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Dietary oleic and palmitic acid exert similar effects on plasma lipids and lipoprotein metabolism in hamsters fed purified diets with low cholesterol but different quantities of fat

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The current study was designed to determine whether the transition from a low-fat (20% en) to a high-fat (40% en) diet through incremental increases in specific fatty acids (16:0 or 18:1) would exert a differential effect on plasma lipids and lipoprotein metabolism. Male Golden Syrian hamsters were fed purified diets in which the dietary fat (fatty acids) content was varied by blending different dietary oils. Animals were fed one of 5 purified diets: a low-fat control diet with 20% en fat; two diets with 30%en from fat; and two diets with 40% en from fat. In each case the extra fat was supplied either by oleic acid or palmitic acid. Dietary myristic (0 - 0.50% en) and linoleic acid (5.2 -5.9% en) were relatively constant across all diets, which contained a low level of cholesterol (~40 mg/1000 kcal). Diets were formulated so that protein, vitamins and minerals were constant per calorie. All animals were fed a fixed amount of calories for 6-8 week periods. Plasma lipids (n=15-20 per group) and lipoprotein cholesterol concentrations were determined following sequential ultracentrifugation, from individual animals (n=5-6 per group). Increasing dietary fat from 20% en to 30% en to 40% en, by increasing oleic acid (6.9% en to 16.5% en to 24.8% en respectively), did not affect total cholesterol (TC), triglyceride (TG) or lipoprotein cholesterol concentrations. Similarly, increasing dietary fat from 20% en to 30% en to 40% en, by increasing palmitic acid (6.6% en to 12.9% en to 21 % en) had no affect on plasma lipids or lipoprotein cholesterol. The similarity in plasma and lipoprotein cholesterol levels was further confirmed by kinetic studies (at 8 weeks) in which animals were injected simultaneously with either radiolabeled native LDL and methylated LDL or radiolabeled native LDL and HDL. Consistent with the similarities in circulating LDL-C concentrations, there was no difference in the clearance (ie fractional catabolic rates and half-lives) of LDL by either receptor-mediated or receptor-independent pathways. Similarly, in agreement with the similar HDL-C concentrations, no difference was observed in HDL fractional catabolic rates. Thus, if dietary myristic acid is low and linoleic acid is adequate and constant, dietary 16:0 and 18:1 can be readily interchanged, across a wide range of energies without compromising the plasma lipid profile in normocholesterolaemic animals consuming low-cholesterol diets. Whether this 16:0/18:1 equivalence is dependent on the relatively low levels of dietary cholesterol and/or adequate amounts of linoleic acid (~5 to 6% en) remains to be established.

Key words: Dietary fat, oleic acid, palmitic acid, lipoprotein, LDL receptor activity

Introduction

Current dietary guidelines advocate reductions in total fat consumption, saturated fatty acid and dietary cholesterol intake, as a primary means for lowering low density lipoprotein cholesterol concentrations (LDL-C), and thereby reducing subsequent risk from coronary heart disease (CHD). While there is much data on the effects of specific fatty acids on plasma lipids, the role of these individual fatty acids within the context of the total fat load is relatively unexplored. Most studies which have assessed fat quantity in modulating plasma lipids, have utilised, at least in experimental animals, the same basic fat fed at different levels in the diet[1,2]. However, a distinct disadvantage in these types of studies is that while total fat quantity and specific fatty acid content changes, the relative mix or proportion of the various fatty acids remains unaltered. Thus feeding a specific fat at 40% en and subsequently at 30% en, results in decreased consumption of all the fatty acids present in the parent fat, but the relative mix of fatty acids in the parent fat is maintained at both fat loads. Hence the results maintained may reflect decreased total fat consumption or decreases in one or more fatty acids.

