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ScienceDirect
International Dairy Journal 16 (2006) 1374–1382
INTERNATIONAL DAIRY JOURNAL
www.elsevier.com/locate/idairyj

Review

Medium-chain triglycerides

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Received 1 December 2005; accepted 2 June 2006

Abstract

Medium-chain fatty acids (MCFAs) comprise saturated fatty acids with 6–10 carbons. Besides synthetic medium-chain triglyceride (MCT) oils there are natural sources, like coconut oil and dairy fat. Compared with long-chain fatty acids (LCFAs), the chemical and physical properties of MCFAs show substantial metabolic differences. MCFAs do not require binding to proteins such as fatty-acid binding protein, fatty acid transport protein, and/or fatty acid translocase (FAT, homolog to human platelet CD36). MCFAs are a preferred source of energy (β-oxidation). MCFAs are also incorporated into adipose tissue triglycerides, and may influence adipose tissue and other systemic functions more substantially than previously assumed. MCTs reduce fat mass, through down-regulation of adipogenic genes as well as peroxisome proliferator activated receptor-γ. Recent studies confirmed the potential of MCFAs to reduce body weight and particularly body fat. This effect was not transient. MCFAs reduce lipoprotein secretion and attenuate postprandial triglyceride response. It was, however, frequently observed that MCTs increase fasting cholesterol and triglyceride levels. But, given in moderate amounts, in diets with moderate fat supply, MCFAs may actually reduce fasting lipid levels more than oils rich in mono- or polyunsaturated fatty acids. The same is true for glucose levels. MCTs improved several features contributing to enhanced insulin sensitivity. Under certain in vitro conditions, MCTs exert proinflammatory effects, but in vivo MCTs may reduce intestinal injury and protect from hepatotoxicity.

Keywords: Medium-chain fatty acids; Metabolism; Health

Contents

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doi:10.1016/j.idairyj.2006.06.015

1. Introduction

The term medium-chain triacylglycerols refers to mixed triacylglycerols of saturated fatty acids with a chain length of 6–10 carbons, i.e., hexanoic acid (C6:0, common name capronic acid), octanoic acid (C8:0, common name caprylic acid), and decanoic acid (C10:0, common name capric acid). Sometimes, dodecanoic acid (C12:0, common name lauric acid) is included. In the 1950s, medium-chain triglycerides (MCTs) were introduced as a special energy source within a variety of clinical nutrition settings, including pancreatic insufficiency, fat malabsorption, impaired lymphatic chylomicron transport, severe hyperchylomicronemia, and total parenteral nutrition. MCTs are also being used in preterm infant formulas. Since 1994, the use of MCTs in food products is generally recognized as safe (GRAS status) the US Food and Drug Administration (Traul, Driedger, Ingle, & Nakhasi, 2000).

2. Natural occurrence of medium-chain fatty acids and chemical synthesis of MCT oil

Dietary fats contain largely fatty acids with a chain length of 14 carbons and more. However, there are some natural sources of Medium-chain fatty acids (MCFAs). In coconut and palm kernel oil, there are high amounts of MCFAs (>50 wt% of fatty acids). In bovine milk C6:0–C10:0 make up 4–12% of all fatty acids, and C12:0 make up 2–5%, varying with genetics, stage of lactation, and feeding regimens (Jensen, 2002). MCT oils are produced by hydrolysis of coconut or palm kernel oil, filtration of MCFAs, and subsequent re-esterification. These MCT oils contain almost exclusively octanoic and decanoic acid, at a ratio from 50:50 to 80:20 (Bach & Babayan, 1982). Compared with triglycerides containing mainly saturated long-chain fatty acids, MCTs have a lower melting point, smaller molecule size, are liquid at room temperature, and less energy dense (8.4 versus 9.2 kcal g^{-1}). These distinct chemical and physical properties affect the way MCFAs are absorbed and metabolized.

There is an enormous number of studies dealing with the role of MCFAs as well as a number of reviews in this field (Bach & Babayan, 1982; Pfeuffer & Schrezenmeir, 2002; St Onge, 2005; St Onge & Jones, 2002). Most attention has focused on the potential role of MCFAs for weight management. The present paper addresses several aspects of MCFA metabolism that affect features of the metabolic syndrome; these include plasma lipid levels, insulin resistance, inflammatory response, as well as weight management.

3. Intestinal absorption

Intraluminal hydrolysis of MCTs is faster and more efficient than hydrolysis of long-chain triglycerides (LCTs). Likewise, absorption of MCFAs is faster and more efficient than that of long-chain fatty acids (LCFAs). MCFAs stimulate cholecystokinin secretion, bile phospholipid and cholesterol secretion less than LCFAs. In the presence of pancreatic lipase or bile salt deficiency, MCFAs can still be absorbed, as opposed to LCFAs (Bach & Babayan, 1982). In patients with pancreatic insufficiency, steatorrhea was significantly lower during a 5-day intake of a diet supplemented with MCT oil compared with a diet supplemented with LCTs (butter fat) (Caliari et al., 1996).

The majority of absorbed MCFAs are transported in the portal vein to the liver, whereas LCFAs are incorporated into chylomicron triglycerides and reach the systemic circulation via the lymph system (Bach & Babayan, 1982). The proportion of MCFAs in chylomicrons increases with increasing chain length and with chronic administration. Simultaneous administration of MCTs and LCTs increases MCFA appearance in chylomicrons (Lee, Hashim, & Vanitall, 1968).

4. Cellular handling of MCFAs in liver and other organs

In hepatocytes as well as in other cells, esterification of MCFAs is limited (Papamandjaris, MacDougall, & Jones, 1998). Thus, MCFAs have a high propensity for oxidation and seem to behave more like glucose than fat (Babayan, 1987). In contrast to LCFAs, MCFAs do not require carnitine palmitoyl transferase (CPT) for intramitochondrial transport. MCFAs readily cross the mitochondrial membrane, are activated intramitrochondrially by medium-chain acyl CoA synthases (Ikeda, Okamuraikeda, & Tanaka, 1985), and are rapidly oxidized. Consequently, oxidation of MCFAs is higher than that of LCFAs, both in rodents (Crozier, 1988; Noguchi, Takeuchi, Kubota, Tsuji, & Aoyama, 2002) and humans (Metges & Wolfram, 1991; St Onge, Bourque, Jones, Ross, & Parsons, 2003). In order to oxidize fatty acids, sufficient oxaloacetate is required to channel an elevated influx of acetyl CoA into the tricarboxylic acid cycle. An excessive supply of acetyl CoA results in increased ketone body production, as happens from MCFAs as compared to LCFAs (Seaton, Welle, Warenko, & Campbell, 1986; Tsuji et al., 2001). In parallel with increased MCFA oxidation, increased hepatic lipogenesis due to increased de novo fatty acid synthesis and enhanced fatty acid elongation was observed after the consumption of high MCT diets (>38%, w/w; Carnielli et al., 1994; Crozier, 1988; Hill et al., 1990). Increased cytosolic concentration of malonyl CoA down regulates the activity of CPT1 and thus results in reduced intramitochondrial transport and oxidation of LCFAs, while MCFAs bypass this transport process.

