Consumption of a Functional Oil Rich in Phytosterols and Medium-Chain Triglyceride Oil Improves Plasma Lipid Profiles in Men[1]

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ABSTRACT Medium-chain triglycerides (MCT) have been proposed as weight-lowering agents, although there is some concern regarding their hyperlipidemic effect. This study evaluates the effects of a combination of MCT oil, phytosterols and flaxseed oil [functional oil (FctO)] on plasma lipid concentrations and LDL particle size. Twenty-four healthy overweight men (body mass index 28.2 ± 0.4 kg/m^2) consumed controlled diets designed to maintain weight for two periods of 29 d each. Diets contained 40% of energy as fat, 75% of which was added fat, either FctO or olive oil (OL). Body composition and blood samples were analyzed at the baseline and the endpoint of each period. Total cholesterol concentration decreased 12.5% (−0.68 mmol/L; $P < 0.05$) when subjects consumed FctO and 4.7% when they consumed OL. Similarly, FctO consumption lowered LDL cholesterol concentrations by 13.9%, whereas OL consumption did not. There was no difference in absolute change in LDL-cholesterol between FctO and OL consumption. Peak LDL particle size was greater in those who consumed FctO than in those who consumed OL ($P < 0.05$), with no effect of diet on proportion of large, medium or small particles. We conclude that those who consume a diet containing FctO have a better lipid profile than those who consume a diet rich in OL, which also leads to a larger lipoprotein particle size. Functional oil consumption can therefore help reduce the risk of cardiovascular disease. J. Nutr. 133: 1815–1820, 2003.

KEY WORDS: • *cholesterol* • *lipoproteins* • *low-density lipoprotein cholesterol* • *medium-chain triglycerides* • *phytosterols*

Medium-chain triglycerides (MCT)[3] have been the subject of much research for their purported effects on energy metabolism. In fact, many animal (1–4) and human trials (5–10) have shown that consumption of diets rich in MCT increases energy expenditure (EE) and fat oxidation. Animal studies have also demonstrated lower body weight gain and size of fat depots with MCT consumption compared to long-chain triglyceride (LCT) consumption. These effects of MCT on energy metabolism have prompted researchers to propose their use in the prevention or treatment of obesity.

Despite potential benefits in EE, triglycerides (TG) containing medium-chain fatty acids (MCFA) have been shown to unfavorably alter plasma lipid profiles in humans (11–13). Cater et al. (11) showed that in men consuming controlled diets rich in either MCFA (octanoate and decanoate), palm oil or sunflower oil, the diets containing palm oil and MCFA increased total cholesterol (TC) and LDL-cholesterol (LDL-C) concentrations to approximately the same extent. However, the MCFA-containing diet also increased TG concentrations to a greater extent than diets containing palm oil or sunflower oil. Swift et al. (13) also observed increased TG concentrations with MCT consumption compared to a diet containing mostly LCT. However, these investigators observed no difference in TC and LDL-C concentrations but a decrease in HDL-cholesterol (HDL-C) concentrations. After an overfeeding period with a diet containing MCT, Hill et al. (12) reported an increase in circulating TG concentrations in fasting subjects, whereas the same diet containing LCT did not result in any change in TG concentrations. These unfavorable effects of MCT consumption on blood lipid concentrations thus means that the use of MCT for the prevention of obesity is unhealthy from a cardiovascular disease risk perspective.

Therefore, to use MCT in obesity prevention strategies, a functional oil (FctO) containing a blend of vegetable oils and plant sterols, known for their hypocholesterolemic properties, was created. This FctO contains mostly MCT oil but also tall oil phytosterols and flaxseed oil. Flaxseed oil, a rich source of (n-3) fatty acids, decreases TC and LDL-C concentrations (14). Phytosterols also reduce TC and LDL-C concentrations by ~9 and 13%, respectively (15–17). We therefore hypothesized that those who consume a diet containing this FctO would have a favorable lipid profile compared to those who consume a diet containing olive oil (OL) as the main fat source. As a secondary hypothesis, the effects of FctO compared with OL consumption on LDL peak particle size and distribution of LDL particle size were evaluated.

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[3] Abbreviations used: AT, adipose tissue; CNRU, clinical nutrition research unit; EE, energy expenditure; FctO, functional oil; HDL-C, HDL-cholesterol; IMAT, intramuscular adipose tissue; LCT, long-chain triglycerides; LDL-C, LDL-cholesterol; MCFA, medium-chain fatty acids; MCT, medium-chain triglycerides, OL, olive oil; TC, total cholesterol; TG, triglycerides.

