Lymphatic absorption of structured triglycerides vs. physical mix in a rat model of fat malabsorption

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Tso, Patrick, Theresa Lee, and Stephen J. DeMichele. Lymphatic absorption of structured triglycerides vs. physical mix in a rat model of fat malabsorption. Am. J. Physiol. 277 (Gastrointest. Liver Physiol. 40): G333–G340, 1999.—Comparison was made between the intestinal absorption and lymphatic transport of a randomly interesterified fish oil and medium-chain triglyceride (MCT) structured triglycerides (STG) vs. the physical mix in rat small intestine following ischemia and reperfusion (I/R) injury. Under halothane anesthesia, the superior mesenteric artery (SMA) was occluded for 20 min and then reperfused in I/R rats. The SMA was isolated but not occluded in control rats. In both treatment groups, the mesenteric lymph duct was cannulated and a gastric tube was inserted. Each treatment group received 1 ml of the fish oil-MCT STG or physical mix (7 rats/group) through the gastric tube followed by an infusion of PBS at 3 ml/h for 8 h. Lymph was collected hourly for 8 h. Lymph triglyceride, cholesterol, and decanoic and eicosapentaenoic acids increased rapidly and maintained a significantly higher output (P < 0.01) with STG compared with physical mix in control rats over 8 h. After I/R, lymphatic triglyceride output decreased 50% compared with control. Gastric infusion of STG significantly improved lipid transport by having a twofold higher triglyceride, cholesterol, and decanoic and eicosapentaenoic acids output to lymph compared with its physical mix (P < 0.01). We conclude that STG is absorbed into lymph significantly better than physical mix by both the normal intestine and the intestine injured by I/R. Lymph; fat absorption; enteral nutrition; long-chain triglycerides; medium-chain triglycerides; lymph-fistula rat.

AN EXCITING NEW APPROACH to optimize the metabolic benefits of specific lipid mixtures has been the development of structured triglycerides (STG). Considerable advances have been made over the past 10 years that have broadened our knowledge base as to the understanding of the basic chemistry, physiology, and metabolism of these novel lipids. STG are a chemically interesterified mixture of both medium- and long-chain fatty acids incorporated on the same glycerol backbone by hydrolysis and random reesterification (3, 25). These triglyceride molecules are chemically distinct and offer unique advantages from their constituent medium (MCT)- and long (LCT)-chain triglycerides. For example, STG that contain medium-chain fatty acids may provide a useful vehicle for rapid hydrolysis and absorption due to the smaller molecular size and greater water solubility in comparison to LCT. Although STG retain some characteristics of MCT and LCT, they may provide an alternative lipid source that could overcome the gastrointestinal intolerance related to the sole use of MCT or LCT in patients with malabsorptive diseases.

Numerous studies in animal models of trauma, burn injury, and endotoxic shock have demonstrated that STG have metabolic benefits compared with identical physical mixtures of oils that have not been interesterified (10, 11, 24, 28, 33, 34). Rats receiving STG showed the greatest gain in body weight and attenuation of the hypermetabolic and protein catabolic response to injury over comparable groups of rats given either LCT or MCT alone or a physical mixture of LCT and MCT. Metabolic improvements have also been observed with STG compared with a physical mix of oil in rat models of cancer (23, 27) and sepsis-induced liver injury and dysfunction (20). Recently, the first clinical testing of a novel STG composed of fish oil and MCT was performed in patients undergoing major abdominal surgery for upper gastrointestinal malignancies (19, 32). Results showed that the enteral administration of a diet containing the fish oil-MCT STG during the postoperative period significantly reduced the total number of reported gastrointestinal complications and infections as well as improved renal and liver function through modulation of proinflammatory eicosanoid production.

