In vivo triglyceride secretion and hepatic and plasma lipids in rats fed medium-chain triglycerides, tripelargonin, or corn oil

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The relationship between in vivo triglyceride secretion and the concentrations of cholesterol and triglycerides in liver and plasma was studied in fasted, male Sprague Dawley rats (150–170 g) fed 16% fat diets containing 8–16% medium chain triglycerides (68% C 8:0 and 24% C 10:0), 14% tripelargonate (C 9:0), or corn oil. Plasma and liver cholesterol concentrations were 10–20% lower ($P < 0.05$), and hepatic activity of 3-hydroxymethyl-3-glutaryl Coenzyme A reductase was 44–66% lower ($P < 0.05$) with ingestion of 14% medium chain triglycerides or tripelargonin than corn oil. Liver triglyceride concentrations were 19–44% lower ($P < 0.01$) with ingestion of 14% medium chain triglycerides or tripelargonin than corn oil. Using the Triton WR-1339 technique, the rate of triglyceride secretion (mg/min × 100 g body wt), plasma triglyceride pool size, and the fractional rate constant for triglyceride secretion were not significantly different among treatment groups. This suggests that a greater rate of triglyceride secretion is not the primary factor associated with lower hepatic triglyceride levels in rats fed medium chain triglycerides. In summary, 10–20% lower plasma and liver cholesterol concentrations were noted with ingestion of saturated, medium-chain-length fatty acid triglycerides containing 8, 9, or 10 carbons compared to corn oil.

Keywords: MCT; tripelargonin; cholesterol; Triton WR-1339; lipogenesis; triglyceride

Introduction

Ingestion of diets containing medium chain triglycerides (MCT) has been noted to increase energy expenditure and to alter triglyceride and cholesterol metabolism in experimental animals and humans.[1-7] These effects have been attributed to the unique digestion, absorption, and metabolism of triacylglycerols, such as MCT,[8] which contain fatty acids with fewer than 12 carbon atoms. Differences in the metabolism of MCT as compared to traditional long chain dietary fats include bypassing of intestinal chylomicron formation,[8] transport in the portal vein instead of lymph,[9] carnitine-independent transport into hepatic mitochondria, and rapid oxidation in hepatic tissue to acetyl-CoA.[10]

Substitution of MCT for long chain dietary fats has been demonstrated to depress hepatic and serum cholesterol levels in several species.[1-3,5,11] Lower cholesterol levels in the rat have been associated with a lower rate of hepatic cholesterogenesis.[12] In studies using isolated rat hepatocytes, rapid oxidation of medium chain fatty acids resulted in an increase in de novo lipogenesis from acetyl CoA.[4] However, lower hepatic triglyceride concentrations have been noted in rats fed MCT rather than long chain dietary fats.[3]

Ingestion of odd-carbon chain length MCT is associated with unique metabolic effects compared to ingestion of even-chain MCT. Beta oxidation of odd-carbon fatty acids yields propionate residues which provide intermediates for acetyl CoA oxidation by the tricarboxylic acid cycle and which are potentially glucogenic.[13,14] The effects on cholesterol metabolism of increased propionate levels due to oxidation of odd-carbon fatty acids is unclear. Pi-Sunyer has reported no significant difference in serum cholesterol and tri-

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glyceride levels in fed or fasted rats fed corn oil or a 7:3 mixture of triundecanoin (C 11:0) and corn oil for 6 weeks.[13] The effect of tripelargonin (C 9:0) ingestion on cholesterol metabolism has not been reported.

Consequently, a series of experiments was conducted to compare the effects of feeding diets containing MCT, tripelargonin, or corn oil on food intake and growth, and total plasma, lipoprotein, and hepatic cholesterol and triglyceride concentrations in rats. These initial experiments demonstrated lower hepatic triglyceride and cholesterol concentrations, and higher VLDL triglyceride concentrations with ingestion of MCT or tripelargonin rather than corn oil. Therefore, in an additional experiment, the Triton WR-1339 technique was used to determine the relationship between in vivo triglyceride secretion and the concentrations of cholesterol and triglyceride in liver and plasma.