Compared with LCFAs, MCFAs do not require binding to fatty acid-binding protein, fatty acid transport proteins, or fatty acid translocase (FAT). This affects a number of regulatory pathways. For example, in the spontaneously hypertensive rat (SHR), where FAT on rat chromosome 4 was identified as a defective SHR gene (Aitman et al., 1997, 1999), dietary supply of MCFAs resulted in reduced basal insulin levels, normalized glucose tolerance, and attenuated

symptoms of the metabolic syndrome (Hajri et al., 2001). Furthermore, MCFA intake improved the impaired capacity of the SHR heart to withstand acute adrenergic stress due to the contribution of exogenous MCFA oxidation to energy production (Labarthe, Khairallah, Bouchard, Stanley, & Des, 2005). Besides peroxisome proliferator activated receptor-γ (PPARγ) gene expression and protein concentrations of further adipogenic transcription factors, steroid regulatory-binding element protein-1c and CCAAT element-binding protein-α were increased in murine adipocytes after exposure to octanoate (Han et al., 2002), indicating regulatory effects of MCFAs on transcriptional and post-transcriptional level.

5. Extrahepatic storage of MCFAs

The minor fraction of MCFAs which bypasses the liver is distributed to peripheral tissue via the general circulation (Bach & Babayan, 1982; Greenberger & Skillman, 1969). Although it is generally believed that ingested MCFAs are preferably oxidized in the liver, MCFAs were also incorporated into adipose tissue triglycerides of rodents (Han, Hamilton, Kirkland, Corkey, & Guo, 2003), and may influence adipose tissue and consequently systemic function more substantially than previously assumed. Murine 3T3-L1 preadipocytes exposed to octanoic acid accumulated less fat and did not induce cell differentiation compared to oleic acid (Guo, Choi, Kirkland, Corkey, & Hamilton, 2000). When 3T3-L1 and human adipocytes were exposed to octanoic acid, they accumulated less fat and show attenuated adipogenesis than cells exposed to LCFAs (Guo, Lei, Wang, Corkey & Han, 2003; Han et al., 2002). Furthermore, compared with an LCT diet, 2-months' feeding of an MCT diet reduced fat mass in rats, apparently through the down-regulation of adipogenic genes as well as the transcription factor PPARγ, beyond improving insulin sensitivity and glucose tolerance (Han et al., 2003). The decreased fat accumulation in adipocytes could result from preferential lipolysis of MCFAs stored at position sn-1,3 of adipose tissue triacylglycerols (Guo et al., 2000). Because MCFAs are highly ionized at physiological pH, they are much more soluble in aqueous biological fluids compared with LCFAs (Odle, 1997) and could move away faster from lipid droplets to reduce product inhibition of hormone sensitive lipase (Lei et al., 2004).

6. Implications of MCTs for health

6.1. Fasting plasma lipids

Serum lipids are secreted into the circulation from the intestine as chylomicrons and from the liver as very low-density lipoprotein (VLDL). Both lipoproteins carry one molecule of either apolipoprotein (apo) B48 or B100. Long-chain saturated fatty acids as well as oleic acid generally stimulate secretion and at the same time increase intracellular triglycerides. But octanoic (Sato et al., 2005; Tachibana, Sato, Takahashi, & Akiba, 2002), decanoic and dodecanoic acid (Sato et al., 2005) stimulated apoB, triglyceride and cholesterol secretions less than palmitic acid (C16:0) in cultured hepatocytes. At the same time, intracellular apoB mRNA expression was reduced with decanoic and dodecanoic acid, and there was no intracellular triglyceride accumulation. MCFAs even attenuated palmitic acid-stimulated apoB secretion (Sato et al., 2005; Tachibana et al., 2002). ApoB secretion, as well as hepatic triglyceride and cholesterol concentration, was also lower with octanoic as compared with oleic (C18:1) or linoleic acid (C18:2) when these fatty acids were fed as synthetic triglycerides to mice (Xie, Woollett, Turley, & Dietschy, 2002).

Nevertheless, studies frequently found that MCT-, as compared with LCT-, containing diets increased fasting plasma cholesterol as well as triglyceride concentrations in humans. LCTs in these studies were mostly from soybean, corn, or olive oil (Cater, Heller, & Denke, 1997; Hill et al., 1989, 1990; Swift, Hill, Peters, & Greene, 1992; Tholstrup et al., 2004). The problem is that polyunsaturated LCFAs themselves are hypocholesterolemic and hypotriglyceridemic compared to saturated LFCAs (Mensink, Zock, Kester, & Katan, 2003). When an MCT-rich diet was compared with a dodecanoic acid-rich diet, with identical amounts of mono- and polyunsaturated fatty acids, total and LDL cholesterol was less increased by the MCT diet. The MCT- as compared with the dodecanoic acid-rich diet also increased LDL receptor activity significantly (Tsai, Park, Kovacic, & Snook, 1999). However, diets with synthetic triglycerides containing only hexanoic or octanoic acid did not change LDL receptor activity as compared with tristearates in animal experiments (Dietschy, Woollett, & Spady, 1993).

All these experiments were carried out with very high amounts of MCTs in the diet, and in some cases the supply of polyunsaturated fatty acids in these diets was critically low. Two studies chose a different approach and used lower amounts of MCTs. In one case, just 5 g MCTs were given in a standard diet (28% of energy as fat, 2200 kcal per day in total), against an LCT diet enriched in mono- and polyunsaturated fatty acids (Nosaka et al., 2003). During the 12-week intervention, cholesterol and triglyceride levels were gradually reduced in both experimental groups, but somewhat more in the MCT group. VLDL cholesterol was significantly more reduced with the MCT diet. In another study, 10 g MCTs or a non-specified LCT oil was given in a very-low-calorie diet (VLCD) for 4 weeks (Krotkiewski, 2001). Again, both test oils decreased total cholesterol and triglyceride levels significantly, and the effect was more pronounced with MCTs. It is not clear whether the difference between the groups was tested for significance.