The advantages of enterally fed STG may relate to differences in absorption, chylomicron formation, and transport of the triglycerides. Enhanced absorption of linoleic acid [18:2 (n-6)] was observed in cystic fibrosis patients fed STG containing long- and medium-chain fatty acids (13, 26). In vitro lipase digestions and absorption studies using isolated intestinal loops revealed rapid hydrolysis and absorption of a STG containing linoleic acid in the sn-2 position and medium-chain fatty acids in the sn-1 and -3 positions (15). Jensen et al. (16) reported in the lymph-cannulated dog that lymphatic absorption of medium-chain fatty acids from STG was 2.6-fold higher (10:0 in excess of 8:0) compared with its equivalent physical mix. Molecular species analyses revealed that the medium-chain fatty acids in lymph were present on the same triglyceride as long-chain fatty acids. Recently, we assessed the intestinal absorption of STG containing two medium-chain fatty acids (8:0) and one long-chain fatty acid [18:2 (n-6)] using a lymph fistula rat model (35). Conclusions from this study indicate that the chain length of the fatty acid on the STG molecule affected the digestion, absorption, and lymphatic transport of the triglyceride.
Although these observations are very important, few studies have assessed the potential absorptive benefits of STG in malabsorptive syndromes. Christensen et al. (9) showed that defined triglycerides with specific fatty acids in the sn-2 position on the glycerol moiety had a higher lymphatic transport of polyunsaturated fatty acids compared with a similar physical mixture of oils in rats with pancreatic deficiency. However, the benefits of STG consisting of random distributions of long- and medium-chain fatty acids on the glycerol backbone have not been explored in a rat model of fat malabsorption. The goals of this study were to compare the digestion, absorption, and lymphatic transport of a fish oil-MCT STG vs. its physical mix in a normal lymph fistula rat model and in a rat model of lipid malabsorption caused by ischemia and reperfusion (I/R)-induced injury of the small bowel (12).

MATERIALS AND METHODS

Conditioning of animals. Male adult Sprague-Dawley rats weighing 300–350 g were used for the study. When the animals first arrived at the vivarium, they were housed in quarantine for 1 wk and fed Purina rat chow. The light in the room was regulated to give 12:12-h light-dark cycle.

Lymph-fistula rat model and ischemic injury. Approval of this study was granted by the Animal Care Committee of the University of Cincinnati in accordance with guidelines set forth in the National Institutes of Health Guide for the Care and Use of Laboratory Animals.

Rats were fasted overnight before surgical procedures. Under halothane anesthesia, a laparotomy was performed. The superior mesenteric artery (SMA) was occluded for 20 min with a microbulldog clamp. At the end of the ischemic period, the clamp was released and three drops of lidocaine were applied directly on the SMA to facilitate perfusion (12).

In the control (sham) animals, the SMA was isolated in a similar fashion but was not occluded. In both groups of animals, the intestinal lymph duct was cannulated according to the method of Bollman et al. (6). In addition, a second soft silicone gastric tube (1.6 mm outer diameter) was introduced into the fundus of the stomach. The tubing was secured in the stomach by closing the fundal incision with a purse-string suture. Postoperatively, the rats were infused intragastrically at a rate of 3 ml/h with a 5% glucose-saline solution containing 145 mM NaCl, 4 mM KCl, and 0.28 M glucose. The animals were allowed to recover for at least 24 h in restraining cages maintained at a temperature of 30°C before lipid infusion.

Experimental plan. Four groups of rats were studied: two groups of sham-operated controls and two groups of rats with small bowel I/R injury. Seven rats were studied in each group. In the first two groups of sham-operated controls, rats were randomized to gastrically receive either 1 ml of fish oil-MCT STG or its physical mix equivalent. The fish oil-MCT STG was produced by mixing 55% by weight fish oil and 45% by weight fractionated MCT followed by chemical interesterification using sodium methoxide as a catalyst. This commercial process of interesterification leads to randomization so that predominantly all possible new triglyceride structures are found including LML, LMM, LLM, MLM (where L and M represent long- and medium-chain fatty acids, respectively, at the sn-1, sn-2, and sn-3 positions on the triglyceride molecule) with lesser amounts of the starting lipids MMM and LLL (3).

