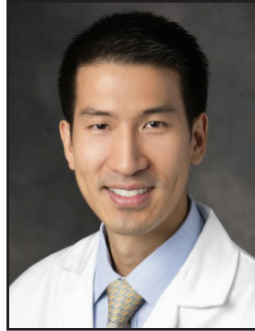


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# The Use of Medium-Chain Triglycerides in Gastrointestinal Disorders



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**Medium-chain triglycerides (MCTs) are lipid molecules that are more readily absorbed and oxidized than most lipids. This unique characteristic of MCTs has led to interest in their use in the management of several gastrointestinal disorders, where MCTs have been primarily used to reduce fat malabsorption and to serve as a source of calories to optimize nutritional status. In this review, we discuss the composition of MCTs, its sources, and the roles that they potentially play in the treatment of various gastrointestinal disorders.**

## INTRODUCTION

**M**edium-chain triglycerides (MCTs) comprise a glycerol molecule attached to 3 fatty acid chains ranging between 6 to 12 carbons in length. Unlike most other lipid molecules that require a complex process of digestion, MCTs are more easily absorbed into the bloodstream from the gastrointestinal tract. These features of MCTs confer unique benefits in the management of gastrointestinal disorders.<sup>1</sup> As such, MCTs have historically been used to treat steatorrhea resulting from malabsorptive disorders, such as pancreatic insufficiency, prior gastrectomy and small

bowel resection. MCTs have also been investigated for their potential to reduce obesity, cardiovascular disease, and neurological disorders. The purpose of this review is to describe the composition, functional characteristics and sources of MCTs, as well as to review the evidence investigating the use of MCTs in the management of gastrointestinal disorders.

## Structure

A fatty acid is a simple lipid molecule with a carboxylic acid group on one end and a hydrocarbon chain on the other.<sup>2</sup> The hydrocarbon chain length may range from 4 to 28 carbons and determines the classification of fatty acids: short chain (< 6 carbons), medium chain (6 to 12 carbons), long chain (13 to 21 carbons), and very long chain ( $\geq$  22 carbons). Triglycerides are lipid

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molecules with three fatty acids attached to a glycerol backbone. Similar to simple fatty acids, the length of the fatty acid group determines the nomenclature of short-chain triglycerides (SCTs), medium-chain triglycerides (MCTs), and long-chain triglycerides (LCTs).

The presence of double bonds can vary within fatty acids. Saturated fatty acids do not contain any double bonds along the hydrocarbon chain, while unsaturated fatty acids do. Monounsaturated fatty acids contain a single double bond, while polyunsaturated fatty acids contain two or more double bonds. Most fatty acids can be endogenously synthesized, except for two long-chain polyunsaturated fatty acids: linoleic acid (18 carbons with 2 *cis* bonds at C9 and C12) and linolenic acid (18 carbons with 3 *cis* bonds at C9, C12, C15); these are considered *essential* fatty acids (EFAs) and must be obtained from the diet.

The fatty acid groups of MCTs include caproic acid, caprylic acid, capric acid, and lauric acid. Compared with LCTs, MCTs are smaller in molecular weight, water soluble, rapidly oxidized for energy, possess a lower smoke point (the temperature when volatile substances are produced and a blue-colored smoke

is seen as a result of oxidation of oil) and are liquid at room temperature. MCTs only contain saturated fatty acids and therefore do not contain either of the EFAs, linoleic and linolenic acid. As MCTs do not contain EFAs, they also do not serve as a precursor to the synthesis of eicosanoids. MCTs provide fewer calories per gram than LCTs, 8.3 vs. 9.2, respectively.

### Digestion and Absorption

The length of the fatty acid influences the process of its digestion and absorption within the gastrointestinal tract. The entry of triglycerides as LCTs from the stomach into the duodenum stimulates the enteric secretion of the hormone cholecystokinin (CCK) and pancreatic enzymes from the pancreas. CCK promotes further release of bile from the gallbladder to help emulsify the triglycerides into smaller fat droplets to maximize its digestion.<sup>3,4</sup> Pancreatic lipase then cleaves the fatty acid chains from the triglycerides to form individual fatty acid molecules that then aggregate into micelles. Micelles are absorbed into the enterocytes along the intestinal brush border via passive diffusion or are shuttled by fatty acid transporters. Once in the