Methods

Animals and diets

Male Sprague Dawley rats weighing 150–170 g (Harlan Sprague Dawley, Madison, WI, USA) were housed individually in stainless steel cages in a room maintained at 25° C with a 12-hr light-dark cycle. Animals were fed a 16% corn oil AIN 76A diet (15,16) for the first five days after delivery to the animal facility to allow for adaptation. They were then assigned to dietary treatment groups (n = 5–10) by controlled randomization such that body weight was not different among groups.

A modified AIN 76A diet[15,16] containing 16% fat and 50% sucrose was used in all studies (*Table 1*). To prevent peroxidation, diets were kept at 4° C and fresh diet was presented biweekly. Food intake was recorded daily in the first experiment, and in subsequent experiments it was calculated weekly based on a 3-day intake period. Body weight was measured biweekly and feed efficiency (g gain/g dietary intake) was calculated. Rats were fasted overnight and anesthetized with CO_2 at the conclusion of each feeding period. Blood (8–10 ml) was then collected by cardiac puncture into syringes containing 1 mg of EDTA and 0.1 mg of gentamicin sulfate per ml of blood.

A series of experiments was conducted to assess the lipogenic effects of ingesting diets supplemented with 8–16% MCT relative to corn oil. In the first experiment, food intake, growth, and feed efficiency were determined in rats fed for 6 weeks. This experiment included 5 dietary groups: 16% corn oil, 8% MCT (68% C 8:0, 24% C 10:0, less than 5% < C 8:0 or > C 10:0) + 8% corn oil, 15% MCT + 1% corn oil, 16% MCT, and a 16% corn oil group pair-fed to the amount of diet consumed by the 16% MCT group. Determination of the fatty acid profile of the total hepatic lipid extract indicated that the triene, C 20:3n9, was present (1–3.4% of fatty acid methyl esters) in rats fed the 15% and 16% MCT diets, respectively. To avoid problems associated with the biochemical effects of essential fatty acid deficiency, the diet composition was modified to 14% MCT + 2% corn oil for subsequent experiments.

In the second experiment, total plasma, lipoprotein, and hepatic cholesterol and triglyceride concentrations were determined in rats fed for 3, 4, or 5 weeks. This experiment included 4 dietary groups: 16% corn oil, 8% MCT + 8% corn oil, 14% MCT + 2% corn oil, and 14% odd-carbon chain length tripelargonin (C 9:0) + 2% corn oil. In the last experiment, in vivo hepatic triglyceride secretion was determined in rats fed 16% corn oil or 14% MCT + 2% corn oil for 4 weeks based on the results from the second experiment.

Table 1 Diet composition[a]

Ingredient	Amount, % by weight
Casein	20.0
DL-methionine	0.3
Sucrose	50.0
Cornstarch	3.98
Cellulose	5.0
Fat source[b]	16.0
Mineral mix—AIN 76	3.5
Vitamin mix—AIN 76A	1.0
Choline dihydrogen citrate	0.2
Butylated hydroxytoluene	0.02

[a] Teklad Test Diets, Madison, WI, USA.
[b] Fat sources include MCT or Captex 300 Capitol City Products Columbus, OH, USA (68% C 8:0, 24% C 10:0, less than 5% < C 8:0 or > C 10:0); tripelargonin (C 9:0) Capitol City Products, Columbus, OH, USA; or corn oil in the following combinations: 16% MCT, 15% MCT + 1% corn oil, 14% MCT + 2% corn oil, 14% tripelargonin + 2% corn oil, 8% MCT + 8% corn oil, and 16% corn oil.

Chemical analyses

Plasma was obtained by centrifugation at 4° C for 20 min at 1200g. Lipoproteins were fractioned from 2-ml plasma samples containing 0.45 mg of 5,5′-dithiobis-2-nitrobenzoic acid and 0.3 mg of phenylmethylsulfonyfluoride by sequential ultracentrifugation at densities: VLDL, d < 1.006 g/ml; LDL, d = 1.006–1.050; and HDL, d = 1.050–1.196.[17]

Triglyceride concentrations in plasma and VLDL were determined using Sigma Triglyceride Kit, No. 336 (Sigma Chemical, St. Louis, MO, USA) with inclusion of standardized triglyceride samples in each assay. The coefficient of variation for the triglyceride assay was 6%. Cholesterol concentrations in plasma, VLDL, LDL, and HDL were determined enzymatically.[18] VLDL total protein concentration was determined using a modification of the Lowry assay with bovine serum albumin as a standard.[19]