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SUBJECTS AND METHODS

Human subjects. Thirty men, aged 26 to 61 y, with TC and TG concentrations below 7.0 and 3.0 mmol/L, respectively, who had no history of diabetes, hypothyroidism, hypertension or other known metabolic disorders, and had a body mass index between 25 and 31 kg/m^2, were recruited into the study. The experimental protocol was approved by the Ethics Committee of the Faculty of Agriculture and Environmental Sciences at McGill University. All subjects were informed of the protocol and had the opportunity to discuss the procedures with the research coordinator before signing a consent form.

Protocol and diet. Subjects were randomly assigned to one of two dietary treatments for 4 wk each in a crossover design. Experimental phases were separated by a 4-wk washout period and differed only in the type of fat incorporated in the diet. (See **Table 1** for diet composition.) Both diets were designed to meet Canadian nutrient recommendations and contained 15, 40 and 45% of protein, fat and carbohydrates, respectively. Of the total dietary fat, 75% was treatment fat, either FctO or OL; the rest of the fat was provided by foods in the basal diet.

The FctO was prepared by heating MCT oil and coconut oil and dissolving tall oil phytosterols (plant sterol composition per 100 g: 64.7 g sitosterol, 10.3 g sitostanol, 6.7 g campesterol and 1.5 g campestanol; Forbes Medi-Tech, Vancouver, Canada), at a concentration of 3.4% of total weight. The concentration of phytosterols was chosen to provide ~22 mg phytosterols/kg body daily (16) when total FctO consumption was adjusted for each subject's energy intake. Subjects thus consumed a mean of 3.38 ± 0.07 g phytosterols/d. Once the phytosterols were dissolved, the oil was allowed to cool, after which olive oil and flaxseed oil were added. The oil was refrigerated at 4°C until use. The fatty acid composition of the FctO was assessed by gas chromatography and that of OL from Jones and Kubow (18) (**Table 2**).

The basal diet consisted of typical North American foods. Diets were designed to maintain weight, and energy intake was calculated on the basis of height, weight and age by use of the Mifflin equation (19) and adjusting for activity level by multiplying by a factor of 1.7. Three isoenergetic meals were provided daily by the staff of the Mary Emily Clinical Nutrition Research Unit (CNRU) of McGill University, two of which were consumed under supervision at the CNRU. Subjects consumed the same amount of energy during both treatment phases.

Body composition and energy expenditure were measured at the baseline and the endpoint of each treatment phase. Whole body magnetic resonance images were acquired at 4-cm intervals using 1-cm slice thickness. The scanner (Siemens, Mississauga, Canada) was landmarked at the L4–L5 vertebrae and at the femoral and humoral heads, allowing for determination of regional body composition. Energy expenditure was assessed by use of indirect calorimetry. A description of the procedures and data obtained for body composition and energy expenditure measurements are described elsewhere (20).

Lipoprotein lipid analyses. Blood samples were collected before breakfast on d 1, 28 and 29 of each experimental phase after a 12-h fast. Samples were immediately centrifuged for 20 min at 250 × *g* and plasma and red blood cells were separated before storing samples at −80°C. Plasma TC, HDL-C and TG concentrations were analyzed using a VP Autoanalyzer and corresponding standards, reagents and enzymatic kits (Abbott Laboratories, Chicago, IL). LDL-cholesterol concentrations were calculated by use of the formula from Friedewald et al. (21).

Determination of LDL peak particle density. Nondenaturing 2–16% polyacrylamide gradient gel electrophoresis was performed on whole plasma as described by St-Pierre et al. (22). Briefly, gels were prepared in batches in our laboratory. Plasma samples (3.5 μL) were mixed with a sampling buffer containing 20% sucrose and 0.25% bromophenol blue in a 1:1 (v/v) ratio. Electrophoresis was performed, after a 15 min prerun, at 150 V for 3 h. Gels were stained for 1 h with Sudan black (0.07%) and stored in a 0.81% acetic acid/4% methanol solution until analysis. The Imagemaster 1-D Prime computer software (Amersham Pharmacia Biotech, Piscataway, NJ) was used to analyze the gels. A mean LDL particle diameter was also computed using the approach described by Tchernof et al. (23). Briefly, the mean LDL particle size was calculated by integrating the relative contribution of each LDL particle subclass within a sample and corresponded to the weighted mean of all LDL subclasses. This integrated LDL particle size was calculated as the sum of LDL subspecies' diameter multiplied by its relative proportion. Identification of the major LDL peak showed a CV of <2% between assays (22). Baseline samples from two subjects were lost during processing of LDL particle size determination and thus changes in concentrations are reported for 22 subjects, whereas endpoint comparisons were done for 24 subjects.