The physical mix was prepared by mixing the same weight proportions of fish oil and MCT as in the STG without interesterification (Fig. 1). The fatty acid composition of the starting oils, STG, and the physical mix is outlined in Table 1. The 2-monoglyceride fatty acid composition and molecular species determination of the fish oil-MCT STG and the physical mix are shown in Tables 2 and 3, respectively. Similarly, 1 ml of either STG or physical mix was given by gavage in the rats injured by I/R.

Experimental procedure. Lymph was collected into precooled conical graduated centrifuge tubes for 2 h before lipid infusion. This sample was analyzed as the fasting lymphatic output of lipid. Additional lymph samples were collected hourly for 8 h and between 8 and 24 h after the beginning of lipid infusion. After the lymph volume was determined, the samples were centrifuged for 15 min at 700 g at room temperature to remove blood cells. Lymph lipid was extracted by the method of Blankenhorn and Ahrens (5), and aliquots of the extract were taken for determination of triglyceride (4), phospholipid, and cholesterol.

Table 1. Fatty acid composition of experimental oils

<table>
<thead>
<tr>
<th>Fatty Acid</th>
<th>MCT Oil</th>
<th>Fish Oil</th>
<th>Physical Mix</th>
<th>Structured Triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:0</td>
<td>55.7</td>
<td>27.6</td>
<td>27.0</td>
<td></td>
</tr>
<tr>
<td>10:0</td>
<td>43.4</td>
<td>20.7</td>
<td>20.5</td>
<td></td>
</tr>
<tr>
<td>12:0</td>
<td>0.8</td>
<td>0.3</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>14:0</td>
<td>0.1</td>
<td>5.9</td>
<td>3.0</td>
<td></td>
</tr>
<tr>
<td>16:0</td>
<td>9.5</td>
<td>4.9</td>
<td>4.7</td>
<td></td>
</tr>
<tr>
<td>16:1 (n-7)</td>
<td>8.3</td>
<td>4.2</td>
<td>4.1</td>
<td></td>
</tr>
<tr>
<td>18:0</td>
<td>12.2</td>
<td>0.6</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>18:1 (n-9)</td>
<td>11.7</td>
<td>6.0</td>
<td>5.7</td>
<td></td>
</tr>
<tr>
<td>18:2 (n-6)</td>
<td>1.7</td>
<td>0.9</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>18:4 (n-3)</td>
<td>2.8</td>
<td>1.1</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>20:1 (n-9)</td>
<td>1.9</td>
<td>1.0</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>20:4 (n-6)</td>
<td>2.8</td>
<td>1.5</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>20:5 (n-3)</td>
<td>28.7</td>
<td>14.7</td>
<td>15.1</td>
<td></td>
</tr>
<tr>
<td>22:5 (n-3)</td>
<td>3.2</td>
<td>1.7</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>22:6 (n-3)</td>
<td>13.1</td>
<td>6.8</td>
<td>8.0</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>8.9</td>
<td>4.4</td>
<td>4.3</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Values are % weight (g/100 g). MCT, medium-chain triglycerides.
phospholipid (29), and cholesterol (30). Aliquots were also taken from a subset of three rats for the analysis of fatty acid composition of the lymph triglycerides.

Analysis of fatty acid composition. Total lipids were extracted according to the official method of the American Official Analytical Chemists' Association (1). Fatty acid methyl esters were prepared and analyzed by gas chromatography as previously described (2, 21). A Hewlett-Packard 5890 gas chromatograph and a fused silica capillary column (230R, 30 m length, 0.32 mm internal diameter, 0.25 micron film thickness; Supelco, Bellefonte, PA) were used throughout the study. A known amount of an internal standard triheptadecanoin was used to quantify the amount of fatty acids in each sample. The results of the fatty acid composition were expressed as grams per 100 grams fatty acids (relative weight percentage).