**Table 1. Comparison of Characteristics between MCTs and LCTs**

Characteristics	Medium Chain Triglycerides	Long Chain Triglycerides
Properties	Water soluble. Lower smoke point. Have no essential fatty acids.	Lipid soluble. Higher smoke point. Contain essential fatty acids.
Structure	6-12 hydrocarbons. All saturated fatty acids.	13 to 21 hydrocarbons (long chain). ≥ 22 hydrocarbons (very long chain). Both are saturated and unsaturated fatty acids.
Caloric Value	8.3 calories per gram.	9.2 calories per gram.
Digestion/ Absorption	Do not stimulate CCK. Do not require bile or pancreatic enzymes. Directly absorbed into portal circulation bound to albumin. Do not require carnitine for transport into the mitochondria.	Stimulate CCK. Require bile and pancreatic enzymes (lipase). Need to be incorporated into micelles, then into chylomicrons for entry into the lymphatic system. Require carnitine for transport into the mitochondria.
Storage	Adipose tissue (less).	Adipose tissue (more).

**Table 2. Examples of Commercial Liquid MCT Oil Products**

Product	Kcal/ 1 TBSP (15 mL)	Kcal/4 TBSP (60 mL)
Nature’s Way® Coconut Premium Oil (20 oz. bottle – 93% MCT, 7% LCT) <a href="http://www.naturesway.com">www.naturesway.com</a>	130 kcal/13 g	520 kcal/52 g
Nestle Health Science® MCT Oil (32 oz. bottle – 100% MCT) <a href="http://www.nestle-nutrition.com">www.nestle-nutrition.com</a>	115 kcal/14 g	460 kcal/56 g
Now Foods® MCT Oil (32 oz. bottle – 100% MCT) <a href="http://www.nowfoods.com">www.nowfoods.com</a>	100 kcal/14 kg	400 kcal/56 g
<ul style="list-style-type: none"> <li>◆ If unopened, the product can be stored in a cool dry place and once opened, can be stored at room temperature or in the refrigerator.</li> <li>◆ The inclusion of these commercial products is not meant to recommend any specific product.</li> </ul>		

enterocytes, the fatty acids are transported into the endoplasmic reticulum, reconverted into triglycerides, and packaged into chylomicrons.

The chylomicrons are released via exocytosis, enters and travels through the lymphatic system and eventually, drains into the subclavian vein to reach the bloodstream. In the intracellular space, long-chain fatty acids bind to carnitine for transport into the mitochondria for subsequent  $\beta$ -oxidation. In carnitine deficiency states that contribute to severe protein malnutrition (e.g., chronic malabsorption, small bowel obstruction, starvation), these long-chain fatty acids cannot be efficiently utilized and instead lead to accumulation of unoxidized fatty acids and impairment of ureogenesis, ketogenesis, and gluconeogenesis.<sup>5</sup> Clinical sequelae may include hepatic steatosis, hepatomegaly, myopathy, and altered mental status.

By contrast, MCT digestion is rapid and simple. MCTs do not stimulate CCK secretion.<sup>3,4</sup> MCT absorption occurs via passive diffusion along the gastrointestinal tract into the portal system bound to albumin. No further packaging or modification of the MCT molecules is required. Moreover, MCTs are not dependent on the carnitine acyltransferase system for transport into the mitochondria for  $\beta$ -oxidation.<sup>5</sup> This provides the ability for more rapid metabolism

of MCTs and improved utilization even in states of protein deficiency (Table 1).

**Sources**

Most fats and oils of animal and plant origin contain LCTs (e.g., fish, avocado, nuts, seeds, corn, peanut, safflower, and soybean oil). By contrast, natural sources of MCTs include coconut oil and palm kernel oil, although these oils also contain LCTs. Commercial MCT formulations may either be comprised of naturally-derived MCT oil, 100% synthetic MCT oil (produced from medium-chain fatty acids that are hydrolyzed from coconut or palm kernel oil, purified, and then re-esterified onto a glycerol backbone), physical mixtures (blend of MCTs and LCTs), or structured lipids<sup>6</sup> (Table 2). Structured lipids are synthetic lipid molecules with a mix of medium-chain and/or long-chain fatty acids attached to a glycerol backbone. In the clinical setting, it is not uncommon for healthcare professionals to tell their patients to use coconut oil to obtain MCTs. However, depending on the circumstance, this may worsen fat malabsorption due to the LCT content. Semi-elemental and elemental enteral formulas typically include MCTs to minimize need for digestion prior to absorption, although LCTs may also be included

*(continued on page 24)*

(continued from page 22)

as a source of EFAs (Table 3). Clinical applications may include malabsorption disorders from pancreatic insufficiency or severe small bowel disease.