Statistical analyses. Baseline values were calculated as the mean of screening value on d 1 for each lipid variable. Endpoint values were calculated as the mean concentration of each given variable on d 28 and 29. Samples from d 1 and d 27 were used to analyze LDL particle size. Mixed-model ANOVA for crossover designs was used to test treatment differences in plasma lipid concentrations and LDL particle characteristics while controlling for initial lipid concentration and change in body weight (SAS/STAT version 8, SAS Institute, Cary, NC). Simple correlations were conducted to assess relationships between changes in body composition and changes in blood lipid variables. Correlations were done on pooled data from the two experimental phases. Upper body adipose tissue (AT) was taken as total AT from images at and above the L4–L5 vertebrae and intramuscular AT (IMAT) consisted of all visible AT around and within muscle fibers but under the muscle fascia. All results are reported as means ± SEM. Significance was set at $P < 0.05$.

TABLE 1

Macronutrient composition of the functional oil (FctO) and olive oil (OL) diets

Nutrient	FctO	OL
	% of energy	
Protein	15	15
Carbohydrate	45	45
Fat	40	40
MCT oil	19.5	0
Coconut oil	1.8	0
Canola oil	2.1	0
Olive oil	3.9	30
Flaxseed oil	2.1	0

TABLE 2

Fatty acid composition of the functional oil (FctO) and olive oil (OL)

Fatty acid	FctO	OL[1]
	g/100 g	
6:0	0.17	0
8:0	36.95	0
10:0	30.35	0
12:0	3.61	0
14:0	1.06	0
16:0	3.52	14
16:1	0.23	0
18:0	0.65	3
18:1	13.81	71
18:2(n-6)	4.62	10
18:3(n-3)	4.94	Tr
20:0	0.05	0

[1] From Jones and Kubow (18). Tr, not detectable.

RESULTS

Twenty-four subjects successfully completed the research trial. Two subjects withdrew from the trial after the first phase

for work ($n = 1$) and health ($n = 1$) related reasons not pertaining to treatments and three were asked to withdraw from the study for observed noncompliance with the research protocol. Data from one subject were not analyzed because of difficulties with the acquisition of images during the last magnetic resonance imaging scan. All subjects consumed at least two meals per day under supervision at the CNRU. For all meals eaten at home, foods were reported to have been entirely consumed. We thus considered compliance with the study protocol to be acceptable. Body weights decreased by 1.03 ± 0.25 kg in subjects who consumed FctO and 0.62 ± 0.29 kg in subjects who consumed OL.

In subjects who consumed the FetO diet there was a decrease in TC of 0.68 ± 0.17 mmol/L compared to 0.25 ± 0.17 mmol/L in those who consumed the OL diet (**Table 3**). There was a significant effect of diet on TC ($P < 0.05$). Endpoint values for TC were lower (CI 4.30 to 5.11 mmol/L, $P < 0.05$) after 28 d in those who consumed a diet containing FctO compared with those who consumed a diet rich in OL (CI 4.58 to 5.46 mmol/L).

Functional oil consumption caused a decrease of 0.48 ± 0.19 mmol/L (CI −0.85 to −0.10 mmol/L) in LDL-C concentrations, whereas OL consumption resulted in a decrease of 0.15 ± 0.15 mmol/L (CI −0.30 to 0.15 mmol/L). LDL-cholesterol concentrations were not significantly affected by diet after controlling for initial concentration and change in body weight (Table 3); however, LDL-C levels were affected by diet when the baseline value and change in body weight were not taken into consideration.

In subjects who consumed FctO there was no change in TG concentrations compared with subjects who consumed OL. Endpoint TG values did not differ in FctO and OL consumption periods. Endpoint HDL-C concentrations after each dietary period were similar (Table 3).