The current study was undertaken to explore what effect the *mix* of fatty acids has when fat quantity alters. Previously, using cholesterol-free purified diets fed to non human primates, or gerbils and hamsters, the results of several studies from this laboratory have revealed that under these conditions, myristic acid (14:0) and linoleic acid (18:2) are key determinants of plasma lipids[3-11]. When LDL receptors are down-regulated (either by feeding excessive dietary cholesterol or for genetic reasons), palmitic acid (16:0) becomes a major determinant of the resulting lipid response. These studies have suggested that if the levels of 14:0 and 18:2 are controlled in situations in which LDL receptor activity is not compromised, 16:0 and oleic acid (18:1) can be readily interchanged without impacting plasma lipids. The results of recent human studies are in support of this tenet[12-15], but only when total fat intake is ~30%en. This interchange does not appear, based on regression analyses[9,10], to depend on the total fat load. However the above mentioned studies from this laboratory were carried out at only one fat level (30% en in non-human primates and 40% en in hamsters and gerbils). Thus to test the applicability of these findings to situations of multiple fat levels (eg 20% en, 30% en and 40% en) the current study was conducted in hamsters. The hypothesis tested was that using low levels of dietary cholesterol, fat quantity could be altered - specifically by manipulating 16:0 and 18:1, without affecting plasma lipids or lipoprotein metabolism provided 14:0 and 18:2 levels were unchanged. To test this objective, hamsters were fed different purified diets in which dietary fat quantity was varied (from 20% en ->30% en ->40% en) by blending different dietary oils such that the increase in fat reflected increases in either 16:0 or 18:1.

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Most importantly, the blends were prepared such that regardless of the fat quantity, 14:0 levels (0-0.5% en) and 18:2 levels (5.2-5.9% en) were essentially constant across diets.

Materials and Methods

Animals, diets and study design. 101 male hamsters (Lakeview strain: age ~6 months) were obtained from Charles River Laboratories. They were housed 3-4 animals per cage and fed laboratory chow (*ad libitum*) for 5 weeks. At this time, fasting plasma cholesterol and triglyceride concentrations were determined in a random subset of 33 animals. All animals were then switched to a cholesterol-free low-fat purified diet (run-in diet) with 20% en from fat, and provided with a fixed amount of diet per day (~52 kcal/animal/ day). After 2 weeks of feeding this diet, fasting plasma cholesterol and triglyceride concentrations were determined in another random subset of 33 animals. Animals were then randomly divided into 5 groups and each group was assigned to one of 5 different purified diets (Table 1).

Table 1. Composition of hamster purified diets (g/100 g)[a]

Ingredient	Diet 1[b]	Diet 2	Diet 3	Diet 4	Diet 5
Casein	22.2	23.7	25.35	23.7	25.35
Cornstarch	34.75	25.9	16.15	25.9	16.15
Glucose	13.3	14.2	15.2	14.2	15.2
Cellulose	15.0	16.0	17.15	16.0	17.15
Fat: (Total)	8.25	13.25	18.75	13.25	18.75
Palm Oil	5.25	3.6	3.75	8.68	1.88
Olive Oil-1 (7% 18:2)	-	-	3.75	-	-
Olive Oil-2 (15% 18:2)	0.9	8.7	13.13	-	-
Palm Stearin	-	-	-	2.65	14.53
Safflower Oil	2.1	0.95	-	1.93	2.35
Mineral mix[c]	5.0	5.34	5.71	5.34	5.71
Vitamin mix[d]	1.2	1.28	1.37	1.28	1.37
Choline Cl_2	0.3	0.32	0.34	0.32	0.34
Cholesterol[e]	0.015	0.016	0.017	0.016	0.017

(a) Diets were prepared in 2 kg batches by adding 120g of cornstarch to 1600mL water to make a gel. Then the remainder of the diet was mixed in as the gel set. (b) Diet codes; 1 - low fat control diet; 2 - medium fat oleic acid-rich diet; 3 - high fat oleic acid-rich diet; 4 - medium fat palmitic acid-rich diet and 5 - high fat palmitic acid-rich diet. (c) Ausman-Hayes mineral mix. (d) Hayes-Cathcart vitamin mix. (e) cholesterol was dissolved in the hot oils prior to mixing with the remaining dietary ingredients.