Lipids were extracted from 1-g hepatic samples with chloroform-methanol[20] and assayed for cholesterol and triglyceride[21] contents. A separate 2-g hepatic sample was homogenized in 18 ml of 0.25 M sucrose to isolate microsomes[22] which were subse-

quently analyzed for 3-hydroxymethyl-3-glutaryl Coenzyme A (HMG-CoA) reductase activity.[23]

In vivo triglyceride secretion

In vivo hepatic triglyceride secretion was determined using Triton WR-1339 (Tyloxapol, Sigma Chemical Co.; St. Louis, MO, USA). Triton WR-1339 is an alkaryl polyether anionic detergent that inhibits lipoprotein lipase activity, and thus provides a quantitative measurement of hepatic triglyceride secretion into the plasma pool of fasted animals.[24-27] Calculation of the rate of increase in plasma triglycerides after intravenous Triton injection has been demonstrated to be in close agreement with techniques utilizing radioactive tracers to assess hepatic triglyceride secretion.[28]

Two blocks of animals underwent surgical placement of catheters in the external jugular vein after 22 and 23 days of feeding. Animals were anesthetized by intramuscular injection with a mixture containing 50 mg/kg body weight ketamine and 10 mg/kg body weight xylazine. Polyethylene catheters (25 cm, PE-50, ID 0.64 mm, OD 1.19 mm; Dow Corning Corp., Midland, MI, USA) fitted with a PE-10 tip (2.5 cm, ID 0.51 mm, OD 0.94 mm) were inserted 2.5 cm into the lumen of the external jugular vein. The free end of the catheter was tunneled under the skin and secured in the midscapular area with two surgical staples. Catheters were flushed daily with 400 μl of a solution containing 1% EDTA and 0.85% NaCl.

Five days after surgery, animals were fasted overnight for 12 hr to ensure chylomicron clearance. The next morning baseline blood samples (400 μl) were collected through the jugular catheters into syringes containing 1 mg of EDTA and 0.1 mg of gentamicin sulfate per ml of blood. Each animal was then infused with 1 ml of 13% Triton in 0.85% saline.[24,25] Subsequent blood samples (300 μl) were collected at 30, 75, and 120 min after Triton infusion as described for baseline blood samples. Plasma triglyceride concentrations were determined in all samples. Animals were not anesthetized during the infusion and sampling period.

The rate of triglyceride secretion [mg/min × 100 g body wt] was calculated as follows:

$$\frac{[TG_f(mg/ml) - TG_i(mg/ml)] \times P(ml)}{Time(min) \times Body\ Weight/0.01\ g} \quad (1)$$

where TG_f = final triglyceride concentration at 120 min, TG_i = initial or baseline triglyceride concentration, P = calculated plasma volume [(Body wt × 0.041) − 1.59].[26]

Statistical analyses

Data were assessed by one-way and two-way analysis of variance (ANOVA) using the SAS general linear model program.[29] Differences between treatments means were compared by the least significant difference technique at $P < 0.05$.[30] Values are expressed as means ± SEM.

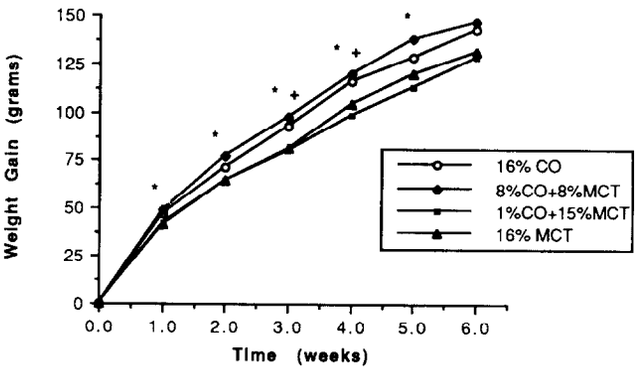

Figure 1 Weekly cumulative weight gain of rats fed 16% fat diets containing medium chain triglycerides (MCT) or corn oil (CO). Cumulative weight gain was significantly lower ($P < 0.05$) with ingestion of the 15% or 16% MCT diets rather than the *8% MCT + 8% CO or ⁻16% CO diets for weeks 1–5, $n = 9$.