Analysis of triglyceride profile by supercritical fluid chromatography. The quantitative determination of triglyceride molecular species using carbon dioxide supercritical fluid chromatography was performed as previously described (22). Triglyceride species were separated according to their equivalent carbon number (ECN), defined as the “sum of the total carbon number in the acyl side-chains of the triglyceride molecule.” A known amount of the triglycerides was dissolved in chloroform-methanol (95:5, vol/vol) solvent and analyzed directly using a supercritical fluid chromatograph (Dionex 602 series; Dionex, Sunnyvale, CA). An SB-100 methyl capillary column (10 m length, 100 µm internal diameter, and 0.25 µm film thickness) with frit restrictor and a flame ionization detector were used for the separation, detection, and quantitation of the triglyceride species. Supercritical fluid carbon dioxide was used as the mobile phase. A known amount of the monoacid triglyceride standards was used for instrument calibration.

2-Monoglyceride analysis. 2-Monoglycerides were analyzed using a method similar to that described by Jensen et al. (16). The triglycerides were hydrolyzed using a freshly prepared lipase solution (Rhizopus arrhizus, Sigma, EC 3.1.1.3, 1 × 10⁶ U/ml). Then 2-monoglycerides were extracted from the reaction mixture and separated using TLC. A solvent mixture containing chloroform-acetone (85:15, vol/vol) was used to separate the triglycerides, diglycerides, 2-monoglycerides, and 1 (3)-monoglycerides (16, 36). The TLC zone for 2-monoglycerides was isolated, and the fatty acid composition was analyzed in the same manner as previously described.

Statistical methods. All values are expressed as means ± SE. A two-way repeated-measures ANOVA was used to determine whether differences existed among groups for each hour of lipid infusion for each dependent variable. If a main effect of group or time was significant, Tukey's studentized range test was carried out to determine where the difference occurred. When a significant interaction was present, a one-way repeated-measures ANOVA was conducted for each group and a one-way ANOVA was conducted at each time. Significant findings were then subjected to the Tukey's test to determine where the differences occurred. Results were considered to be statistically significant at P < 0.05.

RESULTS

Lymph flow. As shown in Fig. 2, the mean fasting lymph flow for all four groups of rats, two I/R (STG and physical mix) and two controls (STG and physical mix), varied between 2.5 and 2.8 ml/h. In all groups, the lymph flow increased significantly as a result of lipid infusion and reached a maximum flow rate between 3.3 and 4.0 ml/h during the 3rd h after feeding the oil by gavage. After peaking at the 3rd h, lymph flow declined slowly and reached a steady output of about 3 ml/h during the 7th and 8th h following lipid feeding. There were no statistically significant differences in the
Lymph flow rates between the STG and physical mix rats in either the control or I/R groups.

Lymphatic triglyceride output. Figure 3 shows the lymphatic triglyceride output during the first 8 h after the gastric feeding of either STG or physical mix. The fasting lymphatic triglyceride output varied between 3.8 and 4.4 µmol/h in all four groups of animals. There was a marked difference in the lymphatic triglyceride output following the feeding of either STG or physical mix in the control animals. Lymphatic triglyceride output in the STG-fed rats increased rapidly and maintained a significantly higher output overall and for all time points during the 8 h after lipid feeding \((P < 0.01)\). The triglyceride output from I/R rats fed STG was similar to the output observed for control rats fed the physical mix.

When the sum of the total number of micromoles of triglyceride transported in lymph during the 8 h following lipid feeding was calculated, the differences between STG and physical mix were obvious. The overall lymphatic triglyceride output during the 8 h after lipid feeding in the control STG group \([268.7 \pm 24.6 (SE) \text{µmol}]\) was significantly higher than control physical mix \([171.1 \pm 14.3 \text{µmol}, P < 0.001]\), as well as the I/R STG group \([157.7 \pm 11.6 \text{µmol}, P < 0.001]\), having an overall significantly higher triglyceride output compared with I/R physical mix \([77.6 \pm 6.5 \text{µmol}]\).