**Dosage**

Excessive intake of oral MCT oil has been associated with gastrointestinal distress, such as abdominal discomfort, cramping, gassiness, bloating, and diarrhea. A tablespoon (15 mL) of MCT oil contains 14 grams of fat and 115 calories. A maximum daily dose of 50-100 grams has been suggested for improved gastrointestinal tolerance; this is equivalent to 4-7 tablespoons (60-100 mL) per day (56-98 grams of fat and 460-805 calories).<sup>1</sup> The daily dose of MCTs should be increased as tolerated to the maximum daily dose, while equally dividing the dose across all meals. The MCTs can be easily mixed into a variety of foods and beverages. If MCTs are used in cooking, the temperature should be kept below 150° C (302° F) to reduce risk of its oxidation, otherwise the flavor of the food could be affected.<sup>1</sup> A tablespoon of MCT oil can also be administered through a feeding tube using a syringe along with a 30 ml water flush before and after its administration (See Table 4). In the severely fat-restricted patient, a source

of EFAs will need to be provided in the diet along with MCT supplementation to prevent EFA deficiency. MCT oil does not require a prescription. Although MCTs possess unique characteristics, it is not considered to be a panacea and its use is intended to be administered along with other therapies to treat a disorder.<sup>1</sup>

**Use in Gastrointestinal Disorders**  
***Pancreatic Insufficiency***

Pancreatic insufficiency is characterized by a disruption in the exocrine function of the pancreas, which may result in decreased synthesis and/or release of pancreatic enzymes that normally assist in digestion of nutrients in the small bowel, particularly dietary LCTs. It may arise in acute or chronic pancreatitis, cystic fibrosis and as a consequence of pancreatic resection. The primary intervention for pancreatic insufficiency is pancreatic enzyme replacement therapy, and occasionally, acid-suppression therapy. There are limited studies at this time investigating the impact of oral MCT oil in pancreatic insufficiency. However, as MCTs do not require pancreatic enzymes for digestion, it is reasonable to consider them as a source of supplemental calories in these patients if needed.<sup>4</sup>

In chronic pancreatitis, there is interest in using

**Table 3. Comparison of MCT vs. LCT Content of Selected Formulas**

Formula	Calories/ mL	Total Fat g/L	MCT g/L	LCT g/L	MCT: LCT Ratio	mL for 1000 kcal
Peptamen®*	1.0	39.0	27.3	11.7	70:30	1000
Peptamen 1.5®*	1.5	56.0	40.0	16.0	70:30	666
Perative®**	1.3	37.3	15.3	22.0	40:60	769
Vital 1.0®**	1.0	38.1	18.0	20.1	47.5:52.5	1000
Vital AF 1.2®**	1.2	53.9	24.0	29.9	45:55	833
Vital 1.5®**	1.5	57.1	27.0	30.1	47.5:52.5	666
Vital HP®**	1.0	23.2	11.6	11.6	50:50	1000
Vivonex RTF®*	1.0	11.6	4.8	6.8	40:60	1000
<b>Standard Polymeric</b>						
Promote®**	1.0	26.0	5.0	21.0	19:81	1000
Replete®*	1.0	34.0	6.8	27.2	20:80	1000
* Nestlé® Nutrition: 800-422-2752 ( <a href="http://nestlenutritionstore.com">nestlenutritionstore.com</a> )						
** Abbott® Nutrition: 800-258-7677 ( <a href="http://abbottnutrition.com">abbottnutrition.com</a> )						

**Table 4. Suggested Guidelines for using MCT Oil**

- ◆ Do not exceed 4-7 tablespoons per day (60-100 ml/day) for gastrointestinal tolerance.
- ◆ Divide the daily dosage equally between all meals.
  - If eating 3 meals a day, this can be 1-2 tablespoons per meal.
- ◆ Do not heat MCT oil over 150° C (302 °F); otherwise it will affect the flavor of the food.
- ◆ Mix MCT oil into a variety of foods and beverages (e.g., hot cereals, soups, sauces, broth, smoothies, fruit/vegetable juices, hot chocolate, coffee, tea).
- ◆ If administered through a feeding tube, one tablespoon of MCT oil can be given with a water flush of 30 ml before and after its administration.
- ◆ MCT supplementation should never be the sole source of fat > 3 weeks. After 3 weeks, high EFA containing vegetable oil should be included in the diet to reduce risk of EFA deficiency.