Results

Growth and liver weight

Results from the first experiment indicated no significant differences in food intake with ingestion of MCT than corn oil diets; thus, pair-fed groups were eliminated in subsequent experiments. Final body weights were not statistically different between treatments in all experiments. However, weekly cumulative weight gain (weekly-initial body weight) was significantly lower in animals fed 15% or 16% MCT diets rather than 8% MCT + 8% corn oil or 16% corn oil diets for weeks one through five (*Figure 1*). Feed efficiency (g gain/g dietary intake) was also significantly lower in animals fed 15% or 16% MCT diets rather than 8% MCT + 8% corn oil or 16% corn oil diets for the first three weeks of feeding. Animals fed the 8% MCT + 8% corn oil diet ate more food, gained more weight, and had a higher feed efficiency than other treatments.

Liver weights (g/100 g body wt) were similar in animals fed corn oil or even-chain MCT for 3, 4, 5, and 6 weeks. However, animals fed 14% tripelargonin for 5, but not 3 and 4 weeks, demonstrated significantly greater liver weights than the 16% corn oil or 14% MCT groups (16% corn oil = 2.9 ± 0.1[a], 14% MCT + 2% corn oil = 3.0 + 0.1[a], 14% tripelargonin + 2% corn oil = 3.4 ± 0.1[b]; g wet wt/100 g body, $P < 0.05$).

Plasma and liver cholesterol and triglyceride concentrations

Plasma triglyceride levels were 39–46% higher in animals fed 14% MCT or tripelargonin than those fed 16% corn oil for 4 weeks (*Table 2*). At five weeks, plasma triglyceride levels were similar among groups. Hepatic triglyceride contents were 19–44% lower ($P < 0.01$) with ingestion of 14% MCT or tripelargonin than 16% corn oil for 3, 4, 5, or 6 weeks.

Plasma cholesterol levels were not different after three weeks of feeding (*Table 2*). However, after 4

Table 2 Plasma and liver cholesterol and triglyceride concentrations

Treatment	Cholesterol		Triglyceride	
	Plasma mg/dl	Liver mg/g wet wt	Plasma mg/dl	Liver mg/g wet wt
Week 3				
16% corn oil	83 ± 5	2.4 ± 0.1	100 ± 4	11.0 ± 0.5[a]
8% corn oil + 8% MCT	82 ± 4	2.4 ± 0.1	87 ± 6	11.1 ± 0.8[a]
2% corn oil + 14% MCT	76 ± 6	2.1 ± 0.1	126 ± 9	8.9 ± 0.6[b]
2% corn oil + 14% C 9:0	73 ± 4	2.3 ± 0.1	105 ± 18	6.2 ± 0.3[c]
Week 4				
16% corn oil	90 ± 4[ab]	2.4 ± 0.1	84 ± 3[a]	10.1 ± 1.0[a]
8% corn oil + 8% MCT	93 ± 3[a]	2.2 ± 0.3	107 ± 11[ab]	8.2 ± 0.6[a]
2% corn oil + 14% MCT	79 ± 3[b]	2.0 ± 0.1	123 ± 9[b]	8.1 ± 0.5[a]
2% corn oil + 14% C 9:0	77 ± 4[b]	2.1 ± 0.1	117 ± 7[ab]	7.4 ± 0.3[b]
Week 5				
16% corn oil	89 ± 5[a]	2.5 ± 0.1	112 ± 3	11.3 ± 0.8[a]
8% corn oil + 8% MCT	92 ± 3[a]	2.4 ± 0.2	134 ± 8	9.5 ± 0.4[ab]
2% corn oil + 14% MCT	73 ± 3[b]	2.1 ± 0.1	136 ± 8	8.0 ± 0.5[bc]
2% corn oil + 14% C 9:0	77 ± 3[b]	2.1 ± 0.1	136 ± 7	7.1 ± 0.3[c]
		2-Way ANOVA		
Diet	0.0001	0.01	0.0008	0.001
Time	NSD	NSD	0.0003	NSD
Diet × Time	NSD	NSD	NSD	0.05

Note: Values are means ± SEM. Values within a column for a given week with a different superscript are significantly different, $P < 0.05$. Means represent 5–6 determinations per group for a given week.

or 5 weeks of feeding, plasma cholesterol levels were 12–20% lower ($P < 0.05$) in animals fed 14% MCT or 14% tripelargonin rather than 8% MCT or 16% corn oil. Plasma cholesterol levels were also 10–20% lower in rats fed 8, 15, or 16% MCT diets for six weeks ($P < 0.05$).

