Chylomicron β-Carotene and Retinyl Palmitate Responses Are Dramatically Diminished When Men Ingest β-Carotene with Medium-Chain Rather than Long-Chain Triglycerides[1,2]

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ABSTRACT The effect of the ingestion of β-carotene with medium-chain triglycerides (MCT) or long-chain triglycerides (LCT) on the bioavailability and the provitamin A activity of β-carotene was investigated in humans. Sixteen healthy young men ingested, on two different days, a test meal containing 120 mg β-carotene incorporated into 40 g LCT (LCT meal) or 40 g MCT (MCT meal). This meal was followed 6 h later by a β-carotene–free meal containing 40 g LCT. Chylomicron β-carotene, retinyl palmitate and triglycerides were measured every hour for 12.5 h after the first meal. No significant increase in chylomicron triglycerides was detected for the 6 h after the MCT meal intake, whereas a significant increase in chylomicron triglycerides was observed after the LCT meal intake. The chylomicron β-carotene and retinyl palmitate responses to the MCT meal (0–6 h area under the curves, AUC) were significantly ($P < 0.05$) lower [AUC = 68.1 ± 26.8 and 43.4 ± 10.4 nmol/(L·h), for β-carotene and retinyl palmitate, respectively] than those obtained after the LCT meal [301.4 ± 64.0 and 166.0 ± 29.0 nmol/(L·h), respectively]. The chylomicron β-carotene and retinyl palmitate responses obtained after the β-carotene–free meal (6–12.5 h AUC) were also significantly lower when the first meal provided MCT rather than LCT. The chylomicron (retinyl palmitate/β-carotene) ratios were constant during the postprandial periods, whatever the meal ingested. We conclude that the chylomicron β-carotene response is markedly diminished when β-carotene is absorbed with MCT instead of LCT. This phenomenon is apparently due to the lack of secretion of chylomicrons in response to MCT; however, a lower intestinal absorption of β-carotene or a higher transport of β-carotene via the portal way in the presence of MCT cannot be ruled out. Finally, the data obtained show that MCT do not affect the rate of intestinal conversion of β-carotene into vitamin A. J. Nutr. 128: 1361–1367, 1998.

KEY WORDS: • *β-carotene bioavailability* • *β-carotene provitamin A activity* • *retinyl palmitate* • *humans*

β-Carotene is one of the most abundant carotenoids present in the human diet. This fat-soluble micronutrient has been studied extensively because of its provitamin A activity and its potential beneficial effect on health (Gey et al. 1993, Riemersma 1994, Ziegler 1989).

The intestinal absorption of β-carotene is not very efficient in humans, ranging between 1 and 50% (Blomstrand and Werner 1967, Goodman et al. 1966, Novotny et al. 1995, Van Vliet et al. 1995). Absorption depends on several dietary and nondietary factors, including the level and origin of dietary fat, the amount of carotenoids, the digestibility of food, the presence of antioxidants or fibers, as well as the vitamin A status (Erdman et al. 1993). Consistent results obtained in animal models and in humans suggest that dietary fat is a key factor in β-carotene absorption. For example, rats fed a low fat diet do not absorb β-carotene efficiently, whereas they do so when the diet contains 10% fat (Bauernfeind et al. 1981). In humans, the role of fat in β-carotene bioavailability was demonstrated by the fact that vitamin A deficiency can be caused by a low fat intake (Roels et al. 1958). Jayarajan et al. (1980) further clarified this result by showing that, in children, an intake of ≥5 g fat/d was required for optimal absorption of β-carotene from green leafy vegetables. The effect of the nature of the dietary fat in β-carotene bioavailability is less clear and studies on this topic have been performed in animal models only. More precisely, butter was found to be a better vehicle for promoting β-carotene absorption than cottonseed oil (Bauernfeind et al. 1981). β-Carotene bioavailability from raw carrots was found to be highest when low molecular weight fatty acids were given and decreased as the chain length of the fatty acid increased (Bauernfeind et al. 1981). These studies suggested that β-carotene bioavailability is better when given with low molecular weight fatty acids than with high molecular weight fatty acids. Nevertheless, a study with isolated rat intestinal segments showed that β-carotene absorption was similar in the presence of medium-chain saturated fatty acids or long-chain polyunsaturated fatty acids (Hollander and Ruble 1978).

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TABLE 1

Subject characteristics[1]

Age, *y*	23.0 ± 0.9
Body mass index, *kg/m*[2]	23.3 ± 0.7
Lean mass[2], *kg*	63.5 ± 2.2
Fat mass[2], *kg*	13.6 ± 2.2
Triglycerides, *mmol/L*	1.20 ± 0.09
Phospholipids, *mmol/L*	2.89 ± 0.13
Cholesterol, *mmol/L*	4.82 ± 0.24
Apoprotein AI, *g/L*	1.16 ± 0.06
Apoprotein B, *g/L*	0.86 ± 0.06
Dietary habits[3]	
Energy, *MJ/d*	11.5 ± 0.6
Protein, *% energy*	14.6 ± 0.7
Fat, *% energy*	36.9 ± 1.1
Carbohydrates, *% energy*	46.3 ± 1.8
Alcohol, *% energy*	2.2 ± 0.9

[1] Values are means ± SEM, $n = 16$.
[2] Lean and fat masses of the subjects were estimated by bioelectric impedance measurements.
[3] Dietary habits were estimated with a 3-d food recall, which was completed in the month before the experiment.