MCTs to help reduce post-prandial pain. A small study of 8 adult pancreatic enzyme-*sufficient* patients with chronic pancreatitis found that consumption of an elemental enteral formula containing MCTs (69% of the total fat content; 9.8 grams per can), at least 3 times per day for 10 weeks, and  $\leq 20$  grams of fat from the diet per day, resulted in minimal increases in serum CCK levels and a significant reduction in post-prandial abdominal pain.<sup>7</sup> A study of 17 children with cystic fibrosis found no difference in absorption rates between a polymeric enteral formula (Isocal) with pancreatic enzyme replacement and elemental enteral formula (Peptamen) containing MCTs without enzyme replacement.<sup>8</sup>

### **Chyle Leaks**

Chyle is a turbid or milk-colored fluid that primarily consists of LCT-containing chylomicrons and lymphatic fluid. Chyle originates in the small bowel where chylomicrons are formed and absorbed into the lymphatic system via the lacteals. Chyle then passes through the lymphatic system and enters the venous circulation via the thoracic duct. An obstruction or injury to the lymphatic system may result in a chyle leak into the pleural, pericardial, or peritoneal space. Common causes of chyle leaks include neoplasia, infection, radiation, and trauma.

The nutritional management of a chyle leak may initially include consumption of a fat-restricted or a fat-free diet, elemental enteral nutrition with MCTs, or a high-protein diet with MCT supplementation.<sup>9,10</sup>

These interventions should only be used for the short term (approximately 2 weeks), as there is a risk of developing EFA deficiency with prolonged restriction of dietary LCTs. Once the chyle leak is closed, foods can be gradually re-introduced into the diet. If the chyle leak continues to persist despite these interventions, then parenteral nutrition is indicated. With parenteral nutrition, there is no need to restrict intravenous lipid emulsions, as they completely bypass the gastrointestinal tract and lymphatic system.

Three cases have been reported on the successful use of oral and/or nasogastric enteral feeding with MCTs for chylous fistulas that developed after neck dissections.<sup>11</sup> The patients had closure of their fistulas after two weeks on MCTs. In a retrospective review of 245 patients that underwent pancreatoduodenectomy or a total pancreatectomy, 40 patients who developed a chyle leak were placed on an MCT-containing enteral formula until they were able to transition to a fat free diet with oral MCT supplementation.<sup>12</sup> All patients experienced a decrease in chyle output without requiring surgical intervention or parenteral nutrition.

### **Short Bowel Syndrome**

Short bowel syndrome (SBS) is defined by a significant anatomic (or functional) reduction in small bowel length, thus leading to compromise in the digestive and absorptive capacity of the small bowel. Significant malabsorption observed in these patients often manifest as diarrhea, unintentional weight loss, and fluid and electrolyte disturbances. The rationale behind the use of

MCTs in SBS is to provide calories that are efficiently absorbed with minimal need for prior digestion.

At this time, there are only a few early case reports that have demonstrated potential benefit of MCTs in SBS. One case involved a 65 year-old woman with 76 cm of jejunum, 20 cm of terminal ileum, and an intact colon, who was admitted for chronic diarrhea and unintentional weight loss 3 years after extensive bowel resection for adhesions.<sup>13</sup> Another case involved a 69-year-old man with 120 cm of remaining small bowel (mostly jejunum), who was admitted with chronic diarrhea and unintentional weight loss 2 years after his extensive bowel resection due to mesenteric thrombosis.<sup>13</sup> Fecal fat excretion was elevated in both patients when given a LCT-rich regular diet or enteral formula. When switched to a sole MCT-containing enteral formula, fecal fat excretion was reduced and the patients experienced weight gain. Both patients afterwards were placed on a fat-restricted (LCTs) diet for 8-10 months that was supplemented with MCT.