Lymphatic phospholipid output. Figure 4 shows the lymphatic phospholipid output in micromoles per hour. In all four groups of rats, lymphatic phospholipid output increased as a result of lipid feeding. Although the lymphatic phospholipid output appeared to be higher in the control STG group compared with the control physical mix rats, the overall differences were not statistically significant \((P = 0.09, \text{repeated measures ANOVA})\). I/R injury to the small bowel significantly reduced lymphatic phospholipid output compared with the control animals regardless of the type of lipid infused. However, lymphatic phospholipid output was significantly higher in the I/R STG group compared with I/R physical mix \((P < 0.001; \text{repeated measures ANOVA})\) and for all time points from 2 to 8 h. Similar differences like those above were observed when the control STG rats had a higher maximal triglyceride output compared with physical mix. As we have previously observed, the lymphatic triglyceride output decreased 50% following I/R injury compared with control animals. Although I/R injury resulted in a significant reduction in the lymphatic absorption of both STG and physical mix, gastric infusion of STG significantly improved triglyceride transport by having a significantly higher triglyceride output overall and for all time points during the 8 h following lipid feeding \((P < 0.01)\). The triglyceride output from I/R rats fed STG was similar to the output observed for control rats fed the physical mix.

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cumulative lymphatic phospholipid in the four groups of rats was calculated. The total lymphatic phospholipid output during the 8 h following lipid feeding in the control STG group was 28.7 ± 1.7 µmol and not statistically different from control physical mix (25.3 ± 1.4 µmol, P = 0.105). In contrast, the overall lymphatic phospholipid output was significantly higher in the I/R STG rats (21.1 ± 1.2 µmol) compared with I/R physical mix (14.8 ± 1.6 µmol, P < 0.01).

Lymphatic cholesterol output. As shown in Fig. 5, lymphatic cholesterol outputs recapitulated the pattern observed with the lymphatic triglyceride outputs. Similar to lymphatic triglyceride output, I/R injury significantly reduced lymphatic cholesterol outputs in rats fed with either STG or physical mix at all time points during the 8 h following lipid feeding (P < 0.01 for comparisons at all time between control STG and I/R STG or control physical mix and I/R physical mix). Lymphatic cholesterol transport was significantly higher overall (P < 0.01) with STG feeding compared with physical mix feeding in both the control and I/R rats (P < 0.01 for comparisons at all time points between control STG and control physical mix or I/R STG and I/R physical mix animals).

The cumulative lymphatic cholesterol outputs showed that during the 8 h following lipid feeding, the control STG rats transported 39.6 ± 1.8 µmol of cholesterol into lymph as compared with 27.1 ± 1.4 µmol in the control physical mix group (P < 0.001). In the I/R group, rats fed STG transport 24.4 ± 1.8 µmol of cholesterol in lymph compared with 14.9 ± 1.5 µmol of cholesterol in the physical mix animals, which was highly significant (P < 0.001).

Lymphatic decanoic acid and eicosapentaenoic acid outputs. The fatty acid composition of lymph triglycerides was measured to assess whether differences exist between rats fed either STG or physical mix in the absorption and lymphatic transport in the individual fatty acids of interest, i.e., decanoic acid (10:0, a medium-chain fatty acid) and eicosapentaenoic acid (20:5 n-3), a long-chain n-3 fatty acid). As shown in Figs. 6 and 7, there was a two- to threefold increase in decanoic and eicosapentaenoic acids transported in lymph during the 8 h following STG feeding compared with physical mix. As observed before with triglyceride output, lymphatic transport of either fatty acid was reduced following I/R injury. However, lymphatic transport results of both decanoic and eicosapentaenoic acids were two- to threefold higher as early as 2 h after feeding STG compared with physical mix. This difference was maintained during the 8-h lymph collection.