Overall, these data are too contradictory and insufficient to allow conclusions to be drawn concerning the effect of medium-chain triglycerides (MCT)[4] on β-carotene bioavailability in humans. Although MCT are far less abundant than long-chain triglycerides (LCT) in the normal human diet, they are commonly incorporated into enteral feeding emulsions. Thus their effect on β-carotene bioavailability should be investigated especially because it is assumed that their processing is different from that of LCT. Indeed, hydrolysis of MCT to free fatty acids in the gut is more rapid and more efficient than that of LCT (Isselbacher 1968), and the products of MCT hydrolysis are very rapidly absorbed. In addition, only a small proportion (Swift et al. 1990) of medium-chain fatty acids (C8:0–C10:0) is incorporated into chylomicrons; most leave the enterocyte via the portal circulation (Bloom et al. 1951, Isselbacher 1968). Conversely, long-chain fatty acids (C12:0–C18:0) are incorporated into triglycerides, packed with chylomicrons and transported via the lymphatic circulation. Because β-carotene has to be incorporated into the chylomicrons to be secreted in the lymph, it can be hypothesized that MCT affect normal β-carotene metabolism. The aim of this study was therefore to compare the effect of MCT and LCT on the bioavailability and provitamin A activity of β-carotene in humans.

SUBJECTS AND METHODS

Subjects. Sixteen young male volunteers were recruited for this study. Informed written consent was obtained and the study was approved by the local medical ethic committee of the regional university hospital complex from Clermont-Ferrand (France). The subjects were apparently healthy, according to clinical examination and disease history, and had no symptoms of fat malabsorption. Their lean and fat masses were estimated by bioelectric impedance measurements using a BIA 101A instrument (RJL Systems, Mt. Clemens, MI). Fasting plasma lipids, apoprotein A1 and apoprotein B were measured to assess the normality of the subjects' lipid metabolism. The subjects had not taken vitamin supplements for ≥3 mo before the experiment. Their usual diets were monitored by a 3-d food recall, which was completed during the month before the experiment. This diary was analyzed for nutrient composition by using diet analyzer software (GENI, Micro 6, Nancy, France). All measured variables are listed in **Table 1**.

Experimental design. The subjects ingested two successive test meals in two separate experiments with a minimum interval of 2 wk. A second meal containing LCT, but no β-carotene was consumed, 6 h after the first meal to permit the secretion into the lymph of β-carotene that could have been absorbed in the enterocyte, but not secreted into the lymph and then into the blood, during the first postprandial period. Indeed, we have recently found that a large fraction of β-carotene can be secreted in the postprandial period after the meal subsequent to a first meal containing a pharmacologic dose of β-carotene (unpublished data). After a 12-h overnight fast, at ~0700 h, an antecubital vein was catheterized with an intravenous cannula equipped with disposable obturators (Becton Dickinson, Meylan, France). A baseline fasting blood sample was collected and the subjects ingested the first test meal within 20 min. Blood samples (10–15 mL) were collected every hour for 6 h. The subjects ingested the second meal and blood samples were collected for 6 h. Triglycerides, β-carotene and retinyl palmitate were measured in chylomicron fractions prepared from all of the blood samples collected.

The composition of the first meal was as follows: bread (40 g), wheat semolina (60 g cooked and hydrated with 120 mL water), cooked egg whites (35 g), nonfat yogurt (125 g), 300 mL water and an oil-in-water emulsion (about 100 mL). This emulsion, prepared by Inocosm (Chatenay-Malabry, France), contained 40 g triglycerides, into which 120 mg of all-*trans* β-carotene in the form of a β-carotene 30% fluid suspension (Hoffmann-La Roche, Basel, Switzerland) had been mixed, 1 g emulsifiers (egg lecithins and plant ceramides) and 60 mL water. Triglycerides were LCT (LCT meal) or MCT (MCT meal), purchased from Société Industrielle des Oléagineux (St-Laurent-Blangy, France). The triglyceride composition of the oils is given in **Table 2**.

The second meal was the same as the first except that it did not contain β-carotene and was composed only of LCT. The meals were ingested within 20 min. Time 0 of each experiment was set halfway through the first meal.

Chylomicron preparation. Blood was collected in EDTA vacutainers and plasma was prepared immediately by centrifugation (910 × g, 4°C, 10 min). The Svedberg flotation unit (Sf) > 1000 fraction, containing mainly chylomicrons plus large chylomicron remnants, was isolated on the day of the experiment from 2 mL plasma layered under 3 mL of 9 g/L NaCl by ultracentrifugation at 10°C (24,000 × g for 1 h) in a Beckman (Palo Alto, CA) 40.3 rotor (Borel et al.

TABLE 2

Fatty acid composition of test-meal triglycerides[1]

Fatty acid	Medium-chain triglycerides	Long-chain triglycerides
	g/100 g fatty acids	
6:0	0.28	—
8:0	59.94	—
10:0	38.70	—
12:0	0.81	—
14:0	0.13	0.05
16:0	0.14	6.75
16:1	—	0.10
18:0	—	4.10
18:1	—	21.65
18:2	—	66.25
18:3	—	0.30
20:0	—	0.25
20:1	—	0.15
22:0	—	0.40

[1] Triglycerides were purchased from Société Industrielle des Oléagineux (SIO), Saint-Laurent-Blangy, France. Their fatty acid composition was measured by gas chromatography by SIO; —, not detected (<0.05%).

[4] Abbrevations used: AUC, area under the curve; LCT, long-chain triglycerides; MCT, medium-chain triglycerides.

1997, Dubois et al. 1994, Weintraub et al. 1987). Chylomicrons were stored at −80°C (Craft et al. 1988) until analysis.

Analytical determinations. Triglycerides (Buccolo and David 1973), cholesterol (Siedel et al. 1983) and phospholipids (Takayama et al. 1977) were determined by enzymatic procedures with commercial kits (Boehringer, Mannheim, Germany). Apoprotein A1 (Sievet-Desrumeaux et al. 1980) and apoprotein B (Sievet-Desrumeaux et al. 1979) were assayed by laser nephelometry (Behring Werke A. G., Marburg, Germany).

β-Carotene was extracted twice with ethanol and hexane and quantified by reverse-phase HPLC in a Kontron (Zurich, Switzerland) apparatus with detection at 450 nm. The column was a Zorbax (250 × 40 mm, 5 μm) purchased from Interchim (Montluçon, France); the mobile phase was a mixture of acetonitrile/dichloromethane/methanol (70:20:10, v/v/v). Echinenone and all-*trans* β-carotene (Hoffmann-La Roche) were used as internal and external standards, respectively. Quantifications were conducted with Kontron MT2 software.