As will be discussed later for the effect on weight loss, consuming a moderate amount may be critical for a hypocholesterolemic (and hypotriglyceridemic) effect to be

seen. Though MCFAs do reduce triglyceride secretion when used in lower amounts, MCFA consumption, especially when fed in excess of caloric needs, might increase de novo lipogenesis. This, in turn, would increase triglyceride secretion, and could thus account for the elevated fasting plasma triglyceride levels (Pfeuffer & Schrezenmeir, 2002). As cholesterol and triglyceride secretion are regulated in a coordinated manner, increased cholesterol secretion may be the consequence of increased triglyceride secretion and this, in the longer run, might also enhance plasma cholesterol levels.

6.2. Postprandial plasma lipids

As outlined before, the inhibitory effect of MCFAs on apoB and triglyceride secretion will acutely affect the postprandial triglyceride response. Plasma triglyceride levels increase after a fat-containing meal and return to baseline 6–12 h later. The degree of postprandial triglyceride response to a fat meal is positively correlated with cardiovascular disease risk and features of the metabolic syndrome (Karpe, 1999; Schrezenmeir et al., 1993). According to conventional wisdom this postprandial triglyceride response, usually expressed as area under the curve (AUC), is more pronounced with saturated rather than polyunsaturated fatty acids. Postprandial triglyceride response was generally lower with intake of MCFAs rather than mono- or polyunsaturated LCFAs, both in animals (Kalogeris, Monroe, Demichele, & Tso, 1996) and man (Asakura et al., 2000; Borel et al., 1998). This diminished postprandial triglyceride response is not simply explained by the fact that MCFAs are transported in the lymph. When an MCT meal was followed by a subsequent LCT meal, the postprandial response to the second meal was unexpectedly pronounced, and the total AUC war approximately equivalent to that of two consecutive LCT meals (Borel et al., 1998). The authors concluded that a fraction of the MCFAs had been stored temporarily in the mucosa and secreted after the second meal, and that LCFAs are absolutely required for chylomicron formation. It may, however, be questioned whether lack of LCFAs is a sufficient explanation, as chylomicron triglycerides are generally enriched in endogenous LCFAs (Lambert, Botham, & Mayes, 1995).

Not surprising, obese subjects benefited more from the attenuating effect of MCFAs than lean subjects, and postprandial cholesterol response was also reduced (Kasai, Maki et al., 2003). The difference was mainly in what the authors called low-density lipoprotein (LDL), but what is probably an atherogenic remnant fraction. The lipid load was small in this study, just 10 g of soybean plus rapeseed oil or pure MCTs in a mixed liquid meal. The postprandial triglyceride response to milk fat as compared with an oil rich in polyunsaturated fatty acids was equal or even less in several studies (Mekki et al., 2002). This attenuated response is most probably due to short-chain fatty acids and MCFAs in dairy fat. In one study, the response to an MCT-enriched meal was not different from that to a cream meal (Thomas et al., 2001).

6.3. Body weight

In animals, feeding MCTs results in less weight gain than feeding isoenergetic diets containing LCTs, and less weight gain was associated with decreased fat deposition (Baba, Bracco & Hashim, 1982; Crozier, Boisjoyeux, Chanez, Girard, & Peret, 1987; Geliebter, Torbay, Bracco, Hashim, & Vanitallie, 1983; St Onge, Ross, Parsons, & Jones, 2003). It is generally believed that MCT-induced weight loss is secondary to hepatic oxidation of MCFAs, which lead to increased energy expenditure. Isoenergetic feeding of MCTs increases thermogenesis to a greater extent than LCTs in rodents (Bach & Babayan, 1982; Dulloo, Mensi, Seydoux, & Girardier, 1995; Geliebter et al., 1983; Noguchi et al., 2002). However, humans on a long-term basis could not consume such high-MCT diets, due to lack of palatability and because of adverse gastrointestinal and other symptoms. Energy expenditure following MCT-based meals was also greater than for LCT-based meals in several studies on humans, within 6 h after a single meal (Kasai et al., 2002; St Onge, Ross et al., 2003) or over 24 h (Dulloo, Fathi, Mensi & Girardier, 1996), and this effect was dose dependent (Dulloo et al., 1996). Higher thermogenesis was still evident after 6 days of overfeeding a liquid formula diet containing MCTs (Hill et al., 1989), but was somewhat attenuated after 4 weeks on an MCT as compared with a control olive oil diet (St Onge, Ross et al., 2003). But when MCTs were compared to beef tallow, an increased energy expenditure was still evident after 4 weeks (St Onge, Bourque et al., 2003).

The question arises how do MCTs affect body weight and body composition in the longer term. Intervention studies were carried out mostly in obese subjects, with an energy supply covering energy needs. In two intervention studies on obese subjects, lasting 4 weeks, there was a high fat (40% of energy) and MCT supply (approximately 80 g per day) (St Onge, Bourque et al., 2003; St Onge, Ross et al., 2003). In one experiment, MCTs were compared against beef tallow (St Onge, Bourque et al., 2003); in the other, a so-called functional MCT oil also containing flaxseed oil and phytosterols was compared against olive oil (St Onge, Ross et al., 2003). In both studies, weight loss was not different between intervention groups. However in the latter study, body fat was significantly more reduced with MCT intervention (St Onge, Ross et al., 2003). In a series of intervention studies from Japan in obese subjects (body mass index (BMI) $>23\,kg\,m^{-2}$), lasting 12 weeks each, dietary fat provided 26–27% of energy and the MCT dose was moderate, either 10 g per day during breakfast (Tsuji et al., 2001), 5 g per day in margarine (Nosaka et al., 2003), or 1.7 g per day in bread (Kasai, Nosaka et al., 2003), against a mixture of rapeseed and soybean oil as control. In all studies, body weight as well as body fat was significantly more reduced with the MCT diet. There was

no indication of an attenuated effect with longer time. The effects were not significant in non-obese subjects, i.e., subjects with BMI $< 23\,kg\,m^{-2}$ (Tsuji et al., 2001). When MCT- or LCT-containing VLCDs were given to obese subjects, with 9.9 or 8.8 g per day test fats, equivalent to 25% of total energy, MCT oil decreased body weight more than LCT oil within the first 2 weeks only. However, throughout the 4-week intervention period, MCT administration reduced body fat significantly more and lean body mass less (Krotkiewski, 2001). Thus, these results do not suggest that the effect of MCTs on body weight and body composition would be lost with longer-term application. It is noteworthy that such small amounts of MCTs per day had such a clear effect. It will have to be found out in further studies whether a low amount of MCTs, the ratio of MCFAs to other fatty acids, the total fat supply, or the food matrix into which MCTs are incorporated is critical. Furthermore, such regimens need to be tested in subjects of different genetic background.