Hepatic cholesterol contents were 10–15% lower with ingestion of 14% MCT or tripelargonin rather than 16% corn oil for 3, 4, and 5 weeks (*Table 2*, 2-way ANOVA, $P < 0.01$). Lower plasma and liver cholesterol contents were associated with lower hepatic HMG-CoA reductase activity in animals fed 14% MCT or tripelargonin than in those fed 8% MCT or 16% corn oil for 4 weeks (*Table 3*).

VLDL composition

VLDL protein, cholesterol, and triglyceride levels were higher with ingestion of 14% MCT or tripelargonin rather than corn oil for 3 or 4 weeks, with little difference after 5 weeks of feeding (*Table 4*). These differences in plasma VLDL composition were consistent with differences in plasma triglyceride levels. Lower plasma cholesterol levels in animals fed MCT or tripelargonate diets were associated with higher VLDL cholesterol levels, but lower LDL and HDL cholesterol contents (data not included) at 3 and 4 weeks. A similar ratio of VLDL protein/cholesterol + triglyceride suggests that higher VLDL levels after 3 weeks of feeding reflected a greater concentration of VLDL rather than an alteration in VLDL composition. After 4 weeks of feeding, higher VLDL levels may have been associated with alterations in VLDL composition in animals fed 14% MCT or tripelargonin.

In vivo triglyceride secretion

Rats fed 14% MCT diets for 4 weeks followed by an overnight fast had 15% higher baseline triglyceride levels prior to Triton infusion than animals fed 16% corn oil (*Table 5*). At 30 min, mean triglyceride levels were 20% higher in animals fed MCT than those fed 16% corn oil; by 120 min, mean triglyceride levels were 11% higher in the MCT group. The calculated rate of triglyceride secretion (mg/min × 100 g body wt) was not different in animals fed 14% MCT or 16% corn oil, $P = 0.37$. Body weight, calculated plasma volume, plasma triglyceride pool size ($P = 0.17$), and the fractional rate constant were also not significantly different.

Table 3 Hepatic 3-hydroxymethyl-3-glutaryl coenzyme A reductase activity*

Treatment	pM/mg protein/min
16% corn oil	172 ± 21[a]
8% MCT + 8% corn oil	177 ± 20[a]
14% MCT + 2% corn oil	97 ± 7[a,b]
14% C 9:0 + 2% corn oil	58 ± 4[b]

* Values are means ± SEM, $n = 5$. Values with a different superscript are significantly different, $P < 0.05$. MCT, medium chain triglyceride; C 9:0, tripelargonin.

Table 4 VLDL composition

Treatment	Protein	Cholesterol (mg/dl plasma)	Triglyceride	Protein Chol + TG
Week 3				
16% corn oil	15.0 ± 1.5[a]	3.3 ± 0.5[a]	51.0 ± 4.5[ab]	0.3 ± 0.1
8% corn oil + 8% MCT	11.4 ± 1.7[a]	2.2 ± 0.2[a]	39.4 ± 1.9[a]	0.3 ± 0.1
2% corn oil + 14% MCT	28.2 ± 3.1[b]	6.1 ± 0.4[b]	81.7 ± 4.9[b]	0.3 ± 0.1
2% corn oil + 14% C 9:0	18.9 ± 3.7[a]	4.4 ± 0.8[c]	59.1 ± 10.2[ab]	0.3 ± 0.1
Week 4				
16% corn oil	14.6 ± 1.2[a]	2.4 ± 0.2[a]	25.0 ± 2.6[a]	0.6 ± 0.1[a]
8% corn oil + 8% MCT	23.6 ± 4.6[ab]	3.4 ± 0.9[a]	23.0 ± 4.3[a]	0.7 ± 0.1[a]
2% corn oil + 14% MCT	26.5 ± 3.9[b]	5.6 ± 0.9[b]	81.6 ± 7.6[b]	0.3 ± 0.1[b]
2% corn oil + 14% C 9:0	29.1 ± 1.6[b]	6.0 ± 0.4[b]	64.9 ± 6.5[b]	0.4 ± 0.1[b]
Week 5				
16% corn oil	22.6 ± 1.3	4.1 ± 0.3	43.8 ± 4.2	0.5 ± 0.1
8% corn oil + 8% MCT	23.0 ± 2.2	3.8 ± 0.4	45.6 ± 4.6	0.5 ± 0.1
2% corn oil + 14% MCT	27.0 ± 2.5	5.0 ± 0.2	54.1 ± 3.1	0.5 ± 0.1
2% corn oil + 14% C 9:0	25.2 ± 0.8	4.5 ± 0.2	57.6 ± 7.1	0.5 ± 0.1
2-Way ANOVA				
Diet	0.0001	0.0001	0.03	0.0001
Time	0.004	NSD	0.0001	NSD
Diet × Time	0.03	0.01	0.0009	0.002