Retinyl palmitate was extracted as described for β-carotene. It was quantified by reverse-phase HPLC with detection at 325 nm. The column was a C18-nucleosil (250 × 4.6 mm, 5 μm) purchased from Touzart et Matignon (Paris, France), and the mobile phase was 100% methanol. Pure retinyl palmitate (Hoffmann-La Roche) was used as the external standard. Retinyl laurate, which had been synthesized according to Azaïs-Braesco et al. (1992), was used as the internal standard.

Statistical analysis. Results are expressed as means ± SEM, $n = 16$. Areas under the curves (AUC) were calculated by the trapezoidal rule. Two-factor ANOVA (meal by time) was used to analyze curves showing patterns of change over time within each experiment. When a time effect was observed with the two-factor ANOVA, the significance ($P < 0.05$) of the differences between the postprandial values and the corresponding fasting values was assessed by using one-way ANOVA for paired values with time as the factor (Winner 1971). When a significant (<0.05) *P*-value was obtained, differences were assessed by the Fisher PLSD (protected least significant difference) test. When a meal effect was observed by the two-factor ANOVA, the significance ($P < 0.05$) of the differences found between the chylomicron responses (AUC) measured after each meal was assessed by using the Student's *t* test for paired values (Winner 1971). These statistical comparisons were performed with the StatView SE+Graphics software Version 1.03 (Abacus, Berkeley, CA).

RESULTS

Chylomicron triglyceride responses. In the first experiment (two successive LCT meals, **Fig. 1***A, B*), the chylomicron triglyceride responses (AUC) obtained after consumption of each meal (0–6 h AUC and 6–12.5 h AUC) were similar, i.e., 1.2 ± 0.2 and 1.4 ± 0.2 mmol/(L·h). In the second experiment (a MCT meal followed by a LCT meal, Fig. 1C, *D*), there was no significant increase in plasma chylomicron triglycerides after consumption of the MCT meal, whereas there was a significant increase in chylomicron triglycerides after consumption of the LCT meal. Note that the chylomicron triglyceride response obtained after the second meal (6–12.5 h AUC) was significantly higher [1.9 ± 0.2 mmol/(L·h)] in the second experiment, i.e., after ingestion of MCT in the first meal (Fig. 1C, *D*), than in the first experiment [1.4 ± 0.2 mmol/(L·h)], i.e., after ingestion of LCT in the first meal (Fig. 1*A, B*).

Chylomicron β-carotene responses. There was a significant increase in the plasma chylomicron β-carotene concentration in the postprandial period after consumption of the β-carotene–rich LCT-meal (0–6 h) (**Fig. 2***A, B*). This concentration reached a peak 3 h after β-carotene intake and then decreased slightly for 2 h. After consumption of the second meal (a LCT meal without β-carotene), the chylomicron β-carotene concentration increased again, reaching a peak after 7.5 h, and then decreased for 5 h. The chylomicron β-carotene