Baseline data did not differ between dietary phases for any of the LDL particle characteristics. Peak LDL particle size and integrated size were greater ($P < 0.05$) in subjects who consumed FctO than in those who consumed OL (**Table 4**). The proportion of large, medium and small LDL particles was not affected by diet, but there was a significant ($P < 0.05$) effect of diet on LDL-C content of medium and small LDL particles.

Correlation analyses showed that the change in upper body AT was positively correlated with the change in TC ($r = 0.383$, $P < 0.01$) and LDL-C ($r = 0.369$, $P < 0.01$) concentrations (**Fig. 1**), but not with changes in TG and HDL-C concentrations, or LDL particle size. Intramuscular AT was also positively correlated with changes in TC ($r = 0.334$, $P < 0.05$) and LDL-C ($r = 0.306$, $P < 0.05$) concentrations (**Fig. 2**). As was observed with the change in upper body AT, there was no correlation between change in IMAT and change in TG and HDL-C concentrations, nor with changes in LDL particle size.

TABLE 3

Plasma lipid concentrations with consumption of diets rich in functional oil (FctO) or olive oil (OL) for 28 d in men[1,2]

Diet	TC	HDL-C	LDL-C	TG
		mmol/L		
FctO				
Baseline	5.38 ± 0.17	1.12 ± 0.06	3.43 ± 0.18	1.81 ± 0.16
Endpoint	4.71 ± 0.21	1.01 ± 0.05	2.96 ± 0.20	1.61 ± 0.15
Change	−0.68 ± 0.17	−0.11 ± 0.05	−0.48 ± 0.19	−0.20 ± 0.14
OL				
Baseline	5.27 ± 0.23	1.05 ± 0.06	3.41 ± 0.20	1.77 ± 0.15
Endpoint	5.02 ± 0.23	1.00 ± 0.06	3.26 ± 0.23	1.67 ± 0.20
Change	−0.25 ± 0.17	−0.05 ± 0.04	−0.15 ± 0.15	−0.10 ± 0.08

[1] Values are means ± SEM, $n = 24$. There was a significant effect of diet on total cholesterol (TC) after controlling for initial TC concentration and change in body weight, $P < 0.05$.

[2] TC, total cholesterol; HDL-C, HDL-cholesterol; LDL-C, LDL-cholesterol; TG, triglycerides.

TABLE 4

LDL size and distribution after consumption of functional oil (FctO) and olive oil (OL) for 28 d in men[1]

LDL characteristics	FctO	OL
LDL peak particle size, *nm*	25.85 ± 0.08	25.77 ± 0.08
LDL integrated (mean) size, *nm*	25.69 ± 0.09	25.45 ± 0.11
Relative proportions of LDL, %		
<25.5, *nm*	42.8 ± 3.1	41.3 ± 3.1
25.5–26.0, *nm*	20.7 ± 0.9	21.1 ± 1.4
>26.0, *nm*	36.4 ± 3.5	37.5 ± 4.0
LDL-C, *mmol/L*	2.96 ± 0.20	3.26 ± 0.23
<25.5, *nm*	1.22 ± 0.11	1.32 ± 0.12
25.5–26.0, *nm*	0.61 ± 0.05	0.70 ± 0.07
>26.0, *nm*	1.13 ± 0.14	1.24 ± 0.16

[1] Values are means ± SEM. There was a significant effect of diet on peak and integrated size of LDL particles and LDL-C concentration of medium (25.5–26.0 nm) and small (<25.5 nm) LDL particles after controlling for initial values and change in body weight, $P < 0.05$.