Besides increased resting metabolic rate (White, Papamandjaris, & Jones, 1999) and postprandial energy expenditure, there is some evidence that MCTs could reduce food intake and enhance satiety and thus alter energy intake in rats (Bray, Lee, & Bray, 1980) and humans (Krotkiewski, 2001; Stubbs & Harbron, 1996). Reduced spontaneous food and thus energy intake at lunch was observed following a high-carbohydrate breakfast supplemented with MCTs as compared to olive oil or lard (Van Wymelbeke, Louis-Sylvestre, & Fantino, 2001); however, energy intake at dinner was no longer different. Of note, resting glucose and lipid oxidation and postprandial lipid oxidation was also higher in butter-fed as compared to soybean oil-fed obese rats, and the butter diet seemed to prevent fat accumulation in the long-term. There was no clear beneficial effect of butter in lean animals (Rolland et al., 2002).

6.4. Effect on glucose metabolism and insulin resistance

Because diets high in long-chain saturated fat are linked to the pathogenesis of insulin resistance (Riccardi, Giacco, & Rivellese, 2004), it is worthwhile to examine if MCFAs improve insulin-mediated glucose metabolism. Octanoic acid stimulated glucose-mediated insulin secretion in the perfused pancreas less than longer-chain fatty acids (Stein et al., 1997). Oxidation rates of LCFAs are also usually depressed when the diet is simultaneously high in carbohydrates. But in an euglycemic clamp study, a high glucose supply decreased oleic but not octanoic acid oxidation (Sidossis, Stuart, Shulman, Lopaschuk, & Wolfe, 1996). This means that glucose controls entry of LCFAs, but not of MCFAs, into mitochondria. On the other hand, MCT/LCT infusion decreased glucose oxidation less than LCT infusion (Stouthard, Endert, Romijn, & Sauerwein, 1994).

But in most animal or human studies there was no clear-cut reduction in plasma glucose or insulin levels (reviewed by Pfeuffer & Schrezenmeir, 2002). In a recent study, when a high dose of 70 g of test fats was consumed for 3 weeks, MCTs as compared with high-oleic sunflower oil increased not only LDL cholesterol, VLDL cholesterol, and plasma triglycerides, but also fasting glucose levels (Tholstrup et al., 2004). Yet in subjects of normal weight the amount of $5\,g\,day^{-1}$ MCTs had no effect as compared with the LCT oil (Nosaka et al., 2003). A moderate supply of MCTs (10 g per day), in a VLCD over 4 weeks, gradually decreased fasting glucose and particularly insulin levels more than an LCT diet in obese subjects (Krotkiewski, 2001). Fasting glucose and insulin fasting levels were not changed in patients with type 2 diabetes after 30 days on a MCT-rich diet, but postprandial glucose excursion was less after MCT intervention (Yost et al., 1994). Euglycemic clamping studies in humans showed improved insulin sensitivity with an MCT diet after short-term (Eckel et al., 1992) and longer-term treatment (Yost & Eckel, 1989), in the latter case within a hypocaloric diet. Insulin sensitivity and glucose tolerance were also improved in rats fed MCTs compared with LCTs for 2 months (Han et al., 2003).

Of note, overfeeding with MCTs as compared with LCTs decreased postprandial free fatty acids (FFAs) (Hill et al., 1990). This is noteworthy as increased levels of FFAs are associated with insulin resistance and the metabolic syndrome. In addition, MCT feeding did not stimulate triglyceride accumulation in hepatocytes in cell culture (Tachibana et al., 2002; Sato et al., 2005) and in liver of animal models (Han et al., 2003; Nagata, Kasai, Watanabe, Ikeda, & Saito, 2003).

6.5. Inflammation

It is believed that atherosclerosis is caused by a chronic low-grade inflammatory state, and coronary heart disease risk is associated with increased levels of markers of inflammation, like interleukin-6, C-reactive protein and soluble adhesion molecules. High levels of some markers are also linked to features of the metabolic syndrome, including adiposity and insulin resistance. Long-chain saturated fatty acids are proinflammatory, while n-3 fatty acids from fish oils dampen inflammatory responses (Plat & Mensink, 2005). In vitro, MCT emulsions increase adhesion molecule and activation marker expression in neutrophils and monocytes (Wanten, Janssen, & Naber, 2002), alter protein kinase C-mediated calcium signalling in human neutrophils (Wanten, van Emst-De Vries, Naber, & Willems, 2001), and exert a number of changes associated with an increased inflammatory response (Bellinati-Pires, Waitzberg, Salgado, & Carneiro-Sampaio, 1993). However, where examined, the effect was not observed with MCFAs (Wanten et al., 2002) or structured triglycerides containing both MCFAs and LCFAs (Wanten et al., 2001). The clinical relevance of these findings remains to be established. Most absorbed MCFAs are transported in

blood bound to albumin and are rapidly cleared by the liver, or are otherwise present in mixed triglycerides.

While decanoic acid, like oleic acid, increased secretion of the proinflammatory mediator interleukin (IL)-8 by Caco-2 cells in one study (Tanaka et al., 2001) octanoic acid and MCTs suppressed IL-8 secretion in another study (Hoshimoto, Suzuki, Katsuno, Nakajima, & Saito, 2002). In fact, MCTs are often administered to patients with Crohn's disease or short-bowel syndrome. Consumption of MCTs protected the gut of rats by modulating the immune response to lipopolysaccharides and enhancing secretory immunoglobulin A expression (Kono et al., 2004). Increasing doses of MCTs, at the expense of corn oil, also reduced alcohol-induced hepatotoxicity, including triglyceride accumulation and oxidative stress in rats (Ronis, Korourian, Zipperman, Hakkak, & Badger, 2004). As the short-chain butyric acid (C4:0) inhibits cytokine-induced adhesion molecule expression in endothelial cells (Zapolska-Downar, Siennicka, Kaczmarczyk, Kolodziej, & Naruszewicz, 2004), it would be interesting to also examine the effect of MCFAs. More work needs to be done in this field, in particular in vivo studies.