DISCUSSION

Under steady-state conditions, we compared the absorption and lymphatic transport of STG and its physical mix under normal conditions and following I/R injury of the small bowel. We clearly demonstrated that intestinal lipid absorption was markedly reduced 24 h...
after I/R injury. The details of this model of fat malabsorption have been previously described (12). A conscious lymph fistula rat model was used as an established method for studying the digestion and transport of lipids. By infusing a physiological quantity of either STG or physical mix into the stomach of rats, the lymphatic triglyceride, phospholipid, cholesterol, and fatty acid output can be collected and quantitatively compared between the two groups.

The data presented in this study show that the amount of triglyceride, cholesterol, and specific fatty acids (decanoic and eicosapentaenoic acids) transported into lymph were significantly higher after STG infusion compared with physical mix in the normal conscious lymph fistula rat. When we examined the lymphatic output data for these parameters, the steady-state outputs occurred earlier with significantly higher maximal outputs for control animals fed STG compared with physical mix. It is felt that these observations are very important, especially the findings that the absorption of lipid and key essential fatty acids under normal conditions with STG. Although I/R significantly reduced the lymphatic transport of triglyceride, phospholipid, cholesterol, and specific fatty acids (decanoic and eicosapentaenoic acids) in both groups of rats, STG infusion resulted in similar absorptive benefits as seen in normal animals. For all parameters measured, the difference between STG- and physical mix-fed rats was greater in the I/R group compared with the controls. The magnitude of this difference is evident from the fact that the lymphatic transport of triglyceride, phospholipid, cholesterol, and decanoic, and eicosapentaenoic acids from I/R rats fed STG was similar to the output observed for control rats fed physical mix. These data clearly demonstrate that STG were digested and transported to lymph more efficiently than the physical mix under normal and I/R injury conditions.

There are a number of possible explanations for these important findings. The enhanced lymphatic absorption of the above lipids from STG most likely reflects the unique molecular structure of its triglycerides that results from interesterification of the fish oil and MCT. Triglyceride molecular species analysis of the two oils was performed to determine the relative distribution of medium-chain fatty acids in the various triglycerides of both oils (Table 3). The calculated ECN represents the sum of the acyl side chains of the triglyceride. The triglyceride species containing a mixture of medium- and long-chain fatty acids (ECNs 32–43) were abundant with STG but were absent in the physical mixture. In contrast, the physical mix had a higher proportion of triglycerides with an ECN number less than 30 or greater than 50, indicating that the triglycerides contain exclusively either medium- or long-chain fatty acids, but not mixed. Thus it is likely that the novel triglyceride species (ECNs 32–43) in STG may be responsible for the increased absorption and transport of triglyceride in lymph for both control and I/R rats. The precise mechanism of these absorptive benefits remains to be investigated but may lie in the packaging and secretion of chylomicrons. Because we were not able to radiolabel the abundance of different triglycerides in STG and physical mix, we could not trace the luminal digestion and mucosal uptake of the lipid digestive products of either oil. However, it is not likely that the difference in the lymphatic transport of triglycerides in rats given either the STG or physical mix is caused by a difference in digestion and mucosal uptake of the lipolytic products. Most likely, it is caused by a difference in the re-esterification and packaging of the absorbed lipid into chylomicrons. The mechanism of why the lipid digestion products from STG is packaged better into chylomicrons vs. physical mix remains to be elucidated and is currently being investigated in our laboratory. In support of this theory, more efficient packaging and either larger or more chylomicrons may be formed as evidenced by the observed increases in lymphatic phospholipid and cholesterol outputs.