The control diet (Diet 1) was relatively low in fat (20% en). Diet 2 was a medium-fat oleic acid enriched diet with 30% en fat. Diet 3 was a high-fat oleic acid-enriched diet with 40% en fat. Diet 4 was a medium-fat palmitic acid-enriched diet with 30% en from fat. Diet 5 was a high-fat palmitic acid-enriched diet with 40% en from fat. All 5 diets also contained cholesterol at 40mg/1000 kcal of diet. Diets were formulated with different blends of fats such that in addition to varying the total fat load (at the expense of carbohydrate), specific fatty acids were also varied. Thus relative to Diet 1, the extra fat in Diets 2 and 3 was specifically oleic acid, whereas the extra fat in Diets 4 and 5 (again c.f. Diet 1), was provided specifically by palmitic acid. Dietary myristic acid (14:0) and linoleic acid (18:2) was relatively uniform across all 5 diets -0 to 0.50% en and 5.2 to 5.9% en, respectively. Diets were formulated with the same nutrient densities (Table 2), and the fatty acid composition of the diet (Table 3) as fed was verified by GLC[5]. Irrespective of the dietary fat load, animals continued to receive a fixed amount of calories (~52 kcal/animal/ day). Hence the design of the study allowed for the evaluation of the effects of increasing the dietary fat load, when only one fatty acid increases. Animals were fed their respective diets for up to 8 weeks during which time plasma and lipoprotein lipids as well as *in vivo* lipoprotein metabolism were evaluated as detailed in subsequent sections. All procedures and protocols were in accordance with the University's Animal Use and Radiation Safety Committees.

Plasma and lipoprotein lipid determinations. Individual hamsters were fasted overnight (~16 hours) in hanging cages. Blood was collected by cardiac puncture (following light anaesthesia with 50% O_2/50% CO_2) using an EDTA-wetted syringe, and transferred to EDTA-containing tubes which were kept on ice. Plasma was isolated by centrifugation at 1000x g, 10 min, 4°C. Lipoprotein fractions were isolated either by discontinuous density gradient or sequential ultracentrifugation as indicated in the text. Cholesterol and triglyceride concentrations in both plasma and lipoprotein fractions were determined enzymatically (kit #352 and #336 respectively, Sigma DiagnosticsR™, St. Louis, MO).

Lipoprotein isolations. Prior to isolation of any lipoprotein, sodium azide, gentamycin sulfate, benzamidine and EDTA were added to all plasma samples[16,17]. Plasma, pooled according to diet, was utilised for separation of lipoproteins using a 5-step salt gradient by density gradient ultracentrifugation exactly as detailed by Goulinet and Chapman[18]. Following ultracentrifugation at 15°C, 35k for 48 hours in a SW 41.1 rotor, 30 fractions were collected (a top fraction of 500 µL, and 29 subsequent fractions of 400 µL each). The cholesterol content of each fraction was determined enzymatically, as well as the density of each fraction as described elsewhere[11]. Based on the above cholesterol and density distributions, subsequent lipoprotein isolations utilised a Ti 50.4 fixed angle rotor to isolate VLDL+IDL (d<1.02 g/mL), LDL (1.02<d<1.05 g/mL) and HDL (1.05<d<1.18 g/mL) by sequential ultracentri-fugation[19]. In the rest of this report the VLDL+IDL fraction will be referred to simply as VLDL.

Table 2. Caloric content of hamster diets (kcal/ 100g diet)

Ingredient	Diet 1	Diet 2, 4	Diet 3, 5
Casein	88.8 (24%en)	94.8 (24.3%en)	101.4 (24.6%en)
Cornstarch	139 (38%en)	103.6 (27%en)	64.6 (16%en)
Glucose	53.2 (14%en)	56.8 (15%en)	60.8 (15%en)
Cellulose	15 (4%en)	16 (4%en)	17.1 (4%en)
Fat	74.25 (20%en)	119.25 (31%en)	168.75 (41%en)
Total	370	390	413
Cholesterol[a]	40.5	40.5	40.5
Minerals[b]	13.5	13.7	13.8
Vitamins[b]	3.24	3.28	3.32

[a] mg/1000 Kcal; [b]g/1000 Kcal

Table 3. Fatty acid composition of hamster purified diets (%energy).