7. Side effects of MCT consumption

The amount of MCTs that can be tolerated within one meal is limited to 25–30 g. Ingestion of larger amounts of MCTs causes adverse gastrointestinal symptoms, including nausea, vomiting, bloating, gastrointestinal discomfort, abdominal cramps, and osmotic diarrhea (Jeukendrup & Aldred, 2004). There is no risk of ketoacidosis or ketonemia with MCTs at levels associated with normal consumption (Traul et al., 2000). Furthermore, rats adapted to long-term feeding of MCT-containing diets, in that hepatic and blood levels of ketone bodies were decreased (Crozier et al., 1987; Papamandjaris et al., 1998). It was concluded from several animal and human studies that MCTs had no toxicological properties, no matter whether administered orally or parenterally, or if consumed as a supplement in a balanced diet, at levels up to 15% of energy (corresponding to >30 g MCTs per day in a 2000 kcal diet) (Traul et al., 2000).

8. Conclusions and perspectives

In a number of studies, but not always, beneficial effects of MCTs on weight control and glucose as well as on lipid metabolism were observed. This may prove the usefulness of natural foods containing relatively high amounts of MCFAs as well as the usefulness of functional foods supplemented with MCTs. A functional oil containing MCTs, phytosterols, and flaxseed oil reduced total and LDL cholesterol levels and LDL particle size in healthy overweight men as compared to olive oil (St Onge, Lamarche, Mauger, & Jones, 2003). As several studies indicate that moderate doses are better than excessive loads, it will have to be examined which dose and food matrix offers the most benefits, and whether naturally occurring MCFAs at position sn-1,3 of a triglyceride molecule and MCT oils have the same effect. Another interesting aspect is whether MCFAs, due to their preferred oxidation, might "spare" polyunsaturated fatty acids from oxidation, as fatty acid tracer exhalation tests and serum fatty acid profiles in preterm infants (Rodriguez et al., 2003) and rats (Nagata et al., 2003) suggest.

Subjects with existing obesity may particularly profit from the consumption of MCFAs. β-oxidation of LCFAs was impaired in obese as compared to normal-weight subjects, but this was not the case for the oxidation of MCFAs (Binnert et al., 1998). A butter diet seemed to prevent fat accumulation in obese rats (Rolland et al., 2002), and obese human subjects lost more weight on an MCT diet than normal-weight subjects (Tsuji et al., 2001). Obese subjects profited more from the attenuating effect of MCTs on the postprandial triglyceride response (Kasai, Maki et al., 2003).

References

Aitman, T. J., Glazier, A. M., Wallace, C. A., Cooper, L. D., Norsworthy, P. J., Wahid, F. N., et al. (1999). Identification of Cd36 (Fat) as an insulin-resistance gene causing defective fatty acid and glucose metabolism in hypertensive rats. *Nature Genetics*, *21*, 76–83.

Aitman, T. J., Gotoda, T., Evans, A. L., Imrie, H., Heath, K. E., Trembling, P. M., et al. (1997). Quantitative trait loci for cellular defects in glucose and fatty acid metabolism in hypertensive rats. *Nature Genetics*, *16*, 197–201.

Asakura, L., Lottenberg, A. M. P., Neves, M. Q. T. S., Nunes, V. S., Rocha, J. C., Passarelli, M., et al. (2000). Dietary medium-chain triacylglycerol prevents the postprandial rise of plasma triacylglycerols but induces hypercholesterolemia in primary hypertriglyceridemic subjects. *American Journal of Clinical Nutrition*, *71*, 701–705.

Baba, N., Bracco, E. F., & Hashim, S. A. (1982). Enhanced thermogenesis and diminished deposition of fat in response to overfeeding with diet containing medium chain triglyceride. *American Journal of Clinical Nutrition*, *35*, 678–682.

Babayan, V. K. (1987). Medium chain triglycerides and structured lipids. *Lipids*, *22*, 417–420.

Bach, A. C., & Babayan, V. K. (1982). Medium-chain triglycerides—An update. *American Journal of Clinical Nutrition*, *36*, 950–962.

Bellinati-Pires, R., Waitzberg, D. L., Salgado, M. M., & Carneiro-Sampaio, M. M. (1993). Functional alterations of human neutrophils by medium-chain triglyceride emulsions: evaluation of phagocytosis, bacterial killing, and oxidative activity. *Journal of Leukocyte Biology*, *53*, 404–410.

Binnert, C., Pachiaudi, C., Beylot, M., Hans, D., Vandermander, J., Chantre, P., et al. (1998). Influence of human obesity on the metabolic fate of dietary long- and medium-chain triacylglycerols. *American Journal of Clinical Nutrition*, *67*, 595–601.

Borel, P., Tyssandier, V., Mekki, N., Grolier, P., Rochette, Y., Alexandre-Gouabau, M. C., et al. (1998). Chylomicron beta-carotene and retinyl palmitate responses are dramatically diminished when men ingest beta-carotene with medium-chain rather than long-chain triglycerides. *Journal of Nutrition*, *128*, 1361–1367.

Bray, G. A., Lee, M., & Bray, T. L. (1980). Weight-gain of rats fed medium-chain triglycerides is less than rats fed long-chain triglycerides. *International Journal of Obesity*, *4*, 27–32.

Caliari, S., Benini, L., Sembenini, C., Gregori, B., Carnielli, V., & Vantini, I. (1996). Medium-chain triglyceride absorption in patients with pancreatic insufficiency. *Scandinavian Journal of Gastroenterology*, *31*, 90–94.

Carnielli, V. P., Sulkers, E. J., Moretti, C., Wattimena, J. L. D., Vangoudoever, J. B., Degenhart, H. J., et al. (1994). Conversion of octanoic-acid into long-chain saturated fatty-acids in premature-infants fed a formula containing medium-chain triglycerides. *Metabolism—Clinical and Experimental*, *43*, 1287–1292.

Cater, N. B., Heller, H. J., & Denke, M. A. (1997). Comparison of the effects of medium-chain triacylglycerols, palm oil, and high oleic acid sunflower oil on plasma triacylglycerol fatty acids and lipid and lipoprotein concentrations in humans. *American Journal of Clinical Nutrition*, *65*, 41–45.