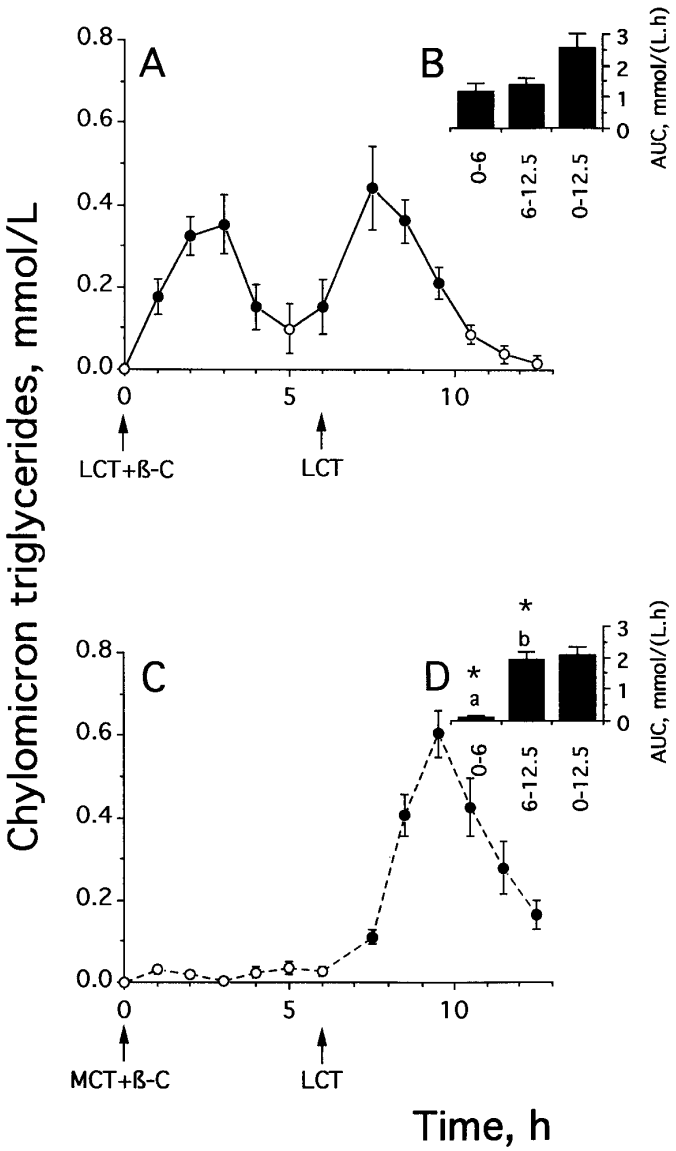

FIGURE 1 Plasma chylomicron triglyceride responses in 16 healthy young men, measured after the intake of two successive meals on two different days. In the first experiment (*A*, *B*), the first meal provided 120 mg β-carotene (β-C) dissolved in 40 g long-chain triglycerides (LCT), and the second meal 40 g LCT without β-carotene. In the second experiment (*C*, *D*) the first meal provided 120 mg β-carotene dissolved in 40 g medium-chain triglycerides (MCT) and the second meal 40 g LCT without β-carotene. The arrows indicate the times at which the meals were ingested. Points represent the means ± SEM, $n = 16$. *Inserts*: area under the curves (AUC) of the response obtained after the first meal (0–6 h), the second meal (6–12.5 h) and after both meals (0–12.5 h). Two-factor ANOVA gave a meal effect of $P = 0.0013$, a time effect of $P = 0.0001$ and a meal × time interaction of $P = 0.0001$. A filled symbol indicates that the value is significantly different from the fasting (0 h) value ($P < 0.05$, one-way ANOVA for paired values). Different letters indicate that the 0–6 h AUC and the 6–12.5 h AUC of the same experiment were significantly different ($P < 0.05$, Student's *t* test for paired values). Asterisks indicate that corresponding AUC were significantly different between Experiments 1 and 2 ($P < 0.05$, Student's *t* test for paired values).

response obtained after the second LCT meal was significantly higher than that observed after the first LCT meal. In the second experiment (Fig. 2C, *D*), the response to the first meal accounted for 22.6% of the corresponding response obtained

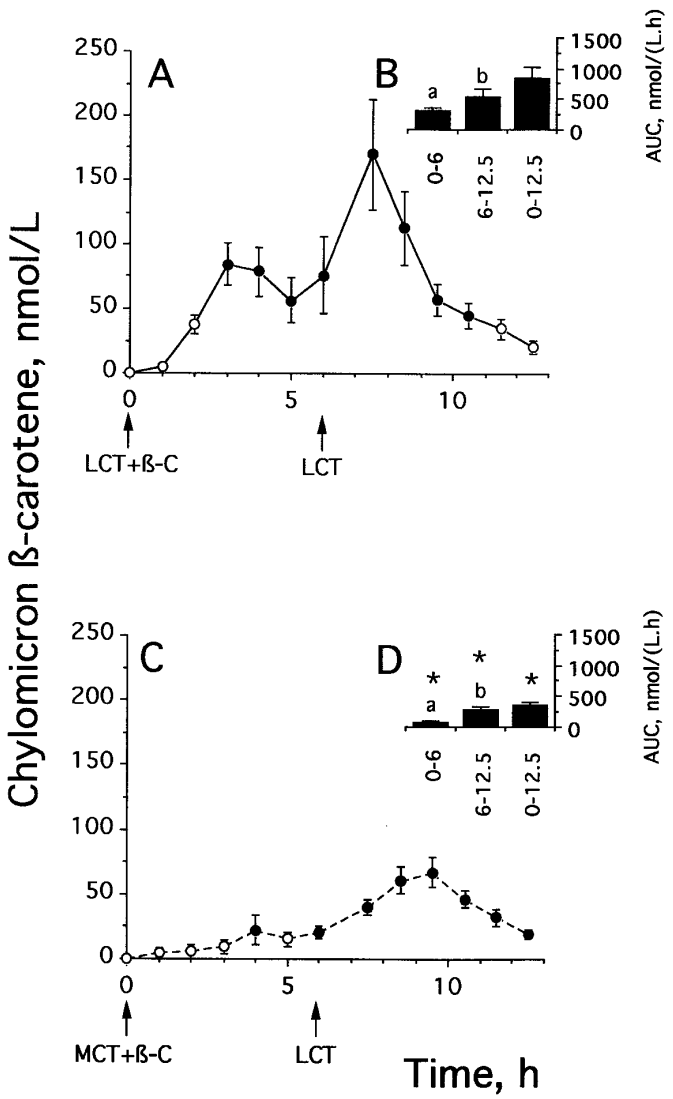

FIGURE 2 Plasma chylomicron β-carotene (β-C) responses in 16 healthy young men, measured after the intake of two successive meals on two different days. In the first experiment (*A*, *B*), the first meal provided 120 mg β-carotene dissolved in 40 g long-chain triglycerides (LCT) and the second meal 40 g LCT without β-carotene. In the second experiment (*C*, *D*) the first meal provided 120 mg β-carotene dissolved in 40 g medium-chain triglycerides (MCT) and the second meal 40 g LCT without β-carotene. Points represent the means ± SEM, n = 16. Two-factor ANOVA gave a meal effect of P = 0.0073, a time effect of P = 0.0001 and a meal × time interaction of P = 0.0006. For details see the legend of Figure 1.

in the first experiment, and the response to the second meal accounted for 53.2% of that obtained in the first experiment (Fig. 2*A*, *B*). Consequently, when β-carotene was provided with MCT, the overall chylomicron β-carotene response (0–12.5 h AUC) accounted for 42.1% ($P < 0.05$) of the response obtained when it was provided with LCT.

Chylomicron retinyl palmitate responses. The chylomicron retinyl palmitate responses to the two successive meals were similar to those observed for chylomicron β-carotene responses (**Fig. 3**). The chylomicron retinyl palmitate concentration increased after ingestion of β-carotene as the only source of vitamin A, but the ingestion of β-carotene with MCT led to a significantly lower chylomicron retinyl palmitate response (0–12.5 h AUC) than with LCT.

Chylomicron retinyl palmitate/β-carotene ratios. The ratios of chylomicron retinyl palmitate to chylomicron β-carotene were calculated for each time point and for each subject throughout the postprandial period. There were no time or meal effects on this ratio, which ranged between 0.2 and 1 (**Fig. 4**).