Fatty acid	Diet 1	Diet 2	Diet 3	Diet 4	Diet 5
14:0	0.4	0	0.1	0.3	0.5
16:0	6.6	6.7	7.7	12.9	21.9
18:1	6.9	16.5	24.8	9.5	9.9
18:2	5.2	5.9	5.4	5.6	5.9

Diets were analysed by GLC.

Preparation of lipoprotein tracers. Six days prior to commencement of the turnover study, several hamsters from each group were fasted individually for 16h in hanging cages. Following anaesthesia with 50%O_2/50%CO_2, they were exsanguinated by cardiac puncture. Plasma was harvested following centrifugation, and LDL (1.02 < d < 1.05 g/mL) and HDL (1.05 < d < 1. 18 g/mL) were isolated from pooled plasma by sequential ultracentrifugation and washed and concentrated by recentrifugation at their appropriate densities. Following dialysis

(0.15 M NaCl/ 1mM EDTA pH 7.4), lipoprotein protein concentration was determined using Markwell's modification[20] of the Lowry procedure[21]. The LDL was divided into two aliquots, which were radiolabeled with $Na^{125}I$ and $Na^{131}I$ (Amersham, Chicago, IL) respectively. The ^{131}I-LDL was subsequently reductively methylated as detailed previously[7]. Additionally, an aliquot of HDL was radiolabeled with $Na^{131}I$. All three tracers were extensively dialyzed against saline prior to injection. For all three tracers the intramolecular distribution of radioactivity was determined[7]. For both the native ^{125}I-LDL and methylated ^{131}I-LDL, apo B associated radioactivity was ~88%, while for ^{131}I-HDL, protein-bound radioactivity was in excess of 97%.

Protocol for metabolic studies. Potassium iodide (0.1 g /100mL) was added to the drinking water of all hamsters 48 hours before injection of tracers. Hamsters were injected simultaneously with either ^{125}I-LDL and methylated ^{131}I-LDL or ^{125}I-LDL and ^{131}I-HDL via the jugular vein. A 100 µL blood sample was obtained by cardiac puncture at 2 min post-injection. Subsequent blood samples (100µL) were obtained periodically by cardiac puncture over the next 48 hours. At each instance the hamsters were lightly anaesthetised with $50\%O_2/50\%CO_2$. All animals continued to have access to KI-supplemented water until 2 days after collection of the last blood sample. All blood samples were kept on ice until the separation of plasma. Duplicate aliquots of plasma (20-50 µL) were counted for determination of ^{125}I- and ^{131}I-associated radio activities.

Kinetic analyses Plasma ^{125}I- and ^{131}I radioactivity data were bi-exponential for all three tracers, and were therefore analysed in accordance with a 2-pool model[22] and their half-lives and fractional catabolic rates (FCR) were calculated[23]. The assumptions and rationale for using the 2-pool model have been detailed previously[7,8]. Additionally, the limitations of the analyses in using HDL concentrations and the FCR for whole HDL, as a measure of HDL apo A1 metabolism have been discussed[8].

Statistical Analyses All statistical analyses were performed using a Power Macintosh 6100R ™ computer (Apple Systems Inc., Cupertino, CA) with the Statview 512+™ (Brain Power Inc., Calabasca, CA) statistical package. Significant differences were calculated using a one way analysis of variance test. Results are presented as the mean±SD.

Results

Body weights, plasma cholesterol and triglyceride concentrations averaged 157 ± 17 g, 149 ± 16 mg/dL and 136 ± 40 mg/dL, respectively (mean ± SD, n=33) in the hamsters at the end of the 2-week run-in period.

Body weights and plasma lipids after 6 weeks of feeding the test diets are shown in Table 4. There were no significant dietary effects on any of the measured parameters. The 6 week data was not significantly different from the 4 week data (results not shown), indicating that the animals had achieved a steady-state with respect to their plasma lipid concentrations. In accordance with the plasma lipid data, there were no discernible differences in the lipoprotein cholesterol concentrations measured after sequential ultracentrifugation of plasma from individual animals (Table 5). For all diets, VLDL-C averaged ~13% of total lipoprotein cholesterol, while the figures for LDL and HDL were ~21% and ~66%, respectively.