Note: Values are means ± SEM. Values within a column for a given week with a different superscript are significantly different, $P < 0.05$. Means represent 5–6 animals per group for a given week.

Table 5 In vivo rate of triglyceride secretion into plasma

Parameters	16% corn oil	14% MCT + 2% Corn oil
Body wt, g	260 ± 7	249 ± 8
Plasma volume,† ml	9.1 ± 0.3	8.6 ± 0.3
Initial TG concentration, mg/dl	65 ± 3[a]	75 ± 3[b]
Rate of TG secretion,‡ mg/min × 100 g body wt	0.088 ± 0.006	0.097 ± 0.007
Plasma TG pool size,§ mg/100 g body wt	2.3 ± 0.2	2.6 ± 0.1
Fractional rate constant,** min^{-1}	0.039 ± 0.003	0.037 ± 0.002

Note: Values are means ± SEM, $n = 8$. Values within a row with a different superscript are significantly different, $P < 0.05$.

† Calculation: (Body Wt × 0.041 − 1.59)

‡ Calculation: $\frac{\{TG_f(mg/ml) - TG_i(mg/ml)\} \times \text{Plasma Vol. (ml)}}{\text{Time (minutes)} \times \text{(Body Wt) 0.01 g}}$

§ Calculation: $\frac{TG_i(mg/ml) \times \text{Plasma Vol. (ml)}}{\text{(Body Wt) 0.01 g}}$

** Calculation: Rate of TG secretion/plasma TG pool size

Discussion

This report summarizes the effects associated with chronic ingestion of diets containing moderate amounts of MCT (8–16%) on plasma and hepatic lipid contents, and growth of rats. In vivo plasma triglyceride secretion was measured to determine if a higher rate of triglyceride secretion was associated with lower hepatic and higher plasma triglyceride levels.

The rate of plasma triglyceride secretion in fasted rats fed 14% MCT diets for 4 weeks was approximately 10% higher than in rats fed the corn oil diet. However, this response was not statistically significant and not large enough to account for the 19–44% lower concentrations of triglyceride observed in hepatic tissue from rats fed MCT. Previous authors have also noted lower hepatic triglyceride concentrations in rats fed MCT rather than corn oil.[3,31] In addition, evidence from assays of the rate limiting enzymes in fatty acid synthesis,[12,32] work with isolated hepatocytes,[4] and in vivo determination of hepatic lipogenesis from acetate[1,31] all suggest greater hepatic fatty acid synthesis with ingestion of MCT rather than long chain dietary fats. These observations of greater hepatic fatty acid synthesis and lower hepatic triglyceride

concentrations are consistent with the hypothesis that the rate of heptic triglyceride secretion is increased with ingestion of MCT.

Several factors may account for the modest differences in triglyceride secretion which we noted. Our calculated values for the plasma triglyceride pool size and the rate of triglyceride secretion were approximately 30% lower than previous reports using the Triton technique, while our values for the fractional rate constants were similar.[26-28] This may be associated with our use of fasted animals, as Williams et al. have noted higher triglyceride secretion into plasma with fed rather than fasted rats.[33] Fasted animals were used to focus on hepatic triglyceride secretion by controlling for differences in lipid absorption and intestinal secretion of triglycerides.[34] The intake of 16% fat rather than 5–10% used in most reports[25-28,33] is associated with a decrease in hepatic lipogenesis,[35] which may also account for our lower rate of triglyceride secretion. Our data suggest that an increase in the rate of triglyceride secretion into plasma is not the primary factor associated with lower hepatic concentrations of triglycerides in fasted rats fed MCT.