DISCUSSION

We decided to assess the effect of MCT on β-carotene bioavailability and provitamin A activity by measuring the appearance of β-carotene and retinyl palmitate in the chylomicron fraction. Indeed, this noninvasive methodology makes it possible to compare β-carotene intestinal absorption and can give valuable information on the efficiency of β-carotene con-

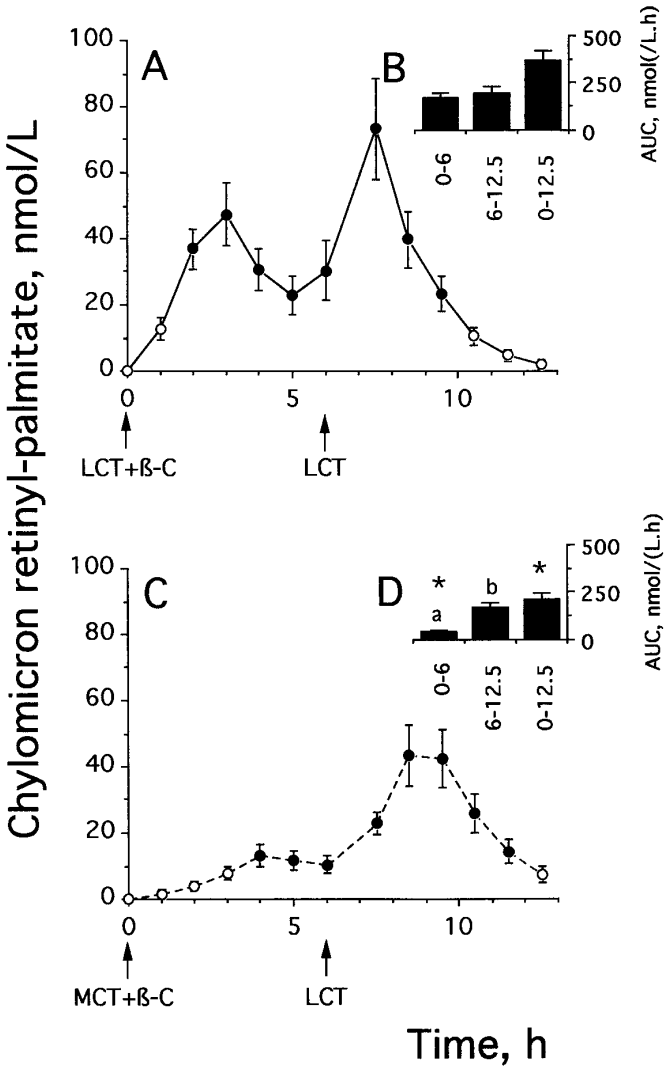

FIGURE 3 Plasma chylomicron retinyl palmitate responses in 16 healthy young men, measured after the intake of two successive meals on two different days. In the first experiment (*A*, *B*), the first meal provided 120 mg β-carotene (β-C) dissolved in 40 g long-chain triglycerides (LCT) and the second meal 40 g LCT without β-carotene. In the second experiment (*C*, *D*) the first meal provided 120 mg β-carotene dissolved in 40 g medium-chain triglycerides (MCT) and the second meal 40 g LCT without β-carotene. Points represent the means ± SEM, n = 16. Two-factor ANOVA gave a meal effect of P = 0.0004, a time effect of P = 0.0001 and a meal × time interaction of P = 0.0001. For details see the legend of Figure 1.

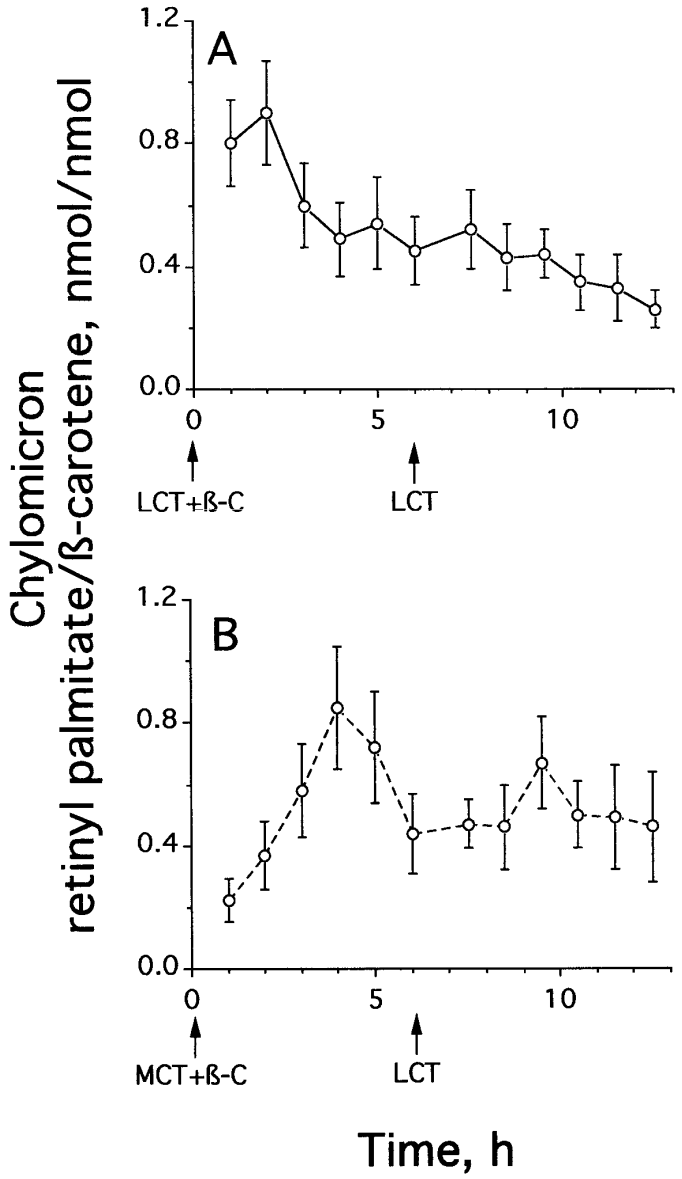

FIGURE 4 Retinyl palmitate/β-carotene (β-C) ratios in 16 healthy young men, measured in the plasma chylomicrons collected after the intake of two successive meals on two different days. In the first experiment (*A*), the first meal provided 120 mg β-carotene dissolved in 40 g long-chain triglycerides (LCT) and the second meal 40 g LCT without β-carotene. In the second experiment (*B*), the first meal provided 120 mg β-carotene dissolved in 40 g medium-chain triglycerides (MCT) and the second meal 40 g LCT without β-carotene. Points represent the means ± SEM, $n = 16$. Two-factor ANOVA revealed no significant effect of time or meal on the chylomicron retinyl palmitate/β-carotene response. For details see the legend of Figure 1.