The 6 week lipoprotein isolations were carried out by sequential ultracentrifugation and VLDL, LDL and HDL were isolated at the density intervals $d<1.02$g/mL, $1.02<d<1.05$ g/mL and $1.05<d<1.18$ g/mL, respectively. These density cuts were based on the 4 week lipoprotein isolations carried out by discontinuous density gradient ultracentrifugation (Figure 1) which also revealed no diet effects.

Clearance of native LDL, methylated LDL and HDL was assessed in a subset of 33 animals after ~8 weeks on diet, and the resulting data is shown in Table 6. Consistent with the plasma lipid data, there were no dietary influences on the FCR of native LDL, methylated LDL or HDL. Receptor-independent clearance represented ~48% of total clearance and thus receptor-dependent clearance accounted for ~52% of the total clearance. The half-life of the methylated LDL (irrespective of diet) was significantly longer than the half-life of the native LDL (21.7 ± 3.6 hrs vs.13.4 ± 1.7 hrs, p = 0.0001), indicative of its longer residence time in the plasma. The half-life of whole HDL (25.4 ± 3.5 hrs) was significantly longer than the half-life for both the methylated and native LDL.

Table 4. Body weights and plasma lipid concentrations after 6 weeks.

Diet	BW (g)	TC (mg/dL)	TG (mg/dL)
#1 (18)	166±20	141±21	125±28
#2 (15)	174±13	145±16	138±26
#3 (20)	180±15	142±21	126±25
#4 (13)	169±20	151±27	147±40
#5 (14)	176±20	130±17	120±28

Values are the mean ± SD of the number of animals given in parentheses. There was no significant difference between dietary groups for any of the three parameters (assessed by ANOVA).

Table 5. Plasma and lipoprotein cholesterol concentrations (µg/dL).

Diet	TC	VLDL	LDL	HDL
#1	137±13	17±4	33±4	87±11
		(13%±2%)	(24%±3%)	(63%±2%)
#2	131±16	17±4	28±5	86±7
		(13%±2%)	(21%±2%)	(66%±3%)
#3	137±8	20±6	27±3	90±7
		(14%±5%)	(20%±2%)	(66%±5%)
#4	139±30	19±8	29±7	91±18
		(13%±3%)	(21%±4%)	(66%±4%)
#5	133±30	18±13	31±11	84±7
		(13%±6%)	(23%±3%)	(64%±8%)

Lipoproteins were isolated by sequential ultracentrifugation from the plasma of individual hamsters at the following density intervals - VLDL $d<1.02$ g/mL; LDL $1.02<d<1.05$ g/mL and HDL $1.05<d<1.18$ g/m L.
Values are the mean ± SD for 5-6 hamsters per dietary group. Percentage of total lipoprotein cholesterol in parenthesis.

Discussion

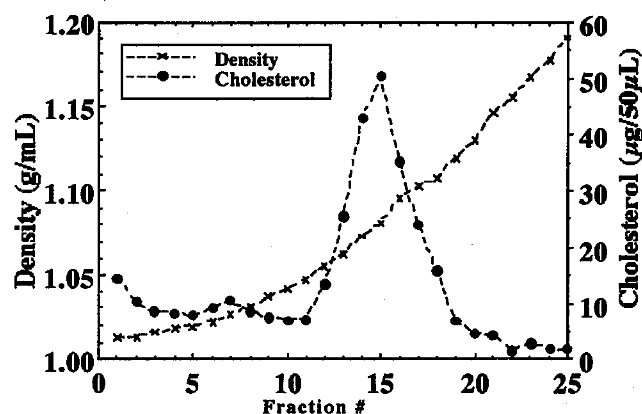
The current study was conducted in order to evaluate the effects of increasing dietary fat quantity - specifically by increasing only one fatty acid - on plasma lipids. Theoretically, the study might have started with a control diet of 40% en (with equivalent contributions from SFA, MUFA and PUFA) in which fat quantity decreased to 30% en and 20% en by decreasing either 16:0 or 18:1. However, this design was not possible given the limitation that we wished to utilise naturally occurring oils, as opposed to artificially generated triglycerides, on the assumption that triglyceride structure may affect lipoprotein metabolism. Thus a 20% control diet was selected in which SFA, MUFA and PUFA were roughly in a 1/1/1 ratio. With this control diet as a starting point, it was possible to formulate diets with 30% en or 40% en from fat, in which the excess fat was contributed by either 18:1 or 16:0, but, 14:0 and 18:2 were held constant. Within this design frame, the results clearly show that within a 20% en to 40% en dietary fat load, 16:0 and 18:1 can be readily interchanged without having any effect on plasma total or lipoprotein cholesterol concentrations. This was further reflected in the *in vivo* kinetic data, which revealed no dietary effects on LDL and HDL clearance rates.