Crozier, G. L. (1988). Medium-chain triglyceride feeding over the long-term—The metabolic-fate of [C-14] octanoate and [C-14] oleate in isolated rat hepatocytes. *Journal of Nutrition*, *118*, 297–304.

Crozier, G., Boisjoyeux, B., Chanez, M., Girard, J., & Peret, J. (1987). Metabolic effects induced by long-term feeding of medium-chain triglycerides in the rat. *Metabolism—Clinical and Experimental*, *36*, 807–814.

Dietschy, J. M., Woollett, L. A., & Spady, D. K. (1993). The interaction of dietary-cholesterol and specific fatty-acids in the regulation of ldl receptor activity and plasma LDL-cholesterol concentrations. *Annals of the New York Academy of Sciences*, *676*, 11–26.

Dulloo, A. G., Fathi, M., Mensi, N., & Girardier, L. (1996). Twenty-four-hour energy expenditure and urinary catecholamines of humans consuming low-to-moderate amounts of medium-chain triglycerides: A dose–response study in a human respiratory chamber. *European Journal of Clinical Nutrition*, *50*, 152–158.

Dulloo, A. G., Mensi, N., Seydoux, J., & Girardier, L. (1995). Differential-effects of high-fat diets varying in fatty-acid composition on the efficiency of lean and fat tissue deposition during weight recovery after low food-intake. *Metabolism—Clinical and Experimental*, *44*, 273–279.

Eckel, R. H., Hanson, A. S., Chen, A. Y., Berman, J. N., Yost, T. J., & Brass, E. P. (1992). Dietary substitution of medium-chain triglycerides improves insulin-mediated glucose-metabolism in NIDDM subjects. *Diabetes*, *41*, 641–647.

Geliebter, A., Torbay, N., Bracco, E. F., Hashim, S. A., & Vanitallie, T. B. (1983). Overfeeding with medium-chain triglyceride diet results in diminished deposition of fat. *American Journal of Clinical Nutrition*, *37*, 1–4.

Greenberger, N. J., & Skillman, T. G. (1969). Medium-chain triglycerides—Physiologic considerations and clinical implications. *New England Journal of Medicine*, *280*, 1045.

Guo, W., Choi, J. K., Kirkland, J. L., Corkey, B. E., & Hamilton, J. A. (2000). Esterification of free fatty acids in adipocytes: a comparison between octanoate and oleate. *Biochemical Journal*, *349*, 463–471.

Guo, W., Lei, T. G., Wang, T., Corkey, B. E., & Han, J. R. (2003). Octanoate inhibits triglyceride synthesis in 3T3-L1 and human adipocytes. *Journal of Nutrition*, *133*, 2512–2518.

Hajri, T., Ibrahimi, A., Coburn, C. T., Knapp, F. F., Kurtz, T., Pravenec, M., et al. (2001). Defective fatty acid uptake in the spontaneously hypertensive rat is a primary determinant of altered glucose metabolism, hyperinsulinemia, and myocardial hypertrophy. *Journal of Biological Chemistry*, *276*, 23661–23666.

Han, J. R., Farmer, S. R., Kirkland, J. L., Corkey, B. E., Yoon, R., Pirtskhalava, T., et al. (2002). Octanoate attenuates adipogenesis in 3T3-L1 preadipocytes. *Journal of Nutrition*, *132*, 904–910.

Han, J. R., Hamilton, J. A., Kirkland, J. L., Corkey, B. E., & Guo, W. (2003). Medium-chain oil reduces fat mass and down-regulates expression of adipogenic genes in rats. *Obesity Research*, *11*, 734–744.

Hill, J. O., Peters, J. C., Swift, L. L., Yang, D., Sharp, T., Abumrad, N., et al. (1990). Changes in blood-lipids during 6 days of overfeeding with medium or long-chain triglycerides. *Journal of Lipid Research*, *31*, 407–416.

Hill, J. O., Peters, J. C., Yang, D., Sharp, T., Kaler, M., Abumrad, N. N., et al. (1989). Thermogenesis in humans during overfeeding with medium-chain triglycerides. *Metabolism—Clinical and Experimental*, *38*, 641–648.

Hoshimoto, A., Suzuki, Y., Katsuno, T., Nakajima, H., & Saito, Y. (2002). Caprylic acid and medium-chain triglycerides inhibit IL-8 gene transcription in Caco-2 cells: Comparison with the potent histone deacetylase inhibitor trichostatin A. *British Journal of Pharmacology*, *136*, 280–286.

Ikeda, Y., Okamuraikeda, K., & Tanaka, K. (1985). Purification and characterization of short-chain, medium-chain, and long-chain acyl-CoA dehydrogenases from rat-liver mitochondria—Isolation of the holoenzymes and apoenzymes and conversion of the apoenzyme to the holoenzyme. *Journal of Biological Chemistry*, *260*, 1311–1325.

Jensen, R. G. (2002). The composition of bovine milk lipids: January 1995 to December 2000. *Journal of Dairy Science*, *85*, 295–350.

Jeukendrup, A. E., & Aldred, S. (2004). Fat supplementation, health, and endurance performance. *Nutrition*, *20*, 678–688.

Kalogeris, T. J., Monroe, F., Demichele, S. J., & Tso, P. (1996). Intestinal synthesis and lymphatic secretion of apolipoprotein A-IV vary with chain length of intestinally infused fatty acids in rats. *Journal of Nutrition*, *126*, 2720–2729.

Karpe, F. (1999). Postprandial lipoprotein metabolism and atherosclerosis. *Journal of Internal Medicine*, *246*, 341–355.

Kasai, M., Maki, H., Nosaka, N., Aoyama, T., Ooyama, K., Uto, H., et al. (2003). Effect of medium-chain triglycerides on the postprandial triglyceride concentration in healthy men. *Bioscience, Biotechnology and Biochemistry*, *67*, 46–53.

Kasai, M., Nosaka, N., Maki, H., Negishi, S., Aoyama, T., Nakamura, M., et al. (2003). Effect of dietary medium- and long-chain triacylglycerols (MLCT) on accumulation of body fat in healthy humans. *Asia Pacific Journal of Clinical Nutrition*, *12*, 151–160.

Kasai, M., Nosaka, N., Maki, H., Suzuki, Y., Takeuchi, H., Aoyama, T., et al. (2002). Comparison of diet-induced thermogenesis of foods containing medium-versus long-chain triacylglycerols. *Journal of Nutritional Science and Vitaminology*, *48*, 536–540.