version into vitamin A at the intestinal level (Van Vliet et al. 1995). We decided to use 120 mg β-carotene, which is much higher than the estimated intake of 5 mg/d from typical diets, because pharmacologic doses of β-carotene, i.e., from 9 times (Dimitrov et al. 1988) to 60 times (Prince et al. 1991) the intake estimates, have been commonly used in studies on β-carotene metabolism in humans (Dimitrov et al. 1988, Gaziano et al. 1995, Johnson and Russell 1992, Johnson et al. 1996 and 1997, Mathews-Roth 1990, Nierenberg et al. 1991, Prince et al. 1991, Stahl et al. 1995, Tamai et al. 1995, Tang et al. 1996), mainly because of the relatively low sensitivity of β-carotene measurements with HPLC coupled with spectrophotometric detection. Moreover, extradietary doses of β-carotene are used in the treatment of erythropoeitic protoporphyria (Todd 1994) and were used in recent intervention studies performed to assess the effect of β-carotene on cancers (Heinonen and Albanes 1994, Omenn et al. 1996).

The data obtained here show that a large fraction of β-carotene can be incorporated into the chylomicrons secreted during the postprandial period after the meal subsequent to a meal providing a pharmacologic dose of β-carotene. This can be explained by the fact that, when a high dose of β-carotene is ingested, a large fraction of β-carotene can be stored temporarily in the enterocyte until the LCT of the next meal enable its packaging into the chylomicrons.

The fact that no chylomicron triglycerides were detected during the postprandial period after consumption of the MCT meal was not surprising. Indeed, it is generally assumed that medium-chain fatty acids are almost exclusively transported via the portal vein (Isselbacher 1968), and it was shown that after 6 d of continued MCT consumption (40% of total energy), chylomicron triglyceride medium-chain fatty acid content was only 13% (Swift et al. 1990). Nevertheless, the fact that the chylomicron triglyceride response to the second meal was significantly higher (43%) when the first meal provided MCT rather than LCT was noteworthy. We suggest that a fraction of the medium-chain fatty acids that had been absorbed after the MCT meal was temporarily stored in the enterocyte and incorporated into the chylomicrons secreted after the second meal. Moreover, the fact that no secretion of chylomicrons was observed after the MCT meal suggests that LCT are absolutely required for the formation of chylomicrons and that MCT could be incorporated into LCT chylomicrons but could not form chylomicrons alone.

The dramatically lower chylomicron β-carotene response observed when β-carotene was ingested with MCT rather than LCT can be explained by several mechanisms. The most likely is that the lack of chylomicron secretion that was observed after the MCT meal did not enable β-carotene to be secreted into the circulation. Indeed, newly absorbed β-carotene must be incorporated into the chylomicrons to be secreted in the lymph and then in blood (Olson 1994). However, this is a large dose of β-carotene to be stored in the enterocyte. Moreover, if this mechanism was the only one involved, we would expect to observe a higher β-carotene plus retinyl palmitate response after the second LCT meal, when the first meal provided MCT rather than LCT. This was not the case. On the contrary, the chylomicron β-carotene response to the second LCT meal was significantly lower when the first meal provided MCT rather than LCT. Thus, another mechanism was probably involved.

The intestinal absorption of β-carotene may have been lower in the presence of MCT than in the presence of LCT. This cannot be explained by the very different solubility of β-carotene in MCT than in LCT, leading to a suspension of β-carotene in MCT and to a solution of β-carotene in LCT, because we have previously shown (Borel et al. 1996) that the solubility of β-carotene is similar, even slightly higher, in MCT than in LCT. This can be explained by the lower solubility of β-carotene in mixed micelles containing medium-chain fatty acids than in mixed micelles containing long-chain fatty acids. Nevertheless, this later hypothesis disagrees with the results of early studies in animals, suggesting that β-carotene absorption was similar (Hollander and Ruble 1978) or higher in the presence of medium-chain fatty acids than in the presence of long-chain fatty acids (Bauernfeind et al. 1981). This discrepancy could result from the fact that observations made in animal models could not reflect what happens in humans.

Another mechanism that can be proposed suggests that, in the presence of medium-chain fatty acids, there could be a very efficient cleavage of β-carotene to vitamin A. However, the lower chylomicron retinyl palmitate responses observed after the MCT meal and the similar chylomicron retinyl palmitate/β-carotene ratios measured in all chylomicron fractions collected in both experiments suggest that this mechanism is very unlikely.

Finally, it is possible that in the presence of medium-chain fatty acids, a large proportion of β-carotene and/or its metabolites were transported via the portal system. Indeed, medium-chain fatty acids are much more soluble in water than are long-chain fatty acids, and they likely can solubilize a fraction of β-carotene or its metabolites, allowing them to be transported via the portal pathway. Although additional experiments are required to determine the correct hypothesis, this experiment clearly shows that MCT affect the normal metabolic route of β-carotene in humans.