Table 6. Clearance of native LDL, methylated LDL and HDL.

Diet		nat LDL			meth LDL			HDL	
		FCR pools/day	t 1/2 hrs		FCR pools/day	t 1/2 hrs		FCR pools/day	t 1/2 hrs
#1	(7)a	1.805+0.297	14.30±1.81	(3)	0.89±0.12	22.8±2.0	(4)	0.74±0.09	28.3±0.7
# 2	(5)	1.960±0.518	13.81±1.76	(2)	0.76,0.84	23.5,23.1	(3)	0.89±0.07	27.7±6.5
#3	(7)	2.080±0.672	13.50±1.30	(3)	0.86±0.33	23.7±6.6	(4)	0.95±0.10	23.4±2.0
#4	(6)	1.833±0.317	13.63±1.64	(3)	1.02±0.35	20.0±1.9	(3)	0.79+0.12	25.0±2.7
#5	(7)	2.542±0.898	12.04±1.35	(3)	1.24±0.21	19.6±2.4	(4)	1.08±0.30	23.1±1.9
All	(32)	2.056±0.625	13.43±1.67	(14)	0.99±0.27	21.7±3.6	(18)	0.89±0.19	25.4±3.5

[a] Number of animals. A total of 33 animals were injected with ^{125}I-LDL, and either methylated ^{131}I-LDL (n=15) or ^{131}I-HDL (n=18). One animal from Diet 2 (injected with native and methylated LDL) died during the course of the turnover. Thus complete data were available from 32 animals. Values are presented as mean±SD, except for the diet 2 animals injected with methylated LDL, for whom individual values are listed. FCR's and half-lives were calculated as indicated in the text. One way ANOVA indicated no significant difference between diets for any of the measured parameters. For all animals combined, the half life for the native LDL was significantly lower than the half-life of the methylated LDL and HDL (p=0.0001). Additionally, the half-life of the methylated LDL was significantly lower than the HDL half life (p=0.0001).

Figure 1. Cholesterol and density distribution of plasma lipoproteins isolated by discontinuous density gradient ultracentrifugation (DDGUC).



Lipoproteins were isolated by DDGUC and 30 fractions collected. The cholesterol content of each fraction as well as its density was determined. Profile shown is from the control diet (Diet 1). Similar results were obtained with the plasma from the other diets.

In previous studies in hamsters[2] and guinea pigs[1,24], the effects of decreasing dietary fat quantity on plasma lipids were dependent largely on the basal fat employed. In the hamster, plasma LDL decreased when the basal fat was principally hydrogenated coconut oil (HCO) and fat quantity was decreased from 40% en to 20% en[2]. While the above effect was attributed to the SFA content of the diet, the current data suggests that altered intake of 14:0 and 18:2 may have been responsible, especially as HCO a) has a very high 14:0 content and b) no 18:2. Although safflower oil was blended into the HCO-based diet, the levels of 18:2 were considerably less than the ~5% en employed in the current study. Similarly, in the guinea pig studies, varying fat quantity between 19% en and 35% en modulated plasma lipids differentially depending on whether the basal fat was lard, olive oil or corn oil. However, in each of these fats the levels of 14:0 or 18:2 were not constant.