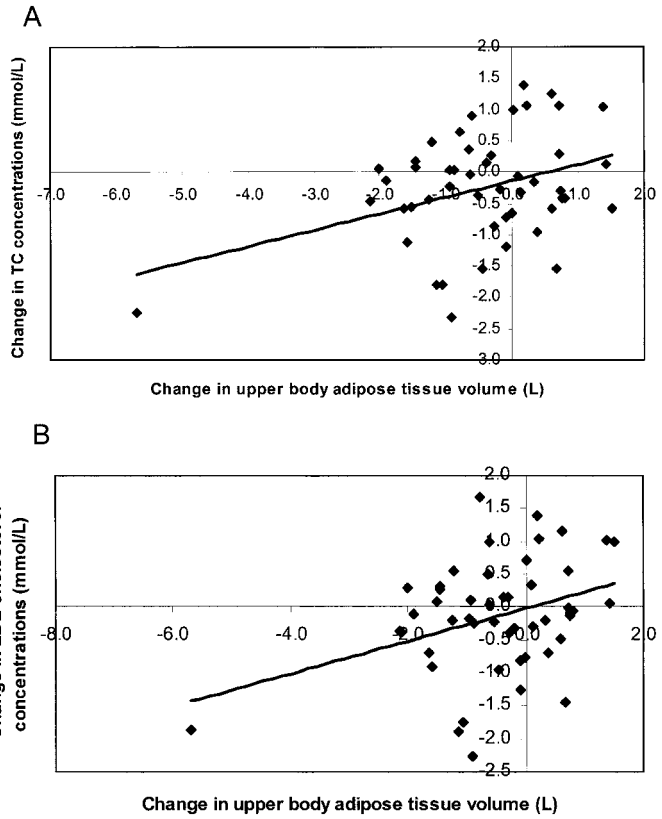

FIGURE 1 Correlation between change in upper body adipose tissue and total cholesterol (TC) (*A*) and LDL-cholesterol (*B*) concentrations in men. Correlations were done by use of pooled data from the two experimental phases.

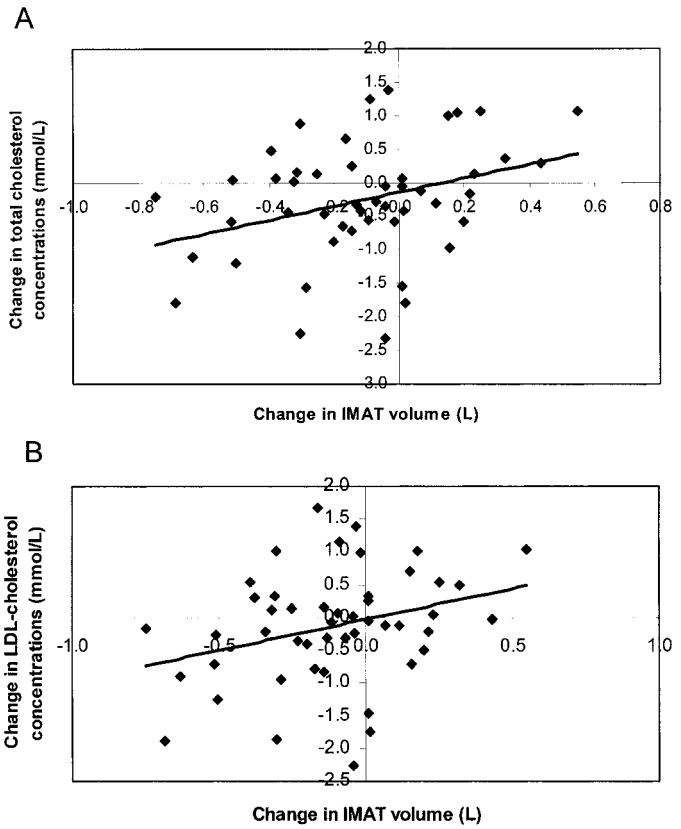

FIGURE 2 Correlation between change in intramuscular adipose tissue (IMAT) and total cholesterol (*A*) and LDL-cholesterol (*B*) concentrations in men. Correlations were done by use of pooled data from the two experimental phases.

DISCUSSION

This study shows for the first time that consumption of a combination of MCT oil, phytosterols and flaxseed oil creates a more beneficial lipid profile and favorably alters LDL particle size compared with consumption of OL in mildly hypercholesterolemic men using a randomized crossover design with strictly controlled diets. In addition, only one study to date has examined diets supplemented with phytosterols on LDL particle size (24) and only one trial has looked at dietary fatty acid composition in relation to LDL particle size (25). We showed that, compared with consumption of OL, which has been proposed to improve circulatory lipid patterns (26), consumption of FctO caused lower endpoint TC and LDL-C concentrations and led to greater LDL particle size. Therefore, FctO may be considered a healthy alternative to other dietary fats. Furthermore, this study is the first to establish a link between change in IMAT and change in TC and LDL-C concentrations.