Because β-carotene is a major source of dietary vitamin A, it was important to verify whether MCT can affect the conversion of β-carotene to vitamin A. This was done by comparing the chylomicron retinyl palmitate/β-carotene ratios measured in the postprandial period after the LCT or the MCT meal. Indeed, in humans, the intestine and liver are the major sites of cleavage of β-carotene into vitamin A (Novotny et al. 1995, Olson 1994, Parker 1996) and most uncleaved β-carotene and retinyl esters are secreted in the chylomicrons. The data obtained clearly show that substituting MCT for LCT does not significantly affect the intestinal conversion of β-carotene to vitamin A. However, although MCT do not affect the intestinal conversion of β-carotene to vitamin A, they might have affected the provitamin A activity of β-carotene by diminishing the intestinal absorption of β-carotene. The question arises whether the fraction of β-carotene and retinyl palmitate that was not secreted in the chylomicrons was in fact secreted into the portal system (see above).

Ingestion of β-carotene with MCT as the only source of dietary triglycerides dramatically impairs chylomicron β-carotene response compared with the ingestion of β-carotene with LCT. This is apparently due mainly to the lack of, or the very low secretion of chylomicrons in response to the ingestion of MCT, but this is also due to another mechanism, which could be a lower intestinal absorption of β-carotene or a higher transport of β-carotene or β-carotene metabolites via the portal blood in the presence of MCT. To our knowledge, this is the first time that such an effect of MCT on a lipophilic micronutrient has been described. Although this result was obtained with a pharmacologic dose of β-carotene, similar results might be obtained with smaller doses of β-carotene. Indeed β-carotene is absorbed via passive diffusion (Hollander and Ruble 1978). Nevertheless, this should be verified. From a practical point of view, because most enteral feeding supplements are mixtures of MCT and LCT, we can speculate that the effect of MCT on chylomicron β-carotene response would be proportional to the level of MCT in the enteral feeding mixture. Again, additional experiments should be performed to verify this hypothesis. Finally, the question arises whether a similar effect would be observed with other lipophilic micronutrients such as lipid-soluble vitamins.

LITERATURE CITED

Azaïs-Braesco, V., Forget, A., Mercier, M. & Grolier, P. (1992) Rapid synthesis and purification of vitamin A esters. J. Am. Oil Chem. Soc. 69: 1272–1273.

Bauernfeind, J. C., Adams, C. R. & Marusich, W. L. (1981) Carotenes and vitamin A precursors in animal feed. In: Carotenoids as Colorants and Vitamin A Precursors (Bauernfeind, J. C., ed.), pp. 563–653. Academic Press, San Diego, CA.

Blomstrand, R. & Werner, B. (1967) Studies on the intestinal absorption of radioactive β-carotene and vitamin A in man. Scand. J. Clin. Lab. Invest. 19: 339–345.

Bloom, B., Chaikoff, I. L. & Reinhardt, W. O. (1951) Intestinal lymph as pathway for transport of absorbed fatty acids of different chain lengths. Am. J. Physiol. 166: 451–455.

Borel, P., Grolier, P., Armand, M., Partier, A., Lafont, H., Lairon, D. & Azaïs-Braesco, V. (1996) Carotenoids in biological emulsions: solubility, surface-to-core distribution, and release from lipid droplets. J. Lipid Res. 37: 250–261.

Borel, P., Mekki, N., Boirie, Y., Partier, A., Grolier, P., Alexandre-Gouabau, M. C., Beaufrere, B., Armand, M., Lairon, D. & Azaïs-Braesco, V. (1997) Postprandial chylomicron and plasma vitamin E responses in healthy older subjects compared with younger ones. Eur. J. Clin. Invest. 27: 812–821.

Buccolo, G. & David, H. (1973) Quantitative determination of serum triglycerides by the use of enzymes. Clin. Chem. 19: 476–482.

Craft, N. E., Brown, E. D. & Smith, J. C. (1988) Effects of storage and handling conditions on concentrations of individual carotenoids, retinol, and tocopherol in plasma. Clin. Chem. 34: 44–48.

Dimitrov, N. V., Meyer, C., Ullrey, D. E., Chenoweth, W., Michelakis, A., Malone, W., Boone, C. & Fink, G. (1988) Bioavailability of β-carotene in humans. Am. J. Clin. Nutr. 48: 298–304.

Dubois, C., Armand, M., Azaïs-Braesco, V., Portugal, H., Pauli, A. M., Bernard, P. M., Latge, C., Lafont, H., Borel, P. & Lairon, D. (1994) Effects of moderate amounts of emulsified dietary fat on postprandial lipemia and lipoproteins in normolipidemic adults. Am. J. Clin. Nutr. 60: 374–382.

Erdman, J. W., Bierer, L. & Gugger, E. T. (1993) Absorption and transport of carotenoids. In: Carotenoids in Human Health. Ann. N. Y. Acad. Sci. 691: 76–85.

Gaziano, J. M., Johnson, E. J., Russell, R. M., Manson, J. E., Stampfer, M. J., Ridker, P. M., Frei , B., Hennekens, C. H. & Krinsky, N. (1995) Discrimination in absorption or transport of β-carotene isomers after oral supplementation with either all-*trans*- or 9-*cis*-β-carotene. Am. J. Clin. Nutr. 61: 1248–1252.

Gey, K. F., Moser, U. K., Jordan, P., Stahelin, H. B., Eichholzer, M. & Ludin, E. (1993) Increased risk of cardiovascular disease at suboptimal plasma concentrations of essential antioxidants: an epidemiological update with special attention to carotene and vitamin C. Am. J. Clin. Nutr. 57: 787S–797S.

Goodman, D. S., Blomstrand, R., Werner, B., Huang, H. S. & Shiratori, T. (1966) The intestinal absorption and metabolism of vitamin A and β-carotene in man. J. Clin. Invest. 45: 1615–1623.

Heinonen, O. P. & Albanes, D. (1994) The effect of vitamin E and beta-carotene on the incidence of lung cancer and other cancers in male smokers. N. Engl. J. Med. 330: 1029–1035.

Hollander, D. & Ruble, P. E. (1978) Beta-carotene intestinal absorption: bile, fatty acid, pH and flow rate effects on transport. Am. J. Physiol. 235: E686–E692.