Kono, H., Fujii, H., Asakawa, M., Maki, A., Amemiya, H., Hirai, Y., et al. (2004). Medium-chain triglycerides enhance secretory IgA expression in rat intestine after administration of endotoxin. *American Journal of Physiology Gastrointestinal and Liver Physiology*, *286*, G1081–G1089.

Krotkiewski, M. (2001). Value of VLCD supplementation with medium chain triglycerides. *International Journal of Obesity*, *25*, 1393–1400.

Labarthe, F., Khairallah, M., Bouchard, B., Stanley, W. C., & Des, R. C. (2005). Fatty acid oxidation and its impact on response of spontaneously hypertensive rat hearts to an adrenergic stress: Benefits of a medium-chain fatty acid. *American Journal of Physiology Heart and Circulatory Physiology*, *288*, H1425–H1436.

Lambert, M. S., Botham, K. M., & Mayes, P. A. (1995). Variations in composition of dietary fats affect hepatic-uptake and metabolism of chylomicron remnants. *Biochemical Journal*, *310*, 845–852.

Lee, D. S., Hashim, S. A., & Vanitall, T. B. (1968). Effect of long chain triglyceride on chylous transport of medium chain fatty acids. *American Journal of Physiology*, *214*, 294.

Lei, T. G., Xie, W. S., Han, J. R., Corkey, B. E., Hamilton, J. A., & Guo, W. (2004). Medium-chain fatty acids attenuate agonist-stimulated lipolysis, mimicking the effects of starvation. *Obesity Research*, *12*, 599–611.

Mekki, N., Charbonnier, M., Borel, P., Leonardi, J., Juhel, C., Portugal, H., et al. (2002). Butter differs from olive oil and sunflower oil in its effects on postprandial lipemia and triacylglycerol-rich lipoproteins after single mixed meals in healthy young men. *Journal of Nutrition*, *132*, 3642–3649.

Mensink, R. P., Zock, P. L., Kester, A. D. M., & Katan, M. B. (2003). Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: A meta-analysis of 60 controlled trials. *American Journal of Clinical Nutrition*, *77*, 1146–1155.

Metges, C. C., & Wolfram, G. (1991). Medium-chain and long-chain triglycerides labeled with C-13—A comparison of oxidation after oral or parenteral administration in humans. *Journal of Nutrition*, *121*, 31–36.

Nagata, J., Kasai, M., Watanabe, S., Ikeda, I., & Saito, M. (2003). Effects of highly purified structured lipids containing medium-chain fatty acids and linoleic acid on lipid profiles in rats. *Bioscience, Biotechnology and Biochemistry*, *67*, 1937–1943.

Noguchi, O., Takeuchi, H., Kubota, F., Tsuji, H., & Aoyama, T. (2002). Larger diet-induced thermogenesis and less body fat accumulation in rats fed medium-chain triacylglycerols than in those fed long-chain triacylglycerols. *Journal of Nutritional Science and Vitaminology*, *48*, 524–529.

Nosaka, N., Maki, H., Suzuki, Y., Haruna, H., Ohara, A., Kasai, M., et al. (2003). Effects of margarine containing medium-chain triacylglycerols on body fat reduction in humans. *Journal of Atherosclerosis and Thrombosis*, *10*, 290–298.

Odle, J. (1997). New insights into the utilization of medium-chain triglycerides by the neonate: Observations from a piglet model. *Journal of Nutrition*, *127*, 1061–1067.

Papamandjaris, A. A., MacDougall, D. E., & Jones, P. J. H. (1998). Medium chain fatty acid metabolism and energy expenditure: Obesity treatment implications. *Life Sciences*, *62*, 1203–1215.

Pfeuffer, M., & Schrezenmeir, J. (2002). Milk lipids in diet and health—Medium chain fatty acids (MCFA). *IDF Bulletin*, *377*, 32–42.

Plat, J., & Mensink, R. P. (2005). Food components and immune function. *Current Opinion in Lipidology*, *16*, 31–37.

Riccardi, G., Giacco, R., & Rivellese, A. A. (2004). Dietary fat, insulin sensitivity and the metabolic syndrome. *Clinical Nutrition*, *23*, 447–456.

Rodriguez, M., Funke, S., Fink, M., Demmelmair, H., Turini, M., Crozier, G., et al. (2003). Plasma fatty acids and [C-13]linoleic acid metabolism in preterm infants fed a formula with medium-chain triglycerides. *Journal of Lipid Research*, *44*, 41–48.

Rolland, V., Roseau, S., Fromentin, G., Nicolaidis, S. V., Tome, D., & Even, P. C. (2002). Body weight, body composition, and energy metabolism in lean and obese Zucker rats fed soybean oil or butter. *American Journal of Clinical Nutrition*, *75*, 21–30.

Ronis, M. J. J., Korourian, S., Zipperman, M., Hakkak, R., & Badger, T. M. (2004). Dietary saturated fat reduces alcoholic hepatotoxicity in rats by altering fatty acid metabolism and membrane composition. *Journal of Nutrition*, *134*, 904–912.

Sato, K., Cho, Y., Tachibana, S., Chiba, T., Schneider, W. J., & Akiba, Y. (2005). Impairment of VLDL secretion by medium-chain fatty acids in chicken primary hepatocytes is affected by the chain length. *Journal of Nutrition*, *135*, 1636–1641.

Schrezenmeir, J., Keppler, I., Fenselau, S., Weber, P., Biesalski, H. K., Probst, R., et al. (1993). The phenomenon of a high triglyceride response to an oral lipid load in healthy-subjects and its link to the metabolic syndrome. *Annals of the New York Academy of Sciences*, *683*, 302–314.

Seaton, T. B., Welle, S. L., Warenko, M. K., & Campbell, R. G. (1986). Thermal effect of medium-chain and long-chain triglycerides in man. *American Journal of Clinical Nutrition*, *44*, 630–634.

Sidossis, L. S., Stuart, C. A., Shulman, G. I., Lopaschuk, G. D., & Wolfe, R. R. (1996). Glucose plus insulin regulate fat oxidation by controlling the rate of fatty acid entry into the mitochondria. *Journal of Clinical Investigation*, *98*, 2244–2250.

St Onge, M. P. (2005). Dietary fats, teas, dairy, and nuts: potential functional foods for weight control? *American Journal of Clinical Nutrition*, *81*, 7–15.