The finding that changes in IMAT are correlated with changes in TC and LDL-C concentrations is highly novel. The few trials that have focused on the metabolic effects of IMAT have examined its relationship with insulin sensitivity (27–30). No previous trial has examined the relationship between IMAT and lipid concentrations. Nevertheless, the trials that have been conducted to date demonstrate that IMAT is a metabolically active depot. Furthermore, IMAT increases in obesity and responds to weight loss (28). Results obtained in this trial show that reductions in IMAT are associated with positive changes in plasma TC and LDL-C concentrations.

Plant sterols were important ingredients of the blended FctO. Decreases in TC and LDL-C concentrations in this study are in agreement with data from other studies that examined the effects of phytosterols on blood lipid concentrations (15–17). In a controlled feeding experiment in which subjects consumed 1.8 g tall oil phytosterols/d, phytosterols caused a decrease in TC and LDL-C concentrations of 19.5 and 24.4%, respectively, compared to 10.4 and 8.9%, respectively, for the control diet not containing phytosterols (16). In other controlled feeding studies, overall decreases in TC were 4.9–6.8% (15) and 7.4% (17). These results are similar to those obtained in the present study, in which TC and LDL-C concentrations were decreased by 12.6 and 13.9%, respectively, in subjects who consumed the phytosterol-containing diet FctO. Therefore, it can be assumed that the dose of phytosterols given in this trial, ~3.4 g/d, was appropriate and effective in optimizing changes in TC and LDL-C concentrations and was most likely the major factor responsible for the observed changes in TC and LDL-C concentrations. However, because body weight change weakened the effect of diet on TC and LDL-C concentrations, the effect of diet on body weight as another likely factor mediating changes in plasma lipid concentrations cannot be excluded.

In this study, consumption of FctO did not cause any change in TG concentrations. This agrees with results in previous research examining the effects of plant sterols on plasma lipid concentrations (15–17). However, the intake of MCT was expected to increase TG concentrations as was previously observed in humans (11–13), although in a hamster model, octanoate had similar effects as *cis-* and *trans-*oleate consumption on TG levels (35). However, in human studies, MCT consumption levels were higher than those in the present study. Effects of MCT consumption on TG may depend on the absolute amount ingested or, as in our study, may have been offset by the presence of other sources of fat. Although flaxseed oil was added to the MCT diet in an attempt to diminish TG concentrations, previous studies have also shown the lack of effect of flaxseed (n-3) fatty acids in decreasing TG concentrations (36–38). Conversely, others have found that providing large amounts of flaxseed oil (39) or flaxseed oil in combination with a low saturated fat diet (40) produced a decrease in TG concentrations. When Pedersen et al. (41) compared diets that differed in fat type, it was found that the diet resulting in the most favorable lipid profile was the rapeseed oil diet, which contained 6% of total fat as α-linolenic acid. Our FctO diet contained ~5% of total fat as flaxseed oil and ~3.7% of α-linolenic acid, a level of α-linolenic acid similar to that recommended by de Deckere et al. (42) to decrease coronary heart disease risk.

Another novel aspect of this study is the analysis of LDL particle characteristics. It has been shown that small, dense LDL are associated with increased risk of coronary heart disease (21,43–45), yet few intervention studies have examined the role of lipid-lowering dietary agents on LDL particle size. In this study, the FctO diet increased LDL particle size. A recent trial (25) reported that unsaturated fats lower LDL peak particle size relative to saturated fatty acids. It is therefore possible that the high saturated fatty acid content of the FctO caused the beneficial change in LDL peak particle size. Phytosterol consumption has recently been shown not to affect LDL particle size compared to placebo (24). It is thus unlikely that phytosterols contained in the FctO diet had any impact on LDL particle size because phytosterols do not affect

TG or HDL-C concentrations (15–17). Plasma TG concentrations are positively associated with small dense LDL particles, whereas plasma HDL-C concentrations have been shown to be negatively correlated with the small dense LDL phenotype (23).

Finally, although our study does not allow precise determination of the effects of specific fat-soluble constituents included in FctO on individual plasma lipid concentrations, it does demonstrate that this combination of oils and plant sterols is healthy from a cardiovascular perspective. Therefore, given the recent interest in the use of MCT as agents that upregulate energy expenditure and fat oxidation (5–10), the inclusion of FctO in a typical North American diet in place of oils containing LCT might be expected to produce favorable health effects through actions directed to energy balance and weight control. In conclusion, the present study demonstrates that an MCT-containing oil blend possesses substantial potential to reduce cardiovascular disease risk through its beneficial actions in modulation of lipid concentrations.

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