identical results with regard to fatty acid composition and TG structure.

In Table III are given the fatty acid compositions of the S_3 bands of the epididymal TG. Among the animals fed the fat-free diet, feeding of additional linoleic acid did not alter the composition of this band; additional linoleate led to higher medium-chain levels in the rats fed MCT and a higher stearate level in the group fed LCT. One may speculate as to the biological properties of triglycerides containing more than 30% of stearate.

In Table IV are given the results of the pancreatic lipase hydrolyses of the epididymal TG. As one would have expected, palmitate and stearate were preferentially attached to the 1,3 carbons and oleate and linoleate to the 2 carbon. The C 8–14 acids were also preferentially attached to the 1,3 carbons, and it seemed that their tendency to go into the 2 position increased with the chain length.

The heart TG (Table V) differed from the epididymal TG in having lower palmitoleate and higher

TABLE IV

Fatty Acid Compositions of 1,3 and 2 Positions in Triglycerides from Epididymal Fat of Rats Fed Diets Containing no Fat, 20% of MCT, or 20% of LCT and Supplemented with 0.1 or 2% of Linoleic Acid (LA)

	Low-Fat Diet				20% MCT Diet				20% LCT Diet			
	+ 0.1% LA		+ 2% LA		+ 0.1% LA		+ 2% LA		+ 0.1% LA		+ 2% LA	
	Carbons		Carbons		Carbons		Carbons		Carbons		Carbons	
Fatty acid	2	1,3	2	1,3	2	1,3	2	1,3	2	1,3	2	1,3
8:0	....	....	....	....	....	1.3	....	2.7	....	....	....	....
10:0	....	....	....	.1	.4	1.6	1.0	10.6	....	.1	....	.1
12:0	....	.1	....	.3	.4	1.6	.6	2.8	....	1.2	....	.9
14:0	1.7	2.3	1.2	2.8	2.8	4.0	2.6	4.1	1.6	3.1	1.1	2.8
16:0	12.9	39.6	10.3	39.6	18.0	44.9	15.5	38.9	14.0	37.4	11.1	33.2
16:1	17.6	14.6	13.2	12.6	14.9	10.4	7.3	7.0	10.0	8.7	5.3	6.5
18:0	1.4	5.8	1.4	4.7	3.0	6.8	2.2	7.0	3.2	14.4	3.1	16.8
18:1	62.9	34.6	42.3	29.3	55.0	28.6	29.2	19.8	58.9	32.1	37.5	26.7
18:2	3.2	1.4	27.8	10.4	4.1	.2	26.4	11.1	11.4	3.6	41.6	11.6

TABLE V

Fatty Acid Composition (% of Fatty Acids) of Triglycerides from Hearts of Rats Fed Diets Containing no Fat, 20% of MCT, or 20% of LCT and Supplemented with 0.1 or 2% of Linoleic Acid (LA)

Fatty acid	Low-Fat Diet + 0.1% LA	20% MCT Diet + 0.1% LA	20% MCT Diet + 2% LA	20% LCT Diet + 0.1% LA	20% LCT Diet + 2% LA
8:0	....	....	.1	....	....
10:0	....	.6	.8	....	....
12:0	.2	.4	.8	.3	....
14:0	2.2	2.2	2.8	1.4	.8
16:0	31.2	34.7	30.9	32.6	34.9
16:1	8.9	5.1	4.6	2.6	1.3
18:0	6.1	7.2	8.2	21.1	23.9
18:1	45.2	42.4	27.3	33.6	22.1
18:2	2.5	3.0	17.9	4.8	16.7
20:4	....	....	2.6	....	.3

TABLE VI

Structural Patterns (% of Molecules) of Triglycerides from Hearts of Rats Fed Diets Containing no Fat, 20% of MCT, or 20% of LCT and Supplemented with 0.1% or 2% of Linoleic Acid (LA)

Triglyceride type	Low-Fat Diet 0.1% LA	20% MCT Diet 0.1% LA	20% MCT Diet 2% LA	20% LCT Diet 2% LA
S_3	2.8	7.7	8.9	14.0
S_2O	36.2	27.4	18.3	22.4
SO_2	36.4	34.9	10.0	11.2
S_2L	2.5	3.8	15.5	28.1
SOL	4.9	7.2	15.8	3.1
O_3	16.2	14.9	7.9	17.8
SL_2	1.0	......	3.8	......
O_2L	......	1.2	5.9	......
OL_2	......	......	.2	......
L_3	......	......	2.5	.3
S_2A	......	......	3.2	.7
SAL	......	......	7.5	......
$O_2A + L_2A$	......	......	.5	......
Others	......	2.9	......	......

stearate levels. Furthermore additional linoleate did not lead to increased deposition of the MCT and LCT acids. Arachidonate was found in the TG of the linoleate-supplemented group fed MCT.

Table VI gives the structural patterns of the heart TG. The patterns were different from those of the epididymal fats, i.e., the heart TG of the rats fed MCT + 2% LA included more than 10% of TG-containing arachidonate, and those of the rats fed LCT + 2% LA contained 14% of S_3. Table III shows that, in rats fed MCT, dietary influences on the S_3 band were less pronounced than in the epididymal TG; in particular, higher linoleate supplementation had hardly any influence.

Discussion

The structural analyses have shown that the feeding of the various diets led to the appearance of entirely different TG in the epididymal fat and the heart. If it could be assumed that the effects of a dietary fat are mainly mediated by TG in the various fat depots, the structure of the latter TG may be of importance for the modification of the specific TG in the heart and, presumably, in other organs. Before one can draw any conclusions, it will be necessary to examine whether or not the absorbed products of dietary MCT must first be incorporated in the adipose tissues as are conventional fats. Furthermore it will be necessary to examine whether or not the feeding of MCT leads to the occurrence of structurally different TG from those resulting from the feeding of the free fatty acids which compose MCT. In any event, the study of the TG from various organs will probably lead to a better understanding of the biological effects of specific TG.

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