Isselbacher, K. J. (1968) Mechanisms of absorption of long and medium chain triglycerides. In: Medium Chain Triglycerides (Senior, J. R., ed.). University of Pennsylvania Press, Philadelphia, PA.

Jayarajan, P., Reddy, V. & Mohanram, M. (1980) Effect of dietary fat on absorption of β-carotene from green leafy vegetables in children. Ind. J. Med. Res. 71: 53–56.

Johnson, E. J., Krinsky, N. & Russell, R. M. (1996) Serum response of all-*trans* and 9-*cis* isomers of β-carotene in humans. J. Am. Coll. Nutr. 15: 620–624.

Johnson, E. J., Qin, J., Krinsky, N. & Russell, R. M. (1997) Ingestion by men of a combined dose of β-carotene and lycopene does not affect the absorption of β-carotene but improves that of lycopene. J. Nutr. 127: 1833–1837.

Johnson, E. J. & Russell, R. M. (1992) Distribution of orally administered beta-carotene among lipoproteins in healthy men. Am. J. Clin. Nutr. 56: 128–135.

Mathews-Roth, M. M. (1990) Plasma concentrations of carotenoids after large doses of β-carotene. Am. J. Clin. Nutr. 52: 500–501

Nierenberg, D. W., Stukel, T. A., Baron, J. A., Dain, B. J. & Greenberg, E. R. (1991) The Skin Cancer Prevention Study Group. Determinants of increase in plasma concentration of β-carotene after chronic oral supplementation. Am. J. Clin. Nutr. 53: 1443–1449.

Novotny, J. A., Dueker, S. R., Zech, L. A. & Clifford, A. J. (1995) Compartmental analysis of the dynamics of β-carotene metabolism in an adult volunteer. J. Lipid Res. 36: 1825–1838.

Olson, J. A. (1994) Absorption, transport and metabolism of carotenoids in humans. Pure Appl. Chem. 66: 1011–1015.

Omenn, G. S., Goodman, G. E., Thornquist, M. D., Balmes, J., Cullen, M. R., Glass, A., Keogh, J. P., Meyskens, F. L., Williams, J. H., Burnhart, S. & Hamman, S. (1996) Effect of a combination of beta-carotene and vitamin A on lung cancer and cardiovascular disease. N. Engl. J. Med. 18: 1550–1555.

Parker, R. S. (1996) Absorption, metabolism, and transport of carotenoids. FASEB J. 10: 542–551.

Prince, M. R., Frisoli, J. K., Goetschkes, M. M., Stringham, J. M. & LaMuraglia, G. M. (1991) Rapid serum carotene loading with high-dose β-carotene: clinical implications. J. Cardiovasc. Pharmacol. 17: 343–347.

Riemersma, R. A. (1994) Epidemiology and the role of antioxidants in preventing coronary heart disease: a brief overview. Proc. Nutr. Soc. 53: 59–65.

Roels, O. A., Trout, M. & Dujacquier, R. (1958) Carotenes balances in boys in Ruanda where vitamin A deficiency is prevalent. J. Nutr. 65: 115–127.

Siedel, J., Haëgele, E. O., Ziegenhorn, J. & Wahlefeld, A. W. (1983) Reagent for the enzymatic determination of serum total cholesterol with improved lipolytic efficiency. Clin. Chem. 29: 1075–1080.
Sievet-Desrumeaux, C., Dedomder-Decoopman, E., Fruchart, J. C., Dewailli, P. & Sezille, G. (1979) Immunochemical determination of human apolipoprotein B by laser nephelometry. Clin. Chim. Acta 95: 405–408.
Sievet-Desrumeaux, C., Dedomder-Decoopman, E., Fruchart, J. C., Dewailli, P., Sezille, G. & Jaillard, J. (1980) Immunochemical determination of human apolipoprotein A-1 by laser nephelometry. Clin. Chim. Acta 107: 145–148.
Stahl W., Schwarz, W., Laar, J. & Sies, H. (1995) All-*trans* β-carotene preferentially accumulates in human chylomicrons and very low density lipoproteins compared with the 9-*cis* geometrical isomer. J. Nutr. 125: 2128–2133.
Swift, L. L., Hill, J. O., Peters, J. C. & Greene, H. L. (1990) Medium-chain fatty acids: evidence for incorporation into chylomicron triglycerides in humans. Am. J. Clin. Nutr. 52: 834–836.
Takayama, M., Itoh, S., Nagasaki, T. & Tanimizu, I. (1977) A new enzymatic method for choline containing phospholipids. Clin. Chim. Acta 79: 93–98.
Tamai, H., Morinobu, T., Murata, T., Manago, M. & Mino, M. (1995) 9-*cis* β-Carotene in human plasma and blood cells after ingestion of β-carotene. Lipids 30: 493–498.
Tang, G., Serfaty-Lacrosniere, C., Ermelinda, C. M. & Russell, R. M. (1996) Gastric acidity influences the blood response to a β-carotene dose in humans. Am. J. Clin. Nutr. 64: 622–626.
Todd, D. J. (1994) Review: erythropoietic protoporphyria. Br. J. Dermatol. 131: 751–766.
Van Vliet, T., Schreurs, W.H.P. & Van den Berg, H. (1995) Intestinal β-carotene absorption and cleavage in men: response of β-carotene and retinyl esters in the triglyceride-rich lipoprotein fraction after a single dose of β-carotene. Am. J. Clin. Nutr. 62: 110–116.
Weintraub, M. S., Einsenberg, S. & Breslow, J. L. (1987) Different patterns of postprandial lipoprotein metabolism in normal, type IIa, type III, and type IV hyperlipoproteinemic individuals. Effect of treatment with cholestyramine and gemfibrozil. J. Clin. Invest. 79: 1110–1119.
Winner, B. J. (1971) Statistical Principles in Experimental Design. McGraw-Hill, New York, NY.
Ziegler, R. G. (1989) A review of epidemiologic evidence that carotenoids reduce the risk of cancer. J. Nutr. 119: 116–122.