This present investigation confirms previous STG studies demonstrating the absorptive benefits of STG consisting of a randomized distribution of long- and medium-chain fatty acids on the glycerol moiety. Enhanced absorption of 18:2 (n-6) was observed in cystic fibrosis patients fed STG containing mixed triglycerides (13, 26). Jensen et al. (16) developed a canine model to compare the lymphatic absorption of fish oil-MCT STG and its equivalent physical mix; similar oils were used in this study. Results showed that lymphatic absorption of medium-chain fatty acids from STG was 2.6-fold higher (10.0 in excess of 8.0) compared with the physical mix. Molecular species analyses revealed that the medium-chain fatty acids in lymph were present on the same triglyceride as long-chain fatty acids. In one dog that received a double crossover, a two- to threefold increase in the amount of lipid in lymph was detected with the STG diet compared with the physical mix. Rat absorption studies by Christensen et al. (7–9) and Jensen et al. (17) have shown that defined triglycerides with specific fatty acids in the sn-2 position on the glycerol moiety may provide a means to increase absorption of essential fatty acids in syndromes having reduced pancreatic lipase and/or compromised bile production. Recently, the first clinical testing of fish oil-MCT STG was performed by Kenler and associates (19). They compared the safety, gastrointestinal tolerance, and clinical efficacy of an enteral diet containing STG to an isocaloric formula containing a physical mixture of vegetable oil and MCT in patients undergoing major abdominal surgery for upper gastrointestinal malignancies. Results showed that patients fed fish oil-MCT STG experienced 40% lower total days with reported gastrointestinal complications (P = 0.036) and a 50% decline in the total number of actual reported gastrointestinal complications (P = 0.004) compared with patients fed control diet.

In addition to the increased absorption of triglyceride, phospholipid, and cholesterol, enhanced lymphatic absorption of decanoic and eicosapentaenoic acids was observed with STG compared with physical mix. Positional specificity of fatty acids on the glycerol moiety was likely one of the key factors. Lingual, gastric, and pancreatic lipases hydrolyze medium- or long-chain
fatty acids in the sn-1 and sn-3 positions. The remaining fatty acid in the sn-2 position (2-monoglyceride) is quickly absorbed, reesterified with long-chain fatty acids or longer medium-chain fatty acids, formed into chylomicrons, and transported by the lymphatic system to the systemic circulation for utilization by peripheral tissues (18, 31). The increase in lymphatic eicosapentaenoic acid output after STG feeding was due in part to its higher percentage in the sn-2 position on the glycerol moiety compared with physical mix (Table 2). The overall increase in triglyceride output would also contribute to the increase in eicosapentaenoic acid delivery to lymph. The higher lymphatic transport of decanoic acid after feeding STG, however, cannot be explained by its preferential placement in the sn-2 position of the STG molecule. In fact, the physical mix has a higher percentage of 8:0 and decanoic acid (10:0) in the sn-2 position compared with the physical mix. One explanation may be that the digestion of the physical mix resulted in a higher amount of medium-chain fatty acids being transported via the portal route, resulting in a lower concentration in lymph compared with STG. The increase in lymphatic decanoic acid with STG may be due in part to its unique, mixed triglyceride species containing both medium- and long-chain fatty acids, which are absent in the physical mix. These triglyceride species have been associated with rapid hydrolysis and absorption in both in vitro (15) and in vivo animal models (14, 16, 35). These data suggest that a randomized triglyceride mixture containing either two medium- and one long-chain fatty acid or one medium- and two long-chain fatty acids are absorbed and transported into lymph more efficiently than a mixture of triglycerides containing predominantly either medium- or long-chain fatty acids. These novel triglycerides have been shown to have metabolic benefits in animal models of trauma as described earlier (10, 11, 24, 28, 33, 34). In summary, this study provides important evidence supporting the use of randomly interesterified STG to increase the absorption of triglycerides and essential fatty acids under normal, healthy conditions and following small bowel dysfunction. Provision of oil blends in the form of STG may have improved tolerance and lower gastrointestinal complications in malabsorption syndromes.

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REFERENCES


16. Ling, P. R., N. W. Istfan, S. M. Lopes, V. K. Babayan, G. L. Blackburn, and B. R. Bistrian. Structured lipid made from

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