St Onge, M. P., Bourque, C., Jones, P. J. H., Ross, R., & Parsons, W. E. (2003). Medium- versus long-chain triglycerides for 27 days increases fat oxidation and energy expenditure without resulting in changes in body composition in overweight women. *International Journal of Obesity*, *27*, 95–102.

St Onge, M. P., & Jones, P. J. H. (2002). Physiological effects of medium-chain triglycerides: Potential agents in the prevention of obesity. *Journal of Nutrition*, *132*, 329–332.

St Onge, M. P., Lamarche, B., Mauger, J. F., & Jones, P. J. H. (2003). Consumption of a functional oil rich in phytosterols and medium-chain triglyceride oil improves plasma lipid profiles in men. *Journal of Nutrition*, *133*, 1815–1820.

St Onge, M. P., Ross, R., Parsons, W. D., & Jones, P. J. H. (2003). Medium-chain triglycerides increase energy expenditure and decrease adiposity in overweight men. *Obesity Research*, *11*, 395–402.

Stein, D. T., Stevenson, B. E., Chester, M. W., Basit, M., Daniels, M. B., Turley, S. D., et al. (1997). The insulinotropic potency of fatty acids is influenced profoundly by their chain length and degree of saturation. *Journal of Clinical Investigation*, *100*, 398–403.

Stouthard, J. M. L., Endert, E., Romijn, J. A., & Sauerwein, H. P. (1994). Infusion of long-chain or medium-chain triglycerides inhibits peripheral glucose-metabolism in men. *Journal of Parenteral and Enteral Nutrition*, *18*, 436–441.

Stubbs, R. J., & Harbron, C. G. (1996). Covert manipulation of the ratio of medium- to long-chain triglycerides in isoenergetically dense diets: Effect on food intake in ad libitum feeding men. *International Journal of Obesity*, *20*, 435–444.

Swift, L. L., Hill, J. O., Peters, J. C., & Greene, H. L. (1992). Plasma-lipids and lipoproteins during 6 d of maintenance feeding with long-chain, medium-chain, and mixed-chain triglycerides. *American Journal of Clinical Nutrition*, *56*, 881–886.

Tachibana, S., Sato, K., Takahashi, T., & Akiba, Y. (2002). Octanoate inhibits very low-density lipoprotein secretion in primary cultures of chicken hepatocytes. *Comparative Biochemistry and Physiology A—Molecular and Integrative Physiology*, *132*, 621–627.

Tanaka, S., Saitoh, O., Tabata, K., Matsuse, R., Kojima, K., Sugi, K., et al. (2001). Medium-chain fatty acids stimulate interleukin-8 production in Caco-2 cells with different mechanisms from long-chain fatty acids. *Journal of Gastroenterology and Hepatology*, *16*, 748–754.

Tholstrup, T., Ehnholm, C., Jauhiainen, M., Petersen, M., Hoy, C. E., Lund, P., et al. (2004). Effects of medium-chain fatty acids and oleic acid on blood lipids, lipoproteins, glucose, insulin, and lipid transfer protein activities. *American Journal of Clinical Nutrition*, *79*, 564–569.

Thomas, T. R., Horner, K. E., Langdon, M. M., Zhang, J. Q., Krul, E. S., Sun, G. Y., et al. (2001). Effect of exercise and medium-chain fatty acids on postprandial lipemia. *Journal of Applied Physiology*, *90*, 1239–1246.

Traul, K. A., Driedger, A., Ingle, D. L., & Nakhasi, D. (2000). Review of the toxicologic properties of medium-chain triglycerides. *Food and Chemical Toxicology*, *38*, 79–98.

Tsai, Y. H., Park, S., Kovacic, J., & Snook, J. T. (1999). Mechanisms mediating lipoprotein responses to diets with medium-chain triglyceride and lauric acid. *Lipids*, *34*, 895–905.

Tsuji, H., Kasai, M., Takeuchi, H., Nakamura, M., Okazaki, M., & Kondo, K. (2001). Dietary medium-chain triacylglycerols suppress accumulation of body fat in a double-blind, controlled trial in healthy men and women. *Journal of Nutrition*, *131*, 2853–2859.

Van Wymelbeke, V., Louis-Sylvestre, J., & Fantino, M. (2001). Substrate oxidation and control of food intake in men after a fat-substitute meal compared with meals supplemented with an isoenergetic load of carbohydrate, long-chain triacylglycerols, or medium-chain triacylglycerols. *American Journal of Clinical Nutrition*, *74*, 620–630.

Wanten, G., van Emst-De Vries, S., Naber, T., & Willems, P. (2001). Nutritional lipid emulsions modulate cellular signaling and activation of human neutrophils. *Journal of Lipid Research*, *42*, 428–436.

Wanten, G. J., Janssen, F. P., & Naber, A. H. (2002). Saturated triglycerides and fatty acids activate neutrophils depending on carbon chain-length. *European Journal of Clinical Investigation*, *32*, 285–289.

White, M. D., Papamandjaris, A. A., & Jones, P. J. H. (1999). Enhanced postprandial energy expenditure with medium-chain fatty acid feeding is attenuated after 14 d in premenopausal women. *American Journal of Clinical Nutrition*, *69*, 883–889.

Xie, C. L., Woollett, L. A., Turley, S. D., & Dietschy, J. M. (2002). Fatty acids differentially regulate hepatic cholesteryl ester formation and incorporation into lipoproteins in the liver of the mouse. *Journal of Lipid Research*, *43*, 1508–1519.

Yost, T. J., & Eckel, R. H. (1989). Hypocaloric feeding in obese women—Metabolic effects of medium-chain triglyceride substitution. *American Journal of Clinical Nutrition*, *49*, 326–330.

Yost, T. J., Erskine, J. M., Gregg, T. S., Podlecki, D. L., Brass, E. P., & Eckel, R. H. (1994). Dietary substitution of medium-chain triglycerides in subjects with non-insulin-dependent diabetes-mellitus in an ambulatory setting—Impact on glycemic control and insulin-mediated glucose-metabolism. *Journal of the American College of Nutrition*, *13*, 615–622.

Zapolska-Downar, D., Siennicka, A., Kaczmarczyk, M., Kolodziej, B., & Naruszewicz, M. (2004). Butyrate inhibits cytokine-induced VCAM-1 and ICAM-1 expression in cultured endothelial cells: the role of NF-kappaB and PPARalpha. *Journal of Nutritional Biochemistry*, *15*, 220–228.