The current study which evaluated 16:0 and 18:1 exchanges revealed no effects on plasma lipids even though diets provided cholesterol (albeit at low levels). However, the "lack" of cholesterol was not the factor in determining the response. The hamster when fed a cholesterol-free purified diet based solely on coconut oil (high 14:0, low 18:2) exhibits a plasma cholesterol almost 60-70 mg/dL higher than the levels observed when safflower oil (no 14:0, high 18:2) is the dietary fat source (Pronczuk *et al*, unpublished). This differential response is magnified in the gerbil (almost 120 mg/dL), but a similar study employing the same diets (devoid of cholesterol) also revealed that increasing fat quantity from 20% en to 30% en to 40% en had no effect on plasma lipids when the excess fat was 16:0 or 18:1. However, plasma lipids *increased* when the excess fat was from 14:0 and *decreased* when the excess fat was from 18:2 (Khosla *et al*, unpublished).

Thus the results of the current study lend support to the previous observations from this laboratory[7,10,25] that in situations of normal LDL receptor activity, 16:0 and 18:1 can be readily interchanged without compromising plasma lipids provided 14:0 levels are tightly controlled and 18:2 levels are adequate.

While the current design may be difficult to test using Western type diets in humans, the results may be of relevance to populations accustomed to low levels of fat intake. In India and China, dietary fat constitutes ~15% en. With increasing economic prosperity, fat intake is on the increase in certain sections of the population. The current data, *cautiously* extrapolated to humans, would suggest that if fat consumption increases, it would be prudent to balance the intakes of 14:0 and 18:2 as fatty acids increase.

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Dietary oleic and palmitic acid exert similar effects on plasma lipids and lipoprotein metabolism in hamsters fed purified diets with low cholesterol but different quantities of fat

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膳食油酸與棕櫚酸對血漿脂類和體內脂蛋白代謝的相似作用

摘要

該研究是測定增加不同量的脂肪酸（16: 0和18: 1〕，使膳食從低脂（占總能量20%〕增至高脂（占總能量40%〕，觀察對血漿脂類和脂蛋白代謝的不同影響. 作者選用雄性金Syrian 倉鼠爲對象, 喂以不同脂肪酸的純化膳食. 膳食一爲低脂膳食（占總能量20%〕; 膳食二和四脂肪含量中等（占總能量30%〕; 膳食三和五是高脂膳（占總能量40%〕. 膳食二和三額外補充了油酸, 而膳食四和五額外補充了棕櫚酸. 豆蔻酸（占總能量0-0. 50%〕和亞油酸（占總能量5. 2-5. 9%〕在所有膳食中含量相對穩定, 并含膽固醇40毫克/1000仟卡, 因此每仟卡膳食含蛋白質, 維生素和礦物質是恒定的. 所有動物喂以固定熱量6-8周, 隨后測定血漿脂類（每組15-20只鼠〕和脂蛋白膽固醇濃度（每組5-6只鼠〕. 增加油酸（從占總能量6. 9%分別增至16. 5%, 再增至24. 8%〕, 提高膳食脂肪含量（從占總能量20%增至30%, 再增至40%〕, 并不影響血漿總膽固醇, 甘油三脂或脂蛋白膽固醇濃度. 同樣地, 增加棕櫚酸（占總能量6. 6%增至12. 9%和21%〕, 以提高膳食脂肪含量（占總能量20%增至30%, 再增至40%〕, 亦不影響血漿脂類或脂蛋白膽固醇濃度. 這些結果進一步被同時注射放射性標記的LDL和甲基LDL或放射性標記的LDL和HDL八周動力學研究所確認. 血循環中低密度脂蛋白膽固醇（LDL-c〕濃度是穩定的, 但LDL的清除率（部分分解代謝率和半周期〕沒有改變. 同樣地, 高密度脂蛋白膽固醇（HDL-c〕濃度也是穩定的. 但HDL部分清除率也沒有改變. 該研究指出血液膽固醇正常并進食低膽固醇膳食的動物, 如果嚴格地控制膳食中豆而不影響血漿脂類水平. 這種16: 0/18: 1脂酸的代替互換是否取決于相對的低膽固醇膳食和/或足夠的亞油酸（占總能量5-6%〕仍需進一步研究