The influence of bowel anatomy on the benefits of MCTs is yet unclear, although early studies suggest that the presence of an intact colon plays a significant role. In a randomized cross-over study of 19 SBS patients (9 without a colon; 10 with a colon), participants were initially administered high fat diets with either LCTs alone or an equal mixture of LCTs and MCTs in which the source of the MCT was either a MCT-containing margarine or MCT oil.<sup>14</sup> When switched from the LCT to LCT-MCT diets, patients with an intact colon had no difference in fecal volume, while those without a colon had an increase in fecal volume. Interestingly, patients with a colon also experienced an increase in fat and overall energy absorption on the LCT-MCT diet, although those without a colon only had a marginal increase in fat absorption and no improvement in overall energy absorption. The study investigators suggest that the colon serves as a major organ for absorption of the water-soluble MCTs, similar to short-chain fatty acids and unlike the insoluble LCTs. The lack of improvement in energy absorption among those with ileostomies and jejunostomies was attributed to increased carbohydrate and protein loss. The use of MCTs can be considered in the management of patients with SBS and an intact colon.

### Potential Use in Other Disorders

Due to their integral role in physiologic function, MCTs may have potential benefit in several non-gastrointestinal

disorders. A discussion of these benefits is beyond the scope of this review, although we present a few unique examples of MCT use in diverse conditions.

### **Obesity**

Due to its influence on thermogenesis and satiety, MCTs have been proposed to reduce obesity by increasing energy expenditure, reducing food intake and decreasing fat deposition in adipose tissue.<sup>15,16</sup> A systematic review and meta-analysis of 13 randomized controlled trials in healthy adults showed that when compared with LCTs, MCTs reduced body weight, waist and hip circumference, total body fat, total subcutaneous fat and visceral fat.<sup>17</sup> Serum lipid levels did not differ.

### **Cardiovascular Disease**

In cardiovascular disease, MCTs have been proposed to reduce hyperlipidemia based on observations that indigenous populations with high consumption of coconut flesh have low incidence of cardiovascular disease. However, a review of 8 clinical trials and 13 observational studies on the effect of coconut oil consumption on cardiovascular risk indicated that there is not enough evidence to support this practice.<sup>18</sup>

### **Alzheimer's Disease**

In mild to moderate Alzheimer's disease, MCTs have been investigated to improve cognition based on the theory that decreased glucose metabolism in the brain may result in cognitive and memory impairment, so using MCTs as an alternative energy source as ketones for the brain should potentially counteract this impairment. Small studies have shown modest improvement in memory recall after consumption of MCT.<sup>19</sup>

### **Epilepsy**

The ketogenic diet, which is a high fat, low carbohydrate diet, is often used as a treatment for refractory childhood epilepsy. A Cochrane review of the traditional ketogenic diet for epilepsy concluded that the use of the diet appears promising in treatment of epilepsy, but further studies are needed.<sup>20</sup> While the ketogenic diet often consists of LCTs, the use of MCTs in the ketogenic diet may be more appealing due to their greater potential to yield ketones for rapid oxidation. The MCT-rich ketogenic diet would additionally require less fat in favor of more carbohydrates to afford greater variety in the diet. However, a randomized trial of 145 pediatric

*(continued on page 28)*

(continued from page 26)

patients with refractory epilepsy found no difference in efficacy between the MCT diet and the traditional ketogenic diet.<sup>21</sup>

### CONCLUSION

MCTs possess unique characteristics of digestion, absorption, and oxidation that lead to great interest in their use in the management of gastrointestinal disorders. The facile absorption of MCTs without the need for bile or pancreatic enzymes makes them a good source of calories in the setting of malabsorption and steatorrhea from diseases, such as pancreatic or bile insufficiency. Due to their ability to bypass the lymphatic system, MCTs can also serve as a lipid source for patients with chyle leaks. As MCTs do not contain EFAs, supplementation with EFA containing vegetable oils will be necessary after 3 weeks to avoid deficiency.<sup>10</sup> Although studies are limited, MCTs may be considered as a supplemental calorie source either alone, or as part of an enteral product, in certain gastrointestinal disorders. ■

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