Our data confirm previous reports of lower concentrations of cholesterol in liver and plasma with chronic MCT feeding. However, the 10–20% decrease in plasma cholesterol levels was not as large as previous reports,[1,8] most likely because of feeding adult rats a lower total amount of dietary fat without added cholesterol and cholic acid. In addition, the cholesterol-lowering effect of MCT was only apparent in rats fed for 4–6 weeks. The dietary combination of 8% MCT plus 8% corn oil did not alter plasma cholesterol levels.

The tripelargonin diet was also associated with a cholesterol-lowering effect. These data suggest that increased levels of propionyl-CoA from oxidation of odd-chain length tripelargonin[13] do not alter the hypocholesterolemic effect associated with ingestion of even-chain MCT. The observation of greater liver weight in animals fed tripelargonin rather than corn oil or MCT is unexplained. Guy and Tuley[14] noted that tripelargonin lowers blood and liver β-hydroxybutyrate levels and spares liver glycogen compared to even-chain MCT when dietary carbohydrate is limited. However, our use of 50% dietary carbohydrate is likely to reduce the presence of ketosis and also differences in liver weight due to changes in glycogen stores.

Reduced hepatic cholesterogenesis with MCT feeding has been noted using both in vivo and in vitro experimental approaches.[1,12,31,32] A reduction in hepatic cholesterol synthesis has been suggested to contribute to the lower cholesterol levels observed in animals fed MCT. Our observation of 44% lower hepatic activity of HMG-CoA reductase in conjunction with lower plasma and hepatic cholesterol levels in rats fed even or odd-chain MCT supports this notion.

Evidence also suggests that lower cholesterol levels in animals fed MCT may be associated with rapid hepatic oxidation of MCT and a regulatory shunting of the acetyl-CoA from cholesterogenesis into lipogenesis.[12,35] Using isolated hepatocytes, Crozier et al.[4] have demonstrated simultaneous rapid oxidation and lipogenesis induced by ingestion of MCT. Takase et al.[12] noted significant elevations in the activities of fatty acid synthetase and malic enzyme with concomitant reduction in the activity of hepatic HMG-CoA reductase, and little depletion of essential fatty acids in the liver of animals fed MCT.[32] Hill et al.[6] noted a three-fold increase in fasting serum triglyceride concentrations in men who were overfed MCT rather than long-chain triglyceride (soybean oil) diets for 6 days. Our data also indicated higher fasting plasma triglyceride levels in rats fed MCT rather than corn oil. These observations support evidence suggesting greater de novo synthesis of fatty acids with ingestion of MCT. Further in vivo research is needed to clarify the relative rates of lipogenesis, cholesterogenesis, and ketogenesis during ingestion of MCT-containing diets with different amounts of carbohydrate.

Our observation of a lower feed efficiency but similar final body weights in animals fed MCT or corn oil diets is consistent with evidence of increased thermogenesis in humans[7] and reduced fat deposition in rats fed diets containing 37% MCT and 5% carbohydrate.[3] Lack of a more dramatic effect on growth in our study is most likely associated with inclusion of 50% dietary sucrose and diminished energy expenditure associated with reduced ketogenesis.[36] Greater food intake, weight gain, and feed efficiency in animals fed the 8% MCT plus 8% corn oil diet supports earlier work by Clark and Holt[37] who demonstrated greater intestinal absorption with a 3:4 by weight mixture of trioctanoin and triolein.

In summary, in vivo determination of plasma triglyceride secretion using the Triton WR-1339 technique suggests that greater hepatic triglyceride secretion is not the primary factor associated with the consistent finding of lower hepatic triglyceride concentrations in rats fed MCT. Also, 10–20% lower concentrations of cholesterol in plasma and liver were noted with ingestion of saturated MCT or tripelargonin rather than corn oil. The observation in hamsters[5] that ingestion of cholesterol-supplemented MCT diets was associated with enhanced receptor dependent LDL transport compared to ingestion of longer chain-length saturated triglycerides raises questions about the effects of MCT on cholesterol degradation and